BVSC & AH STUDY BOOK 1 OF 7

General Veterinary Pharmacology

Eleven chapters that build the foundation: what drugs are, how the law treats them, how the body handles them, how they act on cells, why species differ, and how drugs are given, prescribed, stored and tested. Each chapter ends with a 10-question self-test.

11 chapters | **110** practice questions | **No** dose tables

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Start here

Pick a chapter from the list. Chapters 3 to 5 are the scientific core (how drugs move and how they act); the others build around them. Each chapter has six parts: Learn, Concepts, Compare, Species, Quiz and Revise. Your quiz progress is saved on this device only.

CHAPTER 1 OF 11

Introduction, history and sources of drugs

This chapter defines pharmacology and its branches, traces a short history including Indian ethnoveterinary traditions, and covers drug sources, names, development and evidence-based use.

After this chapter you can

- Define pharmacology and list its branches with one-line meanings
- Name the five sources of drugs with examples
- Differentiate chemical, generic (INN) and brand names and explain why generic prescribing is preferred
- Outline how a veterinary drug is discovered, tested and approved
- Explain the idea of evidence-based drug use

What is pharmacology and what does it include?

Pharmacology is the science of drugs: how they are obtained, how they act on living systems, and how they are used to prevent, diagnose or treat disease. In veterinary practice we must also think about the species treated, the owner's economics and the safety of food from treated animals. A **drug** is any substance used for these purposes that changes a body function or structure.

Pharmacology has many branches. Learn each one with a one-line meaning:

- **Pharmacokinetics (PK)**: what the body does to the drug: absorption, distribution, metabolism and excretion.
- **Pharmacodynamics (PD)**: what the drug does to the body: receptors, mechanisms, effects and adverse effects.
- **Therapeutics**: the choice and use of drugs to treat disease in each species.
- **Toxicology**: harmful effects of chemicals, including poisons, overdose and residues.
- **Pharmacy**: preparing, compounding, dispensing and storing drugs in suitable dosage forms.
- **Pharmacognosy**: study of crude drugs from plants, animals and minerals, including identification and active principles.
- **Clinical pharmacology**: study of drugs in patients, including trials, dose selection and drug interactions.
- **Pharmacovigilance**: detecting, assessing and preventing adverse drug reactions after a drug is on the market.

Other terms appear in exams: *pharmacogenetics* (genetic differences in drug response, for example some dog breeds with the MDR1 gene change), *chemotherapy* (drugs against microbes, parasites and cancer) and *pharmacoeconomics* (cost against benefit).

A short history of drugs

Humans and animals used medicines long before science explained them. Early healers relied on plants, minerals and animal products, learned by trial and passed on by word of mouth.

Ethnoveterinary traditions of India. Indian farming communities have long treated livestock with local herbs, oils, turmeric, neem and other materials, and with practices such as bone-setting, branding and massage. Ancient Sanskrit works on the care of horses, elephants and cattle are traditionally attributed to authors such as Shalihotra (horses) and Palakapya (elephants). We have not verified the dates or the exact contents of these texts for this book, so treat names and dates as tradition and consult a veterinary history source before quoting them in an answer. Many folk remedies are now being tested in laboratories; some show promise, but a traditional use is not proof of safety or efficacy.

Milestones of modern pharmacology (widely taught dates):

- Early 1800s: isolation of morphine from opium by Friedrich Sertürner, the first pure active principle from a plant. It moved medicine from crude drugs to pure compounds.
- Mid 1800s: Rudolf Buchheim set up an early experimental pharmacology laboratory, and Oswald Schmiedeberg later built the subject as a modern science.
- 1909: Paul Ehrlich's arsenic compound against syphilis opened the era of chemotherapy ("magic bullet" idea).
- 1920s: insulin discovered and used in diabetes.
- 1928 to 1940s: Fleming noticed penicillin; Florey and Chain developed it for treatment.
- Later decades: discovery of ivermectin-type antiparasitics from soil bacteria, modern anaesthetics, and recombinant DNA products.

Today pharmacology is guided by receptor science, genetics and strict regulation to prove safety and efficacy.

Sources of drugs

Drugs come from five main sources. A drug may have more than one route; for example, vitamins and hormones may be extracted or synthesised.

Source	Meaning	Examples
Plant	Alkaloids, glycosides, oils, tannins, resins from plants	Morphine (opium poppy), atropine (Atropa belladonna), digoxin (foxglove), quinine (cinchona), reserpine (Rauwolfia)
Animal	Hormones, enzymes and extracts from animal tissues	Insulin (from pancreas of animals), heparin, pancreatic enzymes, eCG, cod liver oil, lanolin
Mineral	Inorganic substances from the earth	Magnesium sulphate, copper sulphate, kaolin, sulphur, zinc oxide, sodium chloride
Microbial	Products of fungi and bacteria (often called semisynthetic after modification)	Penicillin (Penicillium), streptomycin, ivermectin (Streptomyces)
Synthetic	Made fully in the laboratory, often designed from a known structure	Xylazine, ketamine, meloxicam, enrofloxacin, albendazole
Biotechnology	Made by genetically modified cells or by recombinant DNA	Recombinant vaccines, recombinant hormones, monoclonal antibodies for pets

Biotechnology products now include recombinant vaccines, hormones and monoclonal antibodies, which are large protein molecules that are usually injected because digestion destroys them. Natural sources still matter, but synthetic and semisynthetic drugs dominate modern practice because they give purity, consistent quality and larger supply.

Drug nomenclature

One drug has several names. Students must know the three types.

1. **Chemical name**: describes the exact molecular structure by chemical rules. It is long and used by chemists, not in prescriptions.
2. **Generic name**: the non-proprietary name. Internationally this is the **International Nonproprietary Name (INN)**, assigned through the World Health Organization. It is public property and belongs to no company.
3. **Brand (trade or proprietary) name**: the name chosen by a company for its own product. It is protected as a trademark and differs from company to company.

Example: the same drug may be sold under many brands, but it has a single INN. Many INNs carry a common *stem* showing the drug family (for example, the stem -mycin marks many antibiotics; the same WHO page gives the example of kanamycin and erythromycin).

Why prescribe by generic name?

- One universal name is understood by every vet, pharmacist and book, so it reduces confusion between look-alike or sound-alike brands.
- It shows the active ingredient at once, which helps avoid duplicate therapy and drug interactions.
- It allows the pharmacist to supply a lower-cost equivalent product, which matters for livestock owners.
- It is stable for the life of the substance, while brand names change or disappear.

Remember that generic does not mean any product is automatically equal. A generic product must meet quality and bioequivalence standards in the species for which it is approved; equal active ingredient does not guarantee equal therapeutic effect in every animal or in off-label use.

How a veterinary drug is discovered, tested and approved

Developing a new animal drug takes many years and is costly. The steps below give the general outline used in most countries; details vary by regulator.

1. **Discovery**: finding a target and a lead compound from plants, microbes, chemical libraries or rational design, followed by screening.
2. **Preclinical studies**: laboratory and animal studies for activity, pharmacokinetics and toxicity.
3. **Studies in the target species**: safety in healthy animals of the species, dose selection and then field studies in diseased animals to prove effectiveness. Veterinary drugs are tested directly in the species they are meant for, so the human Phase I, II and III scheme is only a rough comparison.
4. **Food-animal extras**: residue and depletion studies to set a *withdrawal period*, and safety to the human consumer.
5. **Manufacturing quality, label and environment**: the regulator also reviews the quality of manufacture, the label and, where relevant, environmental effect. A

major regulator such as the US Food and Drug Administration expects a drug to show safety and effectiveness in the target species before approval.

6. **Approval and marketing**, followed by **post-marketing surveillance (pharmacovigilance)**, because rare effects appear only when thousands of animals have been treated.

In India the approving and licensing system is explained in the next chapter. Always check the current rules of the authority concerned.

Evidence-based drug use

A good vet does not use a drug only because a seller recommends it or because it was used earlier. **Evidence-based veterinary medicine** joins three things: the best available research evidence, the clinician's experience, and the owner's situation and values.

- **Ask a clear question**: in this species and condition, does drug A work better than drug B or no treatment?
- **Find the evidence**: use standard textbooks, formularies, reviews and published trials.
- **Judge it**: randomised controlled trials and systematic reviews are stronger than single case reports or opinion. Look at animal numbers, controls and whether the species matches yours.
- **Apply it**: adapt to the patient (age, pregnancy, kidney and liver function, other drugs) and to food safety.
- **Review the result**: record outcome and report unexpected adverse events.

In practice, use antimicrobials only when needed and choose them by the likely organism or by culture and sensitivity. Poor drug use causes treatment failure, residues and antimicrobial resistance, which harms animals and people.

Concept cleared

Concept cleared: Pharmacokinetics vs pharmacodynamics

Think of a courier delivering a parcel. Pharmacokinetics is the journey: how the parcel travels, where it waits and how it leaves. Pharmacodynamics is what happens when the parcel is opened at the door: the effect on the receiver. The body acts on the drug in PK; the drug acts on the body in PD.

Concept cleared: Generic and brand names

A generic name is like the word 'rice', known everywhere. A brand name is like a particular shop's packet of rice with its own label. Many shops sell rice under different labels, but the grain inside is called the same thing. The INN is the grain's name; the brand is the packet.

Concept cleared: Why trials come before approval

Before a new bridge is opened, engineers test it with heavy loads, not just look at the drawing. A drug is the same: laboratory promise is not enough, so it is tested for safety and effect in the target species before general use.

Concept cleared: Natural does not mean safe

A wild mushroom is natural, yet some can kill. Plant drugs such as digitalis and atropine are useful only because their dose is measured carefully. Origin from nature says nothing about safety; only testing and correct dosing do.

Memory aid: Five sources of drugs

Remember PAMS-B: Plant, Animal, Mineral, Synthetic, Biotechnology. Microbial products are often counted under synthetic/semisynthetic or biotechnology, depending on the textbook.

Compare and contrast

Chemical, generic and brand names

Feature	Chemical name	Generic (INN) name	Brand name
Describes	Molecular structure	Active substance	A company's product
Who assigns	Chemical naming rules	WHO INN programme	The manufacturer
Number per drug	One	One	Many
Legal status	Descriptive	Public property	Protected trademark
Use in prescribing	Rarely	Preferred	Allowed, but less clear
Stability over time	Fixed	Lasts for life of the drug	May change or disappear

Drug sources at a glance

Source	Example	Active drug
Plant	Opium poppy	Morphine
Plant	Belladonna	Atropine
Animal	Pancreas	Insulin
Mineral	Magnesium salt	Magnesium sulphate
Microbial	Penicillium mould	Penicillin
Synthetic	Laboratory made	Meloxicam

Species notes

Dog
Some dog breeds (for example collie types) carry an MDR1 gene change, so the same drug can be toxic in them; this is an example of pharmacogenetics.

Cat
Cats are slow at glucuronidation, so drug choice and dosing from other species cannot simply be copied.

Cattle

Poultry

As a food animal, any drug used needs a withdrawal period so milk and meat remain free of residues.

Large flocks are often treated through feed or water, so regulatory limits on antimicrobials matter greatly.

Clinical pearls

Self-test: 10 questions

1. The study of what the body does to a drug is called:

Pharmacokinetics covers absorption, distribution, metabolism and excretion. Pharmacodynamics is the reverse: drug action on the body.

2. Study of crude drugs obtained from plants, animals and minerals is:

Pharmacognosy deals with crude drugs and their active principles.

3. Monitoring adverse drug reactions after a product is marketed is called:

Pharmacovigilance is detection, assessment and prevention of adverse effects after release.

4. Which of the following is a drug of plant origin?

Atropine is an alkaloid from belladonna. Insulin is animal or recombinant, magnesium sulphate is mineral and meloxicam is synthetic.

5. Magnesium sulphate and kaolin are examples of drugs from which source?

Both are inorganic substances obtained from mineral sources.

6. INN stands for:

INN is the International Nonproprietary Name, assigned through the WHO and used as the generic name.

7. Which statement about brand names is correct?

A brand name is a company's trademark, and one drug can have many brands.

8. A major reason for prescribing by generic name is that it:

Generic names reduce confusion and show the active ingredient clearly.

9. Which study is specially needed for a drug to be used in food-producing animals?

Residue depletion studies set the withdrawal period so food is safe for consumers.

10. Evidence-based veterinary medicine combines best research evidence with:

It joins evidence, clinician experience and the owner's situation and values.

Key points to revise

1. Pharmacokinetics is what the body does to the drug; pharmacodynamics is what the drug does to the body.
2. Pharmacognosy deals with crude drugs from natural sources.
3. Pharmacovigilance monitors adverse effects after marketing.
4. Sources of drugs: plant, animal, mineral, synthetic and biotechnology.
5. INN is the WHO-assigned generic name and is public property.
6. Brand names are trademarks and differ between companies.

7. Veterinary drugs are tested for safety and effectiveness in the target species; food-animal drugs also need residue studies.
8. Evidence-based practice combines best evidence, clinical experience and owner circumstances.

Go deeper on this site

- Ch 2. Drug regulation and the law in India (in this book)
- Ch 8. Dosage forms, routes and drug delivery (in this book)
- BVSc & AH syllabus year wise (MSVE-2016)
- Veterinary Drug Concepts Clearly Explained

Sources

- WHO: What's in a name?
- WHO: International Nonproprietary Names (INN) programme
- MSD Veterinary Manual: New animal drugs, extralabel drug use, compounded drugs and generic drugs

CHAPTER 2 OF 11

Drug regulation and the law in India

This chapter explains the main Indian laws and bodies that control veterinary drugs, from the Drugs and Cosmetics Act to the VCI Act, NDPS Act and FSSAI, with examples of banned drugs. Rules change, so always check current notifications.

After this chapter you can

- Describe the Drugs and Cosmetics Act 1940, the Rules 1945 and the idea of schedules
- Distinguish the roles of CDSCO and State Drugs Controllers
- Explain why opioids and ketamine are controlled and where the NDPS Act applies
- State who may prescribe under the Indian Veterinary Council Act 1984
- Define extra-label use and name veterinary drugs reported to be banned or restricted in India

Read this first: rules change

Drug law is not fixed. Acts are amended, schedules are revised, and drugs are added to or removed from banned lists by notification, sometimes only a few months apart. This chapter gives the general framework and a few well-known examples. It is a teaching summary, not legal advice, and it does not give section numbers that we could not confirm. Before you answer a practical question, or use or sell a drug, **check the current notification** on the official websites of the Ministry of Health and Family Welfare, CDSCO, the Gazette of India or your State Drugs Controller. Points marked *reported* rest on news or secondary reports and must be confirmed against the gazette notification.

Drugs and Cosmetics Act 1940 and Rules 1945

The **Drugs and Cosmetics Act, 1940** is the main Indian law that controls the import, manufacture, distribution and sale of drugs and cosmetics. It aims to keep drugs safe, effective and of standard quality. Its definition of a drug is wide and includes substances used for animals as well as humans, so there is no separate national Act just for veterinary medicines. The **Drugs and Cosmetics Rules, 1945** are made under the Act and carry the detailed procedures, licence conditions and **schedules**.

Idea of schedules. A schedule is a list or set of rules attached to the Rules. Each one groups drugs or conditions for a purpose. Commonly taught examples, to be confirmed in the current Rules:

- **Schedule H**: drugs that may be sold only on the prescription of a registered medical practitioner. The Rules use this expression for the practitioner; ask your teacher how it applies to veterinarians and check the text.
- **Schedule H1**: certain antimicrobials and other drugs with stricter sale and record keeping (reported to have been introduced in the early 2010s).
- **Schedule X**: drugs with very strict control, including some psychotropic substances, with special licence and record rules.
- **Schedule M**: good manufacturing practices for factories.

Another important power of the Act allows the Central Government to **prohibit the manufacture, sale and distribution** of a drug in public interest. Several veterinary bans, discussed below, are reported to use this power.

Clinical trials and new drug approval rules were revised by the **New Drugs and Clinical Trials Rules, 2019**, framed under the same Act. Check the current text for how it applies to animal drugs.

CDSCO and State Drugs Controllers

Regulation is shared between the Centre and the States.

- **CDSCO (Central Drugs Standard Control Organisation)**, headed by the Drugs Controller General of India (DCGI), works under the Union Ministry of Health. It approves new drugs and clinical trials, and controls imports and some classes of products.
- **State Drugs Control Departments**, headed by the State Drugs Controller, issue manufacturing and sale licences through State Licensing Authorities and inspect premises through drug inspectors. For veterinary drugs, shops and manufacturers are inspected like others, so a vet who sells drugs from a clinic should check the licence requirements of the State.

For veterinary vaccines and other biologicals, more than one authority may be involved in approval and quality testing. Check the present arrangement before relying on a textbook statement, because responsibilities have been revised from time to time.

Narcotics, psychotropics and the NDPS Act

The **Narcotic Drugs and Psychotropic Substances Act, 1985 (NDPS Act)** controls the cultivation, manufacture, possession, transport, sale and use of narcotic drugs and psychotropic substances. Opioids such as morphine, fentanyl, pethidine and similar potent analgesics are important in veterinary pain control and anaesthesia but are controlled substances. A vet who uses them needs the correct licence, secure storage and accurate record keeping, and must follow the State's rules for medical use.

Ketamine. Ketamine is a widely used veterinary anaesthetic. Reports of a Delhi High Court decision say that ketamine is treated as a *psychotropic substance* under the NDPS Act, through a central notification of 2011, and that the court dismissed a challenge to this. Because this comes from a news report, confirm its present status

and the licence rules from the notified schedule of the NDPS Act and the Rules before practising.

Veterinary Council of India Act 1984 and who may prescribe

The **Indian Veterinary Council Act, 1984** sets up the **Veterinary Council of India (VCI)** and State Veterinary Councils. The VCI sets minimum standards of veterinary education, recognises veterinary qualifications, keeps the Indian Veterinary Practitioners Register and prescribes standards of professional conduct and ethics. State Veterinary Councils keep the State registers. A copy of the Act hosted by a State animal husbandry department states that registered practitioners may practise veterinary medicine, and that unregistered persons are barred from practising it, with limited State permission for trained supervisors or stockmen to give minor services under a registered practitioner.

Take-home points for students: a veterinarian must hold a recognised qualification and be on a State or the Indian register to practise and prescribe, and must follow the code of professional conduct. Always check the present Act, amendments and your State Council rules.

Prevention of Cruelty to Animals Act, FSSAI and residues

The **Prevention of Cruelty to Animals Act, 1960** makes unnecessary pain and suffering to animals an offence and forms the legal base for animal welfare rules. For pharmacology it matters in three ways: treatment must relieve, not cause, avoidable suffering; anaesthesia and analgesia should be used for painful procedures; and animal experiments for drug testing are subject to separate rules and committees.

FSSAI role. The Food Safety and Standards Authority of India, under the Food Safety and Standards Act, 2006, sets standards for food. Its Contaminants, Toxins and Residues Regulations, 2011 (amended from time to time; one summary lists an amendment of August 2020) include tolerance limits for certain antibiotics in food and a list of antibiotics prohibited in meat, poultry, eggs and seafood. The practical rule for a vet: respect the **withdrawal period**, so milk, meat and eggs from treated animals do not exceed residue limits.

Extra-label use, banned drugs and reporting

Extra-label (off-label) use means using a drug in a way that is not on its approved label, for example a different species, dose, route or disease. In the United States the practice is allowed only within a legal framework: it needs a valid veterinarian-client-patient relationship, and in food animals it must not cause illegal residues. There are listed drugs that may never be used in this way in food animals. India has no equal detailed framework that we could verify here, so use professional judgement, choose approved options first, keep records and tell owners about withdrawal times. Use extra-label drugs only when there is no suitable approved product and never for growth promotion.

Banned or restricted veterinary drugs (verify current status).

- **Diclofenac (veterinary use):** reported to have been banned for veterinary use in 2006 and gazetted in 2008, because carcasses of treated cattle poisoned vultures with kidney failure. Meloxicam has been suggested as a substitute.
- **Ketoprofen and aceclofenac (animal use):** reported by a news outlet that a Union Health Ministry notification of 31 July 2023 banned their manufacture, sale and distribution for animal use, under the Act's power to prohibit drugs in public interest. A conservation organisation also reported the ban. The mechanism was described differently in two reports, so read the notification.
- **Colistin in food animals:** reported in July 2019 that the Health Ministry banned the manufacture, sale and distribution of colistin and its formulations for food-producing animals, poultry, aquaculture and animal feed supplements, to protect a last-resort human antibiotic.

Other banned lists, for example for nitrofurans or chloramphenicol in food animals, change with time. We have not verified them for this chapter, so check the current FSSAI and Health Ministry notifications.

Pharmacovigilance and reporting. Veterinary pharmacovigilance reporting systems are weaker in India than for human drugs, so record and report suspected adverse reactions, treatment failures and suspected residue problems to the manufacturer, the veterinary college or the State animal husbandry and drug control authorities. Good reporting helps catch problems, as the vulture case shows.

Concept cleared

Concept cleared: Why schedules exist

A school keeps some items in the open library shelf, others in the locked cupboard, and the most dangerous chemicals in the lab store with a register. Schedules do the same for drugs: they sort drugs by risk and set how strictly each must be sold, stored and recorded.

Concept cleared: Centre and State roles

Think of a national highway and local roads. The Centre (CDSCO) approves new drugs and sets national standards, like highway rules, while State Drugs Controllers license shops and factories and run inspections on the local roads.

Concept cleared: Withdrawal period

Like waiting for a washed vegetable to dry before cooking, a withdrawal period is the waiting time after treatment before milk, meat or eggs are safe for people. Selling food earlier risks leaving residues that can harm consumers.

Concept cleared: Extra-label use

A recipe says bake at one temperature, but a cook may adjust it for a special oven. That is extra-label thinking: using a drug differently from its label. It needs good reasons, careful records and extra caution, and never ignores food safety.

Compare and contrast

Main bodies and laws at a glance

Law or body	Main role for a veterinarian
Drugs and Cosmetics Act 1940 and Rules 1945	Controls manufacture, sale, import and quality of drugs; schedules
CDSCO / DCGI	Central approval of new drugs, clinical trial oversight, national standards
State Drugs Controller	Licences and inspections of manufacture and sale in the State
NDPS Act 1985	Controls narcotic and psychotropic substances such as opioids; ketamine reported as psychotropic
Indian Veterinary Council Act 1984	VCI and State Councils; registration and who may practise
Prevention of Cruelty to Animals Act 1960	Animal welfare; relief of suffering
FSSAI (FSS Act 2006)	Food safety standards, residue limits

Reported veterinary drug restrictions in India

Drug	Reported action	Reason
Diclofenac	Veterinary use banned (2006, gazetted 2008)	Vulture poisoning
Ketoprofen	Animal-use ban reported, July 2023	Vulture protection
Aceclofenac	Animal-use ban reported, July 2023	Vulture protection
Colistin	Food-animal use banned, reported July 2019	Protect human last-resort antibiotic

Species notes

Dog

Opioids and ketamine are often used in dogs for pain and anaesthesia, so a small-animal clinic must follow controlled drug storage and record rules.

Cat

Many analgesics are riskier in cats, so choose approved or well-evidenced options and avoid casual extra-label use.

Cattle
Diclofenac in cattle led to vulture deaths, and treated dairy cattle need strict milk withdrawal periods.

Poultry
Antimicrobials in feed and water are tightly watched; colistin for food animals is reported banned.

Horse
Controlled analgesics and sedatives are used in horses, and competition medication rules may add further limits.

Clinical pearls

Self-test: 10 questions

1. The main Indian law controlling import, manufacture, sale and distribution of drugs is:

The Drugs and Cosmetics Act 1940 with its Rules 1945 regulates drugs and cosmetics.

2. The detailed schedules are found in:

Schedules are attached to the Drugs and Cosmetics Rules 1945.

3. CDSCO functions under which ministry?

CDSCO, headed by the DCGI, is under the Union Ministry of Health and Family Welfare.

4. Manufacturing and sale licences for most drugs are issued by:

State drug control departments license manufacture and sale and inspect premises.

5. Opioids such as morphine and pethidine are mainly controlled under:

The NDPS Act controls narcotic drugs and psychotropic substances.

6. Reports of a Delhi High Court judgment say ketamine is regarded under the NDPS Act as a:

The report says it was upheld as a psychotropic substance; confirm the current notified status.

7. The Veterinary Council of India was set up under:

The IVC Act 1984 establishes the VCI and State Veterinary Councils.

8. Veterinary use of diclofenac was banned in India mainly because it:

Residues in carcasses of treated cattle caused kidney failure and death in vultures.

9. Colistin was reported banned in India in 2019 for use in:

The reported ban covers food-producing animals, poultry, aquaculture and feed supplements, to protect a last-resort human antibiotic.

10. Using a drug in a species, dose or disease not stated on its approved label is called:

This is extra-label (off-label) use, which needs careful justification, especially in food animals.

Key points to revise

1. The Drugs and Cosmetics Act 1940 is the main law for drugs; the Rules 1945 hold the schedules.
2. Schedules group drugs by the level of control needed.
3. CDSCO works at the Centre and State Drugs Controllers license and inspect locally.
4. The NDPS Act 1985 controls narcotics and psychotropics such as opioids; ketamine is reported as psychotropic.
5. The Indian Veterinary Council Act 1984 sets up the VCI and State Councils and regulates registration.
6. The Prevention of Cruelty to Animals Act 1960 supports animal welfare.
7. FSSAI sets food residue and contaminant standards.
8. Veterinary diclofenac, ketoprofen and aceclofenac are reported banned, as is colistin in food animals; always check the current notification.

Go deeper on this site

- Ch 1. Introduction, history and sources of drugs (in this book)
- Ch 9. Prescription writing, calculations and records (in this book)
- Veterinary drugs list: classes, uses and cautions

Sources

- Punjab Animal Husbandry Department: The Indian Veterinary Council Act (text)
- Down To Earth: Centre's move to ban aceclofenac and ketoprofen
- ThePoultrySite: India bans the use of a human-critical antibiotic in poultry farms
- UNEP LEAP: Food Safety and Standards (Contaminants, Toxins and Residues) Regulations
- Health Post: Ketamine to remain in Psychotropic Substances list: HC

CHAPTER 3 OF 11

Pharmacokinetics: how the body handles a drug

How the body handles a drug: absorption, distribution, metabolism and excretion, with the key parameters (bioavailability, volume of distribution, clearance and half-life) and species differences.

> **After this chapter you can**

- Explain absorption, distribution, metabolism and excretion with examples.
- Define bioavailability, first-pass effect, volume of distribution, clearance and half-life, and relate them.
- Apply the ideas of ion trapping and protein binding to drug behaviour.
- Compare routes of administration for speed and reliability.
- Describe ruminant and species differences in drug handling.

Overview: what the body does to the drug

Pharmacokinetics (PK) describes what the body does to a drug over time. It is usually remembered as **ADME**: absorption, distribution, metabolism (biotransformation) and excretion. Metabolism and excretion together are called *elimination*. PK explains why the same drug needs different dosing intervals in a dog, a cow and a hen, and why a drug can work well by one route and fail by another.

A drug must cross biological membranes at almost every step. Most cross by **passive diffusion**, which favours small, lipid-soluble, *non-ionised* molecules. Others use carriers or active transport, and some are pushed back out by efflux pumps such as P-glycoprotein. Because many drugs are weak acids or weak bases, the pH on each side of a membrane decides how much drug is ionised, and therefore where it accumulates. This is the principle of **ion trapping**: a weak base concentrates on the more acidic side of a membrane, and a weak acid on the more alkaline side.

Absorption and bioavailability

Absorption is the movement of drug from the site of administration into the blood. Intravenous (IV) injection skips absorption altogether, so its bioavailability is taken as 100%. **Bioavailability (F)** is the fraction of the dose that reaches the systemic circulation, together with the rate at which it arrives.

- **Oral:** convenient, but the drug must dissolve first, survive gut enzymes and gut flora, and then pass through the liver. Feed can bind some drugs and reduce absorption.
- **Intramuscular (IM) and subcutaneous (SC):** aqueous solutions are absorbed fairly quickly when blood flow is good; SC is usually slower than IM. Oily depot or

long-acting preparations release drug slowly. Poor perfusion, as in shock or dehydration, slows absorption.

- **Topical and transdermal:** the stratum corneum is a strong barrier, so only some drugs penetrate. Damaged skin, heat and certain solvents increase uptake.
- **Inhalation:** gases and volatile anaesthetics enter the blood almost at once through the alveoli.

After oral dosing, blood from the gut goes through the portal vein to the liver before reaching the rest of the body. Drugs that the liver extracts heavily lose much of the dose here; this is **first-pass (presystemic) metabolism**. It is why some drugs are ineffective orally but work by injection, and why portosystemic shunts can unexpectedly raise the oral bioavailability of such drugs. Buccal, sublingual and rectal routes partly avoid first pass.

Distribution

Once in blood, a drug spreads to tissues according to blood flow, lipid solubility, plasma protein binding and special barriers. Organs with rich flow (brain, heart, liver, kidney) receive drug first. Only *unbound* drug can cross membranes, act at receptors and be cleared, so protein binding works like a storage pool in plasma. Two highly bound drugs may compete for albumin, although this rarely matters clinically unless the drug has a narrow safety margin.

The **apparent volume of distribution (Vd)** is a theoretical volume that relates the amount of drug in the body to its plasma concentration. A small Vd suggests a water-soluble drug kept mainly in plasma and extracellular fluid. A large Vd suggests a lipid-soluble drug, or one bound in tissues. Vd does not show where the drug really is; it is a mathematical tool used to work out loading doses. The blood-brain barrier, the blood-milk barrier and the placenta limit or permit passage of drugs, and ion trapping can concentrate weak bases in milk, which is acidic relative to plasma in many species.

Metabolism and excretion

Most biotransformation happens in the liver. **Phase I** reactions (oxidation, reduction, hydrolysis, mostly by cytochrome P450 enzymes) add or expose a reactive group. **Phase II** reactions (conjugation, such as glucuronidation, sulfation and acetylation) attach a large polar group, usually making the product inactive and water-soluble.

The result may be inactivation, conversion of a *prodrug* to its active form, or sometimes a toxic metabolite. Enzyme **inducers** speed up metabolism of other drugs, and **inhibitors** slow it. Liver disease, young or very old age, and thyroid status also change metabolic rate.

The kidney is the main route of excretion, through glomerular filtration, active tubular secretion and passive reabsorption. Changing urine pH can alter excretion of weak acids and bases by ion trapping. Larger molecules are favoured for bile, and drugs reabsorbed from the gut after biliary excretion undergo **enterohepatic recirculation**, which prolongs their action. Milk is a minor route for the animal but important for the consumer, because residues decide **withdrawal periods**. Always follow the product label and current official guidance for withdrawal periods.

Half-life, clearance and steady state

Clearance (Cl) is the volume of plasma completely cleared of drug per unit time. It reflects the efficiency of the liver and kidney and does not depend on the drug concentration for most drugs. **Elimination half-life ($t_{1/2}$)** is the time taken for the plasma concentration to fall by half. The three are linked: $t_{1/2}$ = 0.693 x Vd / Cl. So a drug has a longer half-life if its volume is larger or its clearance is lower.

Most drugs follow *first-order kinetics*: a constant fraction is eliminated per unit time. A few drugs, or any drug at very high doses, saturate their enzymes and follow *zero-order kinetics*, where a constant amount is eliminated per unit time, so small dose increases can cause a disproportionate rise in concentration. With repeated dosing, the drug accumulates until intake equals elimination, called **steady state**, reached in about 3 to 5 half-lives. Likewise, a drug is almost completely eliminated after about 3 to 5 half-lives once dosing stops. Loading doses are used to reach effective levels sooner for drugs with long half-lives.

Ruminant and species differences

Species differences in anatomy and enzymes can change PK drastically, so doses cannot be copied from one species to another. In **ruminants**, the rumen holds large volumes of fluid and microbes. Oral drugs are diluted and absorbed slowly, some are destroyed by rumen microbes, and some can upset the flora. The rumen pH is more acidic than plasma, so weak bases can be trapped there, while the large flow

of alkaline saliva can carry some drugs back into the gut. Drugs excreted in milk need attention for withdrawal times.

Cats have low activity of some glucuronyl transferases, so drugs cleared mainly by glucuronidation can accumulate. **Dogs** have limited acetylation. **Horses and other hindgut fermenters** may absorb orally given drugs differently from simple-stomached animals, and oral antibiotics can disturb the gut flora. In **birds**, a renal portal system exists, and the route of injection may influence how much drug reaches the kidney first; practical importance varies by drug. Neonates and sick animals metabolise and excrete drugs more slowly than healthy adults.

Concept cleared

Concept cleared: Bioavailability
Think of posting a parcel of 100 sweets. Whatever is lost on the way, such as spilled in the sorting office, never reaches the house. An IV injection is hand delivery, so all 100 arrive. An oral tablet may lose many sweets to gut enzymes and the liver. Bioavailability is just the percentage of the dose that arrives.

Concept cleared: Volume of distribution
Pour a known amount of dye into a closed tank of unknown size and measure how dark the water gets. A faint colour means a big tank. Vd works the same way. If the plasma level is low for the dose given, the drug has spread widely or entered tissues, so Vd is large. It is a calculated number, not a real space.

Concept cleared: Half-life and clearance
Imagine a bathtub with a tap draining water. A larger tub takes longer to empty, and a wider drain empties it faster. Vd is the tub size, clearance is the drain width, and half-life is how long half the water takes to go. Big tub plus narrow drain means long half-life.

Concept cleared: Dose volume (illustration only)

Volume to inject = (dose in mg/kg x body weight in kg) / concentration in mg/mL. Illustration only: a made-up dose of 5 mg/kg for a 20 kg animal needs 100 mg; with a solution of 50 mg/mL, the volume is 2 mL. Always use the label dose and units for the real product and species.

Memory aid: ADME

Absorption, Distribution, Metabolism, Excretion: A Drug's Medical Expedition. Remember that M and E together are elimination, and that only unbound drug is free to move, act and be cleared.

Compare and contrast

Phase I versus Phase II metabolism

Feature	Phase I	Phase II
Type of reaction	Oxidation, reduction, hydrolysis	Conjugation
Main enzymes	Cytochrome P450 and others	Transferases (e.g. glucuronyl transferase)
Effect on polarity	Small increase	Large increase
Usual effect on activity	May inactivate, activate or make toxic	Usually inactivates
Species example	Varies with P450 enzymes	Cats: low glucuronidation

Routes of administration

Route	Speed of onset	Key point
Intravenous	Immediate	100% bioavailability; no absorption phase
Intramuscular	Fast to moderate	Depends on blood flow and formulation
Subcutaneous	Moderate	Usually slower than IM
Oral	Slow, variable	Subject to first-pass and gut factors
Topical	Slow, local	Skin barrier limits uptake
Inhalation	Very fast	Gases cross alveoli rapidly

Species notes

Cat

Cats have low activity of some glucuronyl transferases, so drugs cleared by glucuronidation may accumulate; extra caution is needed with such drugs.

Dog

Dogs have limited acetylation ability, and individual dogs vary widely in drug metabolism, so doses must be matched to species and patient.

Cattle

The rumen dilutes, delays and sometimes destroys oral drugs, and traps weak bases by ion trapping; milk residues decide withdrawal periods.

Sheep/Goat

Small ruminants share rumen effects on oral drugs, and doses cannot be assumed to match cattle doses simply by weight.

Poultry

Birds have a renal portal system, and flock medication through water depends on intake, so absorption and exposure can vary.

Clinical pearls

Self-test: 10 questions

1. Which route gives a bioavailability of 100% by definition?

IV injection places the drug directly in blood, so there is no absorption loss.

2. First-pass metabolism occurs mainly in the:

Portal blood from the gut passes through the liver before reaching the systemic circulation.

3. Ion trapping of a weak base is greatest on the side of a membrane that is:

A weak base is ionised in acid, and ionised drug cannot easily diffuse back across.

4. Which relation is correct?

Half-life rises with larger Vd and falls with greater clearance.

5. About how many half-lives are needed to reach steady state on repeated dosing at a fixed interval?

Accumulation is largely complete after roughly 3 to 5 half-lives.

6. Which statement about Vd is true?

Vd is a calculated volume; a large value indicates the drug has left plasma for tissues.

7. Cats are particularly sensitive to drugs cleared by:

Cats have low activity of some glucuronyl transferase enzymes.

8. Phase II metabolism typically:

Conjugation adds a polar group, aiding excretion and usually inactivating the drug.

9. Enterohepatic recirculation generally:

Drug excreted in bile is reabsorbed from the intestine, staying in the body longer.

10. Which fact is correct for ruminants given oral drugs?

The rumen dilutes oral drugs and its microbes can degrade some of them, so absorption is slower and less predictable.

Key points to revise

1. ADME describes the fate of a drug; metabolism plus excretion equals elimination.
2. Non-ionised, lipid-soluble drugs cross membranes by passive diffusion.
3. Bioavailability is the fraction of the dose that reaches the systemic circulation; IV equals 100%.
4. First-pass metabolism lowers oral bioavailability of highly extracted drugs.
5. Vd is a theoretical volume; large Vd means wide tissue distribution.
6. t1/2 = 0.693 x Vd / Cl; steady state takes about 3 to 5 half-lives.
7. Phase II conjugation usually inactivates drugs; cats are poor glucuronidators.
8. Rumen traps weak bases and may inactivate oral drugs.

Go deeper on this site

- Ch 4. Pharmacodynamics: how a drug acts (in this book)
- Ch 7. Drugs in special patients (in this book)
- Veterinary Drug Concepts Clearly Explained
- Drug dose calculation guide

Sources

- Merck Veterinary Manual: Pharmacokinetics
- Merck Veterinary Manual: Disposition and Fate of Drugs
- NCBI Bookshelf (StatPearls): Pharmacokinetics

CHAPTER 4 OF 11

Pharmacodynamics: how a drug acts

How drugs act on the body: receptors, agonists and antagonists, dose-response curves, potency versus efficacy, therapeutic index, drug interactions, tolerance and tachyphylaxis.

After this chapter you can

- Describe the main receptor types and other drug targets.
- Differentiate full agonists, partial agonists, antagonists and inverse agonists.
- Interpret dose-response curves, separating potency from efficacy.
- Define therapeutic index and explain narrow-margin drugs.
- Explain pharmacodynamic interactions, tolerance and tachyphylaxis.

Overview: what the drug does to the body

Pharmacodynamics (PD) is the study of what a drug does to the body: the mechanism of action, the size of the effect and its relation to dose. Pharmacokinetics decides how much drug reaches the site; pharmacodynamics decides what happens when it gets there. Most drugs act by binding to specific target molecules, but some act by simple physical or chemical means, for example antacids neutralising acid, osmotic laxatives holding water in the gut, or chelating agents binding metals.

The targets of most drugs are **receptors**, which are usually proteins. Receptor families include *ion channel receptors* (fast, within milliseconds, such as the nicotinic receptor), *G-protein-coupled receptors* (the largest group, including adrenergic, muscarinic and opioid receptors), *kinase-linked receptors* (such as the insulin receptor) and *intracellular receptors* (steroid and thyroid hormones, which change gene expression over hours). Besides receptors, drugs may act on enzymes (NSAIDs inhibit cyclooxygenase), transport proteins and ion channels (local anaesthetics block sodium channels).

Agonists and antagonists

Two properties describe how a drug interacts with a receptor. **Affinity** is how tightly it binds. **Intrinsic activity (efficacy)** is how well it activates the receptor once bound.

- **Full agonist:** high affinity and high efficacy; it can produce the maximal response of the system.
- **Partial agonist:** binds but produces a smaller maximal response. It has a ceiling effect, and in the presence of a full agonist it can lower the net effect. Buprenorphine at the mu-opioid receptor is an example.
- **Antagonist:** has affinity but no efficacy, so it blocks the agonist and produces no effect of its own.
- **Inverse agonist:** reduces the baseline activity of a receptor that is active even without an agonist.
- **Agonist-antagonist:** acts as an agonist at one receptor subtype and an antagonist at another; butorphanol is a commonly cited opioid example.

A **competitive antagonist** binds reversibly to the same site as the agonist. It shifts the dose-response curve to the right without lowering the maximum, because a higher agonist dose can overcome the block. Atropine blocking acetylcholine at muscarinic receptors is the classic case. A **non-competitive** (or irreversible) antagonist lowers the maximal response, and more agonist cannot restore it. Receptors are finite in number, so responses reach a plateau when most receptors are occupied.

Dose-response, potency and efficacy

When response is plotted against dose, the result is usually a curve that rises and flattens. On a logarithmic dose axis it becomes S-shaped, which makes comparison easy. Two features matter.

- **Potency** is the position of the curve on the dose axis, often expressed as the EC_{50} or ED_{50}, the amount giving half the maximal effect. A curve further to the left means a more potent drug, which means a lower dose is needed.
- **Efficacy (maximal effect, E_{max})** is the height of the plateau, the greatest response the drug can produce.

Potency and efficacy are independent. A very potent drug may have low efficacy, and a weak drug may have high efficacy. For clinical choice, efficacy usually matters more than potency: a mild-effect drug cannot be made to do the job of a strong one just by raising the dose, while a less potent drug only needs a larger dose. Potency also does not mean better; a drug needing a smaller dose is not automatically safer.

The **graded** dose-response curve describes the response in one individual. The **quantal** curve describes how many animals in a group show an all-or-none response, such as sleep or death, and so shows variation between individuals.

Therapeutic index and safety

The **therapeutic index (TI)** compares the dose that causes toxicity with the dose that gives the desired effect. In animal studies it is often written as LD_{50}/ED_{50}, and in the clinic as the minimum toxic concentration over the median effective concentration. A large ratio means a wide margin of safety. A drug with a **narrow therapeutic index**, such as digoxin, needs careful dosing and sometimes monitoring of blood levels, because the effective and toxic doses are close together. A better safety indicator is the **certain safety factor** (LD_1/ED_{99}), which compares the dose lethal to almost none with the dose effective in almost all. The TI is a population value and says nothing about an individual animal with kidney or liver disease, where toxicity may appear at a normal dose.

Drug interactions at the receptor level

When two drugs are given together, the combined effect may be **additive** (sum of the two), **synergistic** (greater than the sum), **potentiation** (one drug with no effect of its own boosts another) or **antagonistic** (reduced effect). Pharmacodynamic antagonism has several types:

- **Competitive (pharmacological):** both drugs compete for the same receptor, as in atropine versus acetylcholine, or naloxone reversing an opioid.
- **Physiological (functional):** two drugs act on different receptors with opposite effects, such as adrenaline raising blood pressure while a vasodilator lowers it.
- **Chemical:** one drug directly binds the other, as when a chelating agent binds a metal.

Do not confuse these with *pharmacokinetic* interactions, where one drug changes the absorption, metabolism or excretion of another. Combining a partial agonist with a full agonist is a receptor-level example: the partial agonist may reduce the effect of the full agonist.

Tolerance, tachyphylaxis and receptor regulation

Receptors are not fixed. With repeated exposure, a drug may produce a smaller response. **Tolerance** is a gradual decrease in effect over days or longer, so a higher dose is needed to match the earlier response. **Tachyphylaxis** is a rapid fall in response within minutes to days, sometimes after only a few doses, as seen with indirectly acting amines that deplete stored transmitter. Mechanisms include receptor *desensitisation*, receptor *down-regulation* (fewer receptors), depletion of mediators and increased metabolism by enzyme induction. The opposite change, *up-regulation* or supersensitivity, can follow long-term blockade, which is why abrupt withdrawal of some drugs, such as beta-blockers, can cause rebound effects. Cross-tolerance may occur between drugs acting on the same receptor. In practice, tolerance may require a dose change or drug rotation, while tachyphylaxis is managed by dosing intervals or by choosing another agent.

Concept cleared

Concept cleared: Receptor as lock

A receptor is a lock and the drug is a key. A full agonist key fits and turns the lock fully. A partial agonist key fits but only turns it halfway. An antagonist key fits but will not turn, and it blocks the lock so the right key cannot enter. Locks are limited in number, so the effect has a ceiling.

Concept cleared: Potency versus efficacy

Two taxi drivers: one reaches the city after a small fare, but only goes 5 km. Another costs more but goes 100 km. Potency is how little fare is needed to start, and efficacy is how far you can finally go. A cheap start does not mean a long journey.

Concept cleared: Therapeutic index

Picture the gap between the dose that works and the dose that harms as the width of a bridge. A wide bridge lets you walk comfortably, but a narrow one leaves little room for error. A narrow therapeutic index drug asks for careful dosing, since a small slip tips the animal over the edge.

Concept cleared: Tolerance and tachyphylaxis

Walk into a room with a strong smell and the smell fades within minutes; that is like tachyphylaxis, a fast loss of response. Living in a house with a mild smell for months and slowly not noticing it is like tolerance. In both, the receptors or signals have adapted.

Memory aid: Competitive versus non-competitive antagonist

Competitive: curve shifts Right, maximum stays the same, and more agonist wins. Non-competitive: maximum goes Down, and more agonist cannot rescue. Think: Competitive equals Contest you can win.

Compare and contrast

Agonists and antagonists

Type	Affinity	Efficacy	Effect
Full agonist	High	High	Maximal response
Partial agonist	High	Low to moderate	Submaximal response, ceiling effect
Competitive antagonist	High	Zero	Rightward shift; surmountable
Non-competitive antagonist	High	Zero	Lower maximum; not surmountable
Inverse agonist	High	Negative	Lowers baseline activity

Potency versus efficacy

Feature	Potency	Efficacy
Meaning	Dose needed for a given effect	Maximum possible effect
Shown on curve as	Position left or right	Height of the plateau
Measure	EC50 or ED50	Emax
Clinical importance	Affects the dose size	Decides if the effect can be achieved at all
Link to safety	None directly	None directly

Species notes

Dog

Buprenorphine and morphine show how a partial agonist differs from a full agonist; dogs are often used to explain opioid ceiling effects.

Cat

Receptor sensitivity to opioids and other drugs can differ in cats, so effect-based titration and species-specific guidance are needed.

Horse

Horses show marked excitation to some opioids, an example that the same drug-receptor action can give different net effects across species.

Cattle

Narrow safety margins of some drugs make accurate weight estimation important in large animals.

Sheep/Goat

Dose-response and safety margins vary between ruminant species, so cattle data should not be copied directly.

Clinical pearls

Self-test: 10 questions

1. A drug that binds a receptor but produces no response is a(n):

An antagonist has affinity but zero intrinsic efficacy.

2. A competitive antagonist causes the dose-response curve of an agonist to:

More agonist can overcome the block, so the maximum is preserved but more drug is needed.

3. Potency is best shown by the:

EC50 or ED50 marks the dose giving half the maximal effect; a lower value means higher potency.

4. The maximal response a drug can produce is its:

Efficacy (Emax) is the plateau of the dose-response curve.

5. A narrow therapeutic index means:

A small ratio between toxic and effective doses leaves little margin for error.

6. Adrenaline raising blood pressure and a vasodilator lowering it is an example of:

They act on different receptors with opposite effects.

7. Which receptor type is a ligand-gated ion channel?

The nicotinic receptor is an ion channel; muscarinic and adrenergic receptors are G-protein-coupled.

8. Rapid loss of response within minutes to days is called:

Tachyphylaxis is acute decrease in response, often from desensitisation or mediator depletion.

9. A partial agonist differs from a full agonist in that it:

It binds but activates the receptor less, so the maximum response is lower.

10. A drug that reduces the baseline activity of a constitutively active receptor is a(n):

Inverse agonists produce an effect opposite to that of an agonist by lowering spontaneous activity.

Key points to revise

1. Pharmacodynamics is the effect of the drug on the body; most drugs act on receptors.
2. Affinity is binding strength; efficacy is the ability to activate the receptor.
3. A full agonist gives maximal response; a partial agonist has a ceiling.
4. Competitive antagonists shift the curve right; non-competitive ones lower the maximum.
5. Potency is the position of the curve (EC50); efficacy is the maximum (Emax).
6. Therapeutic index = toxic dose divided by effective dose; narrow index means little safety room.
7. Tachyphylaxis is a rapid loss of response; tolerance is a slower one.
8. Physiological antagonism uses different receptors with opposite effects.

Go deeper on this site

- Ch 3. Pharmacokinetics: how the body handles a drug (in this book)
- Ch 5. Receptors and signal transduction (in this book)

- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Drug Action and Pharmacodynamics
- Merck Manual Professional: Drug-Receptor Interactions
- Merck Manual Professional: Dose-Response Relationships

CHAPTER 5 OF 11

Receptors and signal transduction

How drug binding becomes a cell response: the four receptor families, second messengers, receptor regulation and non-receptor targets, with MDR1 as a canine pharmacogenetic example.

After this chapter you can

- Classify receptors into the four main families and give a veterinary example of each
- Describe how cAMP, IP3/DAG, Ca2+ and cGMP carry a signal inside the cell
- Explain up-regulation, down-regulation, desensitisation, spare receptors and allosteric modulation
- List drug targets that are not receptors
- Explain the clinical importance of the MDR1 (ABCB1) mutation in dogs

Why receptors matter

Most drugs act by binding to a protein on or inside a cell and changing what that protein does. The commonest such protein is a **receptor**. Earlier chapters described how agonists and antagonists behave and how dose-response curves are drawn. This chapter looks at what happens *after* binding: how a small drug molecule is turned into a cellular response, which is called **signal transduction**.

Knowing the receptor family tells you three useful things at once: how fast the drug will act, how long the effect will last, and which side effects to expect. A drug acting on an ion channel works in milliseconds, while a steroid acting on a nuclear receptor may take hours before the effect is seen.

The four receptor families

Receptors are grouped by the way they link the drug signal to the cell.

1. **Ligand-gated ion channels** (ionotropic receptors). The receptor is itself a channel. Binding opens the pore and ions flow within milliseconds. Examples: the nicotinic acetylcholine receptor at the neuromuscular junction (blocked by atracurium and other relaxants) and the $GABA_A$ receptor, a chloride channel enhanced by benzodiazepines, barbiturates and propofol.
2. **G-protein-coupled receptors** (GPCRs, metabotropic). These have seven transmembrane segments and act through a G protein. They are the largest group of drug targets. Examples: adrenergic receptors (alpha and beta), muscarinic receptors, opioid receptors, histamine H_1 and H_2 receptors, and dopamine receptors. Response takes seconds.
3. **Enzyme-linked receptors**. A single membrane-spanning protein with an enzyme region inside the cell, most often a tyrosine kinase. The insulin receptor and growth-factor receptors are the classical examples. Natriuretic peptide receptors have guanylyl cyclase activity. Response takes minutes to hours.
4. **Nuclear (intracellular) receptors**. Lipid-soluble drugs cross the cell membrane, bind a receptor in the cytoplasm or nucleus, and the complex changes gene transcription. Examples: glucocorticoids, thyroid hormone, sex steroids and vitamin D. Response takes hours to days, and also wears off slowly because new proteins must be made or broken down.

This explains a common exam point: prednisolone given today may reduce inflammation only after some hours, and its benefit lasts longer than its plasma half-life suggests.

Second messengers

When a GPCR is activated it changes a G protein, and the G protein switches an enzyme that makes a **second messenger** inside the cell. The drug is the first messenger. One receptor can activate many G proteins, so the signal is amplified.

- **G_s** stimulates adenylyl cyclase, raising **cAMP**, which activates protein kinase A. Beta-adrenergic stimulation works this way: relaxation of bronchial muscle and faster heart contraction.

- **G_i** inhibits adenylyl cyclase and lowers cAMP. Alpha-2 agonists (xylazine, medetomidine) and opioid receptors act through G_i.
- **G_q** activates phospholipase C, which splits membrane PIP_2 into **IP_3** and **DAG**. IP_3 releases **Ca^{2+}** from stores inside the cell, and DAG activates protein kinase C. Alpha-1 and muscarinic M_3 receptors use this path, causing smooth muscle contraction or secretion.
- **cGMP** is made by guanylyl cyclase. Nitric oxide activates the soluble form, and cGMP relaxes vascular smooth muscle. Sildenafil blocks the breakdown of cGMP (phosphodiesterase 5 inhibition) and is used in dogs with pulmonary hypertension.

Breakdown of messengers is also a drug target. Phosphodiesterase inhibitors, such as theophylline and pimobendan (PDE3), keep cAMP high.

Receptor regulation, spare receptors and allosteric sites

Receptors are not fixed in number or sensitivity. **Down-regulation** is a fall in receptor number after long exposure to an agonist. **Up-regulation** is a rise in number after long blocking, for example after prolonged beta-blocker use. This is why stopping a beta-blocker suddenly can cause rebound tachycardia and hypertension. **Desensitisation** is a quicker loss of response, often within minutes, because the receptor is phosphorylated and uncoupled from its G protein or taken into the cell. It is one cause of tolerance, which was described in the pharmacodynamics chapter.

Spare receptors (receptor reserve) exist when a maximum response needs only a small part of the receptors to be occupied. A tissue with many spare receptors reaches full response at low drug concentration, so its dose-response curve lies to the left of the binding curve. A competitive antagonist must block many receptors before the response falls, and an irreversible antagonist can reduce the maximum only after the reserve is used up.

Allosteric modulators bind at a site different from the agonist site (the orthosteric site). They do not usually activate the receptor alone but change how strongly the natural ligand works. Benzodiazepines are the best example: they bind the $GABA_A$ receptor and increase the effect of GABA, but have little effect if GABA is absent.

This gives a built-in ceiling to some effects, which is one reason they are safer than barbiturates, which at high concentration can open the channel directly.

Targets that are not receptors

Many important drugs do not act on receptors at all.

- **Enzymes:** NSAIDs inhibit cyclo-oxygenase; ACE inhibitors such as enalapril block angiotensin-converting enzyme; organophosphates inhibit acetylcholinesterase; antibacterials such as trimethoprim inhibit bacterial dihydrofolate reductase.
- **Transporters and pumps:** furosemide blocks the Na-K-2Cl carrier in the loop of Henle; omeprazole blocks the gastric proton pump; digoxin inhibits Na^+/K^+-ATPase.
- **Voltage-gated ion channels:** local anaesthetics such as lignocaine block sodium channels; amlodipine blocks calcium channels.
- **Physical or chemical action:** mannitol (osmosis), antacids (neutralisation) and chelating agents (binding metals).
- **Microbial or parasite targets:** ribosomes, cell walls and the parasite chloride channels hit by avermectins. The selectivity of these drugs for the parasite rather than the host is the basis of chemotherapy.

Pharmacogenetics in animals: MDR1 (ABCB1)

Pharmacogenetics studies how inherited differences change drug response. The best-proven veterinary example is the **ABCB1 (MDR1) gene** in dogs. This gene codes for **P-glycoprotein**, an efflux pump in the blood-brain barrier, gut wall, liver and kidney that pushes many drugs back out of cells. A deletion mutation (ABCB1-1Δ, a four-base-pair deletion) causes a frameshift, so a non-functional pump is made. It was first linked to ivermectin sensitivity in Collies and is also found in other herding breeds such as Australian Shepherds, Shetland Sheepdogs, Old English Sheepdogs and some German Shepherds.

Dogs with two mutant copies cannot keep drugs out of the brain, so substrates reach the central nervous system and cause signs such as tremors, ataxia, salivation and coma. Drugs of concern include high-dose ivermectin, loperamide, and sedatives such as acepromazine and butorphanol, which need cautious,

reduced dosing. Some anticancer drugs are also affected. Inhibitors of P-glycoprotein such as ketoconazole and cyclosporine can add to the risk. The standard low doses of avermectin heartworm preventives are considered safe. A cheek-swab DNA test identifies normal, carrier and affected dogs, and breeders and clinicians can use it before drug choice.

Other animal pharmacogenetic differences are real but less well proven, so this chapter does not list them. The cat's weak glucuronidation is a species difference, covered in the species chapter.

Concept cleared

Concept cleared: Second messengers
Think of a doorbell. The drug presses the button outside the house (the receptor), but you hear the bell all over the house (the second messenger inside the cell). One press can make a loud ring in every room, which is amplification. The ring stops when the bell is switched off, like a phosphodiesterase breaking down cAMP.

Concept cleared: Spare receptors
A hall has 100 light switches but the room is fully lit when only 20 are on. The other 80 are spare. A small amount of agonist gives a full effect, and a blocker must switch off many switches before the light dims. Spare receptors make a tissue very sensitive to its agonist.

Concept cleared: Allosteric modulation
The agonist is the person who turns the car key. An allosteric modulator is the power steering or volume control: it does not start the car, but it changes how strongly the driver's action is felt. Benzodiazepines boost GABA in this way and do little when GABA is absent.

Concept cleared: MDR1 pump

P-glycoprotein is a security guard at the brain's door who sends unwanted drugs back out. In a dog with the MDR1 deletion the guard is absent, so drugs such as ivermectin walk in and reach the brain. Same dose, very different result.

Memory aid: G protein quick code

Gs = Stimulates cAMP; Gi = Inhibits cAMP; Gq = IP3 and Calcium (think Q for the second messenger Quartet of PIP2, IP3, DAG, Ca). Remember the receptor families by speed: Channel, G-protein, Kinase, Nucleus - fastest to slowest.

Compare and contrast

The four receptor families

Family	Example	Speed	Link to effect
Ligand-gated ion channel	Nicotinic ACh, GABA-A	Milliseconds	Receptor is the channel; ion flow
G-protein-coupled receptor	Beta-adrenergic, muscarinic, opioid	Seconds	G protein, then second messenger
Enzyme-linked receptor	Insulin, growth factor, natriuretic peptide	Minutes to hours	Kinase or cyclase activity inside cell
Nuclear receptor	Glucocorticoid, thyroid, sex steroid	Hours to days	Changes gene transcription

G protein pathways

G protein	Enzyme effect	Messenger	Example drug action
Gs	Stimulates adenylyl cyclase	cAMP up	Beta agonist: bronchodilation
Gi	Inhibits adenylyl cyclase	cAMP down	Xylazine, opioids
Gq	Activates phospholipase C	IP3, DAG, Ca2+ up	Alpha-1: vasoconstriction
Guanylyl cyclase (not a G protein)	Makes cGMP	cGMP up	Nitric oxide, sildenafil effect

Species notes

Dog

Collies and related herding breeds may carry the ABCB1 deletion; test or use reduced doses of P-glycoprotein substrates such as ivermectin at high dose, loperamide, acepromazine and butorphanol.

Cat

Alpha-2 agonists act through Gi and commonly cause vomiting in cats, and their effects can be reversed with an alpha-2 antagonist such as atipamezole.

Cattle

Corticosteroids act on nuclear receptors, so effects last days; late in pregnancy they can induce parturition in cows, an effect used in practice and a risk when unintended.

Horse

Beta-2 agonists such as clenbuterol act through Gs and cAMP to relax airway smooth muscle in recurrent airway obstruction.

Clinical pearls

Self-test: 10 questions

1. The nicotinic acetylcholine receptor belongs to which family?

The nicotinic receptor is itself an ion channel, opened by acetylcholine within milliseconds.

2. Which receptor family has the slowest onset of action?

Nuclear receptors change gene transcription and protein synthesis, which takes hours to days.

3. Activation of Gq leads directly to formation of:

Gq activates phospholipase C, which splits PIP2 into IP3 and DAG.

4. Xylazine and medetomidine act through which G protein?

Alpha-2 receptors couple to Gi, which lowers cAMP.

5. Sildenafil increases which messenger by blocking its breakdown?

Sildenafil inhibits phosphodiesterase 5, which breaks down cGMP.

6. Sudden stopping of a long-term beta-blocker may cause rebound tachycardia mainly because of:

Long-term blockade increases receptor number, so the sudden return of catecholamine effect is exaggerated.

7. Benzodiazepines enhance the effect of GABA by:

They bind a different site on the GABA-A receptor and increase its response to GABA.

8. Spare receptors mean that:

With receptor reserve, only a fraction of receptors need to be occupied for the full response.

9. Which drug acts on an enzyme rather than a receptor?

Enalapril inhibits angiotensin-converting enzyme; the others act on receptors.

10. The ABCB1 (MDR1) mutation in dogs causes sensitivity because:

The deletion produces a non-working P-glycoprotein pump, so substrate drugs enter the brain and accumulate.

Key points to revise

1. Four receptor families: ligand-gated channels, GPCRs, enzyme-linked, nuclear.
2. Speed of response: ion channel (ms), GPCR (s), kinase (min-h), nuclear (h-days).
3. Gs raises cAMP, Gi lowers cAMP, Gq raises IP3, DAG and Ca2+.
4. cGMP mediates nitric oxide vasodilation and is broken down by PDE5.
5. Down-regulation, up-regulation and desensitisation change response on repeated dosing.
6. Spare receptors make tissue sensitive; a maximal response needs only partial occupancy.
7. Allosteric modulators change agonist effect without acting at the agonist site.
8. MDR1 (ABCB1) deletion in dogs makes P-glycoprotein non-functional and raises CNS drug entry.

Go deeper on this site

- Ch 4. Pharmacodynamics: how a drug acts (in this book)
- Ch 6. Species differences, adverse reactions and interactions (in this book)
- Veterinary Drug Concepts Clearly Explained

Sources

- Cornell University College of Veterinary Medicine: Drug sensitivity (MDR1)

- University of Minnesota Libraries: Pharmacology, G protein-coupled receptors
- PubMed: Ivermectin sensitivity in collies is associated with a deletion mutation of the mdr1 gene

CHAPTER 6 OF 11

Species differences, adverse reactions and interactions

The same drug can be safe in one species and deadly in another because of differences in metabolism, transporters and digestive anatomy. This chapter also covers types of adverse reactions, drug-drug interactions, extra-label use and reporting.

After this chapter you can

- Explain why cats handle paracetamol and aspirin poorly and why some dogs react badly to ivermectin (MDR1/ABCB1).
- Describe the main drug cautions in ruminants, horses and poultry.
- Differentiate Type A and Type B adverse drug reactions with examples.
- Classify drug interactions as pharmacokinetic or pharmacodynamic and give examples of each.
- Define extra-label use and outline how adverse reactions are reported.

Why species differ in drug response

A drug is not handled the same way by every animal. Four things change from species to species: how the drug is absorbed (a rumen is very different from a simple stomach), how it is carried and bound in blood, how the liver changes it (metabolism), and how it leaves the body (kidney, bile, transporters). The target receptors can also differ. Because of this, a dose or a drug that suits one species cannot be copied blindly to another.

In practice, always read the label for the species you are treating, and treat any extrapolation between species as a calculated risk that needs extra monitoring.

Cats, dogs and the liver and transporter story

Cats and glucuronidation. Many drugs are made water-soluble in the liver by conjugation with glucuronic acid. Cats have a very low capacity for this step

because they have a deficient form of the UGT1A6 glucuronosyltransferase enzyme. Drugs that depend on glucuronidation therefore stay in the body much longer.

- **Paracetamol (acetaminophen):** the cat is forced to use alternative pathways, and a toxic metabolite builds up. This damages red cells (methaemoglobinaemia, Heinz bodies) and the liver. Paracetamol is considered unsafe in cats.
- **Aspirin:** the half-life is much longer in cats than in dogs, so dosing intervals must be stretched and the drug used only with great care.
- Other examples are some opioids and phenolic compounds, and propylene glycol and onion-type compounds also damage feline red cells.

Dogs and MDR1 (ABCB1). The ABCB1 gene codes for P-glycoprotein, a pump on the blood-brain barrier and gut wall that throws certain drugs back out. Some dogs, especially collies and other herding breeds, carry a mutation that gives a non-working pump. In these dogs, drugs that are normally kept out of the brain can enter and cause neurological toxicity.

- Macrocyclic lactones such as ivermectin (at higher, non-preventive exposure), loperamide and some anticancer drugs are examples.
- Sedatives such as acepromazine and butorphanol may need a reduced dose.
- Genetic testing can identify carrier and affected dogs.

Ruminants, horses and poultry

Ruminants. The rumen contains billions of microbes that digest fibre. Oral antibiotics, especially broad-spectrum ones, can upset this flora, causing rumen stasis and indigestion. Drugs given by mouth may also be diluted, adsorbed or broken down in the rumen, so oral absorption is unpredictable. On the other hand, the rumen can be used on purpose, for example in slow-release intraruminal boluses. Residues in milk and meat, and therefore withdrawal periods, are major concerns in food animals.

Horses. The horse depends on its large-intestine bacteria (hindgut fermenter). Oral antibiotics, and sometimes even injectable ones, can cause severe antibiotic-associated colitis. Oral lincosamides are particularly dangerous. Horses are also highly sensitive to the ionophore monensin, which can cause fatal heart and muscle damage, so feed meant for cattle or poultry must never be given to them.

Poultry. Ionophore coccidiostats (monensin, salinomycin, narasin) are widely used in feed. If they are combined with certain other drugs, particularly tiamulin, serious toxicity (weakness, paralysis, deaths) can result, because the other drug slows ionophore metabolism. Always check compatibility before adding a new drug to medicated feed. Residues and withdrawal times in eggs and meat also apply.

Types of adverse drug reactions

An adverse drug reaction (ADR) is a harmful, unintended response to a drug given at a normal therapeutic dose. Two broad types are recognised.

Feature	Type A (augmented)	Type B (bizarre)
Relation to pharmacology	Exaggeration of the known action	Unrelated to the known action
Dose dependence	Dose-related	Not clearly dose-related
Predictable?	Yes	No
Frequency	Common	Rare
Examples	Hypotension from an overdose of a sedative; nephrotoxicity from aminoglycosides	Anaphylaxis after penicillin; idiosyncratic reactions

Species-specific toxicity, such as the cat and paracetamol, is usually a Type A reaction in disguise: the effect is dose-related but the safe dose is much lower in that species. Type B reactions include allergy (immune-mediated) and idiosyncrasy (often genetic). Management is to stop the drug, give supportive care, and record the reaction so the animal is not exposed again.

Drug interactions

A drug interaction occurs when one drug changes the effect of another. Interactions are grouped by mechanism.

Pharmacokinetic interactions change what the body does to the drug (absorption, distribution, metabolism, excretion).

- *Enzyme inducers* (for example phenobarbital) speed up liver metabolism of other drugs and can lower their effect.

- *Enzyme inhibitors* (for example ketoconazole and chloramphenicol) slow metabolism, so levels and toxicity rise.
- *Protein binding displacement:* one highly bound drug pushes another off albumin, temporarily raising free drug.
- *Absorption:* divalent cations in antacids or mineral supplements can bind tetracyclines and fluoroquinolones in the gut.
- *Excretion:* competition at kidney transport sites can delay clearance.

Pharmacodynamic interactions occur at the receptor or organ level, without a change in drug concentration.

- *Additive or synergistic:* two nephrotoxic drugs, such as an aminoglycoside with an NSAID or furosemide, increase kidney injury; two sedatives deepen CNS depression.
- *Antagonistic:* a bacteriostatic antibiotic may blunt the effect of a bactericidal one; naloxone reverses opioids.

Useful ideas to prevent trouble: keep the number of drugs low, check dehydration and kidney function before nephrotoxic drugs, and consult a reference whenever a new drug is added to a regimen.

Extra-label use and reporting

Extra-label (off-label) use means using a licensed drug differently from its label, for example in another species, for another disease, or at another dose, route or interval. It is often necessary because few drugs are approved for minor species. Good practice is to use it only when no suitable labelled product exists, to base the choice on evidence, to explain the risk to the owner, and to record the decision. In food animals, an extended withdrawal period must be set because the label withdrawal no longer applies. In the USA this is permitted under defined legal conditions (AMDUCA), and some drugs, such as chloramphenicol, are banned from extra-label use in food animals; always check the rules that apply in your own country and state.

Reporting. Report suspected ADRs, lack of efficacy and residue problems to the manufacturer and to the national pharmacovigilance system. In India, the Pharmacovigilance Programme of India (PvPI) is the national programme, and a CDSCO notice in 2019 reportedly asked veterinary product manufacturers to submit

periodic safety update reports; students should confirm current requirements with CDSCO. A good report states the species, age, weight, drug and batch, timing, signs, outcome and any other drugs given.

Concept cleared

Concept cleared: Cat and glucuronidation
Think of the liver as a washing machine with several programs. Most animals have a fast 'glucuronide' wash cycle for many drugs. The cat has that cycle switched mostly off, so the drug waits in the machine for hours or days and the slower, toxic programs take over. That is why a tablet harmless to a person can poison a cat.

Concept cleared: MDR1 pump
The blood-brain barrier is like a nightclub with a bouncer. P-glycoprotein is the bouncer who pushes unwanted drugs back out onto the street. In MDR1-mutant dogs the bouncer is missing, so drugs such as ivermectin at high doses walk straight into the brain and cause tremors, blindness or coma.

Concept cleared: Type A versus Type B
Type A is like turning a radio volume up too high: the sound is the same, only louder, so it is predictable and depends on the dose. Type B is like the radio suddenly playing a different station for no obvious reason: rare, unpredictable and often immune-related, such as penicillin anaphylaxis.

Concept cleared: Enzyme inducer versus inhibitor
Imagine the liver enzymes as workers on a conveyor belt. An inducer hires extra workers, so drugs are cleared faster and may stop working. An inhibitor sends workers on strike, so drugs pile up and may become toxic. The drug itself is unchanged; only the clearance changes.

Memory aid: Remember: Type A and Type B

A = Augmented, Anticipated, Always dose-related. B = Bizarre, Beyond prediction, Bit rare.

Compare and contrast

Pharmacokinetic versus pharmacodynamic interactions

Feature	Pharmacokinetic	Pharmacodynamic
What changes	Drug concentration at the site	Effect at receptor or organ
Stage involved	Absorption, distribution, metabolism, excretion	Receptor binding and response
Typical example	Phenobarbital inducing metabolism of another drug	Aminoglycoside plus NSAID: additive kidney injury
Another example	Calcium or iron binding tetracycline in the gut	Naloxone antagonising an opioid
How to detect	Drug level change, altered duration	Exaggerated or reduced clinical effect

Type A versus Type B adverse reactions

Feature	Type A	Type B
Predictable	Yes	No
Dose-related	Yes	Usually not
Frequency	Common	Rare
Mechanism	Extension of the known pharmacology	Immune or idiosyncratic
Example	Aminoglycoside nephrotoxicity	Penicillin anaphylaxis

Species notes

Dog
Some herding breeds carry an MDR1 (ABCB1) mutation; ivermectin at higher doses, loperamide and some

Cat
Poor glucuronidation makes paracetamol dangerous and prolongs aspirin; cats are also

chemotherapy drugs can cause serious neurotoxicity in them.

sensitive to permethrin-type products meant for dogs.

Cattle
Oral antibiotics can disturb rumen microbes; withdrawal periods for milk and meat must be respected, especially in extra-label use.

Horse
Antibiotic-associated colitis is a major risk, and monensin in feed is highly toxic to horses.

Poultry
Ionophores such as monensin or salinomycin must not be combined with tiamulin or similar interacting drugs.

Clinical pearls

Self-test: 10 questions

1. Cats are especially sensitive to paracetamol mainly because they have:

Cats have deficient UGT1A6 glucuronidation, so paracetamol is cleared slowly and toxic metabolites cause methaemoglobinaemia and liver injury.

2. The MDR1 (ABCB1) gene codes for:

ABCB1 codes for P-glycoprotein, which pumps drugs out of the brain and gut cells.

3. Which breed group is most commonly affected by the MDR1 mutation?

The mutation is frequent in collies and related herding breeds.

4. Which species is highly sensitive to the ionophore monensin?

Horses are very sensitive to monensin, which can cause fatal heart and muscle damage; the poultry feed use is at approved levels.

5. In poultry, serious toxicity may follow combining an ionophore with:

Tiamulin slows ionophore metabolism and can cause toxicity.

6. A Type A adverse reaction is best described as:

Type A reactions are augmented, dose-related and predictable.

7. Anaphylaxis after penicillin injection is an example of:

It is rare, unpredictable and immune-mediated, which is typical of Type B.

8. Phenobarbital reducing the effect of another drug by speeding its metabolism is an example of:

Phenobarbital is a liver enzyme inducer, a pharmacokinetic interaction.

9. Giving an aminoglycoside together with an NSAID raises the risk of kidney damage. This is a:

Both agents harm the kidney, so the effects add up at the organ level without a change in the other drug's levels.

10. Extra-label use of a drug in a food animal requires special attention to:

The label withdrawal period no longer applies, so a longer one based on evidence must be set to avoid residues.

Key points to revise

1. Species differ in absorption, protein binding, metabolism, excretion and receptors.
2. Cats have deficient glucuronidation (UGT1A6), so paracetamol is toxic and aspirin is slowly cleared.
3. MDR1/ABCB1 mutation in dogs means a non-functional P-glycoprotein pump and CNS toxicity from certain drugs.
4. Ruminant oral antibiotics can upset rumen flora; horses risk colitis from antibiotics; monensin is toxic to horses.
5. Type A reactions are dose-related and predictable; Type B are unpredictable, rare and often immune-mediated.
6. Pharmacokinetic interactions change drug levels; pharmacodynamic interactions change the effect.
7. Enzyme inducers lower and inhibitors raise levels of other drugs; additive nephrotoxicity is a pharmacodynamic example.
8. Extra-label use needs justification, records and an extended withdrawal period in food animals; report ADRs through the pharmacovigilance system.

Go deeper on this site

- Ch 3. Pharmacokinetics: how the body handles a drug (in this book)
- Ch 7. Drugs in special patients (in this book)
- Veterinary Drug Concepts Clearly Explained
- Meloxicam in cats: safety cautions

Sources

- Washington State University Veterinary Hospital: Is your pet at risk of an adverse reaction to common drugs?
- Merck Veterinary Manual: New Animal Drugs, Extralabel Drug Use, Compounded Drugs, and Generic Drugs
- FDA: The Ins and Outs of Extra-Label Drug Use in Animals
- Medical Dialogues: CDSCO directs veterinary manufacturers to submit periodic safety reports

CHAPTER 7 OF 11

Drugs in special patients

How pregnancy, lactation, age, kidney and liver disease, dehydration and obesity change drug handling, and how therapeutic drug monitoring helps individual dosing.

After this chapter you can

- Explain placental transfer and why the stage of gestation decides the type of fetal harm
- Describe drug passage into milk, ion trapping and milk withdrawal periods
- Explain why neonates and geriatric animals respond differently to drugs
- Adjust drug choice in kidney disease, liver disease, dehydration and obesity
- State when therapeutic drug monitoring is useful

Why special patients need special thinking

Standard dosing advice assumes a healthy adult animal. Pregnant, lactating, very young, old, sick, dehydrated or fat animals handle drugs differently. The principles of absorption, distribution, metabolism and excretion from the pharmacokinetics chapter still apply; the task here is to see which step changes in each patient and to choose the drug, route and interval accordingly.

Pregnancy

Most drugs cross the placenta, and the ones that cross most easily are small, lipid-soluble and non-ionised, the same properties that favour passage across any membrane. Placental structure differs between species, but little drug-specific information exists for domestic animals, so advice is often borrowed from laboratory animals and human data.

The **stage of gestation** decides the type of harm:

- **Before and around implantation:** an "all or none" effect; the embryo either dies or survives normally.
- **Organogenesis (early gestation):** the teratogenic window, when malformations occur. Examples from veterinary sources: tetracyclines affect bone and teeth,

griseofulvin causes multiple defects (best known in cats), ketoconazole causes skeletal defects and resorption, and chloramphenicol is linked to eye defects.

- **Later fetal period:** growth and organ function are affected rather than structure. Corticosteroids may cause cleft palate early and premature labour or abortion later; in cattle, a corticosteroid late in gestation can start parturition. Fluoroquinolones may harm growing cartilage.
- **Near term:** drugs such as opioids and sedatives reach the fetus and may depress the newborn. Prostaglandins and oxytocin affect the uterus itself.

Human drug labels once used FDA pregnancy categories A, B, C, D and X. These were replaced by narrative risk summaries, and veterinary labels have no such grading. The practical lesson is to weigh benefit to the dam against possible harm to the fetus, use the drug with the most experience, give it for the shortest time, and avoid known teratogens. People handling hormones or prostaglandins must also be aware of their own risk if they are pregnant.

Lactation

Drugs pass from plasma into milk mainly by simple diffusion. Passage is greater for drugs that are **lipid-soluble**, **small**, **poorly protein-bound** and **weak bases**. Milk is a little more acidic than plasma, so weak bases become ionised and are **trapped** there (ion trapping, as described earlier). Macrolides and lincosamides reach higher milk than plasma concentration for this reason, while weak acids such as penicillins reach low milk levels. Highly fat-soluble drugs also collect in milk fat.

There are two separate concerns.

- **The suckling young.** The amount reaching the young is usually small, but newborns clear drugs slowly and may be affected. Examples are sedation of puppies by drugs in the dam's milk, or diarrhoea from antibiotics changing gut flora. Where the drug is important and risky, the young can be given milk replacer.
- **Milk for human use.** In dairy animals the drug residue in milk must fall below the legal limit, so the **milk withdrawal period** must be observed. Intramammary products, injections in cows and goats, and even some oral drugs can leave residues, and treated animal milk may carry resistant bacteria to people.

Neonates and young animals

Newborn calves, foals, lambs, puppies and kittens are not small adults. Their body differs in ways that change dosing:

- **Absorption:** gastric pH and gut motility are different; the gut is unusually permeable in the first day, and in pre-ruminant calves milk goes directly to the abomasum so oral drugs bypass the rumen.
- **Distribution:** total body water is higher and fat is lower, so water-soluble drugs such as aminoglycosides have a larger volume of distribution. Plasma albumin is lower, so less drug is bound and more is free. The blood-brain barrier is more permeable, so CNS drugs act more strongly.
- **Metabolism:** liver enzymes, especially glucuronidation and other conjugation pathways, are immature, so many drugs have a longer half-life. Chloramphenicol is a standard example.
- **Excretion:** kidney function is immature and matures over several weeks.

The result is accumulation, so intervals may need extending or drug choice changed. Neonates also lose heat, water and glucose quickly, so any sedation or fluid problem is dangerous. Adult values are usually reached after several weeks, but the age varies by species.

Geriatric patients

Ageing lowers kidney function, liver blood flow, lean body mass and often albumin, while fat proportion rises. Old animals commonly have several diseases and take several drugs, so interaction risk is high. They may be more sensitive to sedatives and anaesthetics. The advice is to begin cautiously, choose drugs with a wide safety margin, monitor kidney and liver function, and review the need for each drug regularly.

Kidney disease and liver disease

Kidney disease. Drugs and active metabolites that leave by the kidney accumulate when filtration falls. Choose drugs with a wide margin or non-renal elimination, lengthen the interval or reduce the dose of renally cleared ones, and avoid nephrotoxic drugs. Aminoglycosides and NSAIDs are the typical examples to avoid, and tetracyclines other than doxycycline are also best avoided. Ion trapping may

also change: acidic or alkaline urine alters excretion of weak acids and bases. Keep the animal hydrated, because poor renal perfusion makes injury worse.

Liver disease. The liver clears most lipophilic drugs, so liver failure prolongs their action. Several changes occur together. First-pass metabolism falls, so oral bioavailability of some drugs rises. Low albumin raises the free fraction. Prodrugs that need liver activation may work poorly; prednisolone is preferred to prednisone in severe liver disease. Avoid hepatotoxic drugs, for example paracetamol in cats and dogs, and azole antifungals when liver values are raised. Sedatives such as benzodiazepines can worsen hepatic encephalopathy. When a drug is cleared mainly by the kidney, it may be the safer choice in liver disease, and the reverse is also true.

Dehydration, obesity and drug monitoring

Dehydration reduces the volume of distribution of water-soluble drugs, so plasma concentrations rise, and it lowers kidney perfusion, so excretion falls. Correct fluid deficits before or with giving drugs such as NSAIDs and aminoglycosides.

Obesity. Fat takes up lipid-soluble drugs, such as thiopentone, but little water-soluble drug. Doses of polar drugs should be based on estimated lean body weight, otherwise overdose is likely. Lipophilic drugs may be redistributed from fat slowly, prolonging recovery.

Therapeutic drug monitoring (TDM) means measuring the drug in blood to adjust dosing. It is useful when the therapeutic index is narrow, the clinical effect is hard to see, or the relation between dose and concentration varies between patients. Typical candidates are phenobarbital, digoxin, theophylline, cyclosporine and aminoglycosides. Samples are taken at steady state, usually at trough, and sometimes at peak, and interpreted with the clinical picture rather than as a number alone.

Concept cleared

Concept cleared: Teratogenic window

Building a house: if the wall plan is wrong while the walls go up, the house has a structural fault. Once the walls are done, a problem only damages the paint. Early gestation is wall building (organogenesis) so drugs cause malformations; later exposure affects growth and function.

Concept cleared: Ion trapping in milk

A weak base is like a visitor who enters a room that is slightly more acidic. Inside, it picks up a charge and cannot easily leave, so it collects in milk at a higher level than in blood. Milk acts as a one-way room for weak bases.

Concept cleared: Neonates are not small adults

A newborn is a factory not fully commissioned. The machines (liver enzymes) are being installed and the exit door (kidney) is narrow. The same load clears slowly and piles up, so the schedule must change, not just the size.

Concept cleared: Therapeutic drug monitoring

Like checking the fuel gauge rather than guessing from the distance driven. Blood level shows what the individual patient actually has on board, useful when the safe zone is narrow.

Compare and contrast

Neonate versus adult: why drug handling differs

Feature	Neonate	Effect on drug
Total body water	Higher	Larger Vd of water-soluble drugs
Plasma albumin	Lower	More free drug
Liver enzymes	Immature	Slower metabolism, longer half-life
Kidney function	Immature	Slower excretion
Blood-brain barrier	More permeable	Stronger CNS effects
Gut absorption	Very permeable at first	Oral drugs may be absorbed more

Kidney versus liver disease

Point	Kidney disease	Liver disease
Main change	Slower excretion	Slower metabolism, lower albumin
Drugs to avoid	Aminoglycosides, NSAIDs	Paracetamol, azoles, prolonged sedatives
Adjustment	Longer interval or lower dose	Choose renally cleared drugs; avoid prodrugs
Support	Fluids	Treat encephalopathy; watch glucose

Species notes

Dog
Puppies metabolise drugs slowly in the first weeks, and tetracyclines and fluoroquinolones given to pregnant or growing dogs may harm teeth, bone or cartilage.

Cat
Weak glucuronidation is worse in kittens, and griseofulvin in pregnant queens causes congenital defects.

Cattle
Drug residues in milk require strict milk withdrawal periods, and calves are pre-ruminants, so oral drug absorption differs from adult cows.

Horse
Foals are born with immature organ function and drug dosing intervals often need review; NSAID use needs

particular care in dehydrated or sick foals.

Sheep/Goat
Corticosteroids and prostaglandins can cause abortion in pregnant ewes and does, and milk from treated animals must also meet withdrawal times.

Clinical pearls

Self-test: 10 questions

1. Which drug property favours placental transfer?

Lipid-soluble, small, non-ionised molecules cross membranes, including the placenta, most easily.

2. The period most likely to give structural malformations is:

Organs form during organogenesis, so a teratogen at that time causes structural defects.

3. Which antifungal is best known for causing congenital defects in pregnant cats?

Griseofulvin causes multiple congenital abnormalities, documented especially in cats.

4. Weak bases are concentrated in milk because milk is:

In slightly acidic milk, weak bases become ionised and trapped.

5. The main reason for a milk withdrawal period is to:

Residues must fall below legal limits before milk enters the human food chain.

6. Compared with adults, neonates usually have:

Neonatal conjugation enzymes are immature, so many drugs persist longer.

7. Which drug is best avoided in a dehydrated azotaemic dog?

NSAIDs reduce renal blood flow and are nephrotoxic when perfusion is already low.

8. In severe liver failure, which corticosteroid is preferred because it needs no hepatic activation?

Prednisone is a prodrug converted to prednisolone in the liver; prednisolone is already active.

9. In an obese animal, a polar water-soluble drug should be dosed on:

Polar drugs do not distribute into fat, so dosing by total weight overdoses.

10. Therapeutic drug monitoring is most useful for:

Narrow-margin drugs with variable concentrations need blood level checks to avoid toxicity or failure.

Key points to revise

1. Lipid-soluble, small, non-ionised drugs cross the placenta most easily.
2. Early gestation (organogenesis) is the teratogenic window.
3. Weak bases are trapped in milk because milk is slightly acidic.

4. Milk withdrawal periods prevent residues reaching human consumers.
5. Neonates have higher body water, lower albumin and immature liver and kidney function.
6. Geriatric animals have reduced clearance and more drug interactions.
7. Kidney disease: avoid nephrotoxins, adjust dose or interval; liver disease: avoid hepatotoxins and prodrugs.
8. Dose polar drugs on lean weight in obese animals; correct dehydration first.

Go deeper on this site

- Ch 3. Pharmacokinetics: how the body handles a drug (in this book)
- Ch 6. Species differences, adverse reactions and interactions (in this book)
- Veterinary drugs list: classes, uses and cautions

Sources

- Merck Veterinary Manual: Effect of reproductive treatment on the fetus or neonate in animals
- Merck Veterinary Manual: Pharmacokinetics (effects of age, renal and hepatic disease, dehydration)
- Merck Veterinary Manual: Design of dosing regimens for animals (renal disease, therapeutic drug monitoring)

CHAPTER 8 OF 11

Dosage forms, routes and drug delivery

How a drug is given and in what form decides how fast, how much and how long it acts. This chapter covers routes, species differences, dosage forms and long-acting delivery systems.

After this chapter you can

- Compare routes of administration for speed, bioavailability and limitations
- Explain species-specific issues such as rumen effects and IM injection damage in food animals
- Classify veterinary dosage forms including boluses, drenches, premixes and pour-ons

- Describe modified-release, long-acting and novel delivery concepts
- Choose a suitable route and form for a given species and purpose, and avoid common handling errors

Route and form: why the choice matters

A drug reaches its target only if the **route** (where it enters the body) and the **dosage form** (the physical shape of the product) suit the drug, the species and the purpose. The same active ingredient can act in seconds when given intravenously, in an hour when given orally, or over days when given as a depot injection. Route also decides bioavailability, the fraction of the dose that reaches the systemic circulation. By definition, IV bioavailability is 100 percent; every other route is equal or lower.

Three questions guide the choice: *Where is the target* (local or systemic)? *How fast is the effect needed* (emergency or maintenance)? *Who will give it* (veterinarian, farmer or pet owner) and to which species? A fourth, often forgotten in food animals, is *residue risk*: the route and site decide how long the drug stays in tissue and milk.

Enteral routes: oral, rumen and rectal

Oral (PO) is the commonest route in cattle, pigs, poultry and companion animals because it is cheap, simple and safe. Its drawbacks are slow and variable onset, destruction of some drugs by gastric acid or enzymes, and first-pass metabolism in the liver. Food can bind or delay absorption, and in horses oral bioavailability of several drugs is poor.

Ruminants are different. The rumen acts like a large fermentation vat that dilutes the dose and delays its arrival in the small intestine. Rumen microbes may destroy some drugs (for example, certain oral penicillins and many oral protein or peptide drugs) and some oral antibiotics can upset the rumen flora and cause indigestion. Sheep and goats given a drench may also lose part of it by spillage or regurgitation. On the other hand, the rumen allows **intraruminal boluses** that sit in the reticulorumen and release drug for weeks to months. To stay put and avoid regurgitation during rumination, they must be dense enough or have a shape that keeps them in the forestomach. In young pre-ruminant calves, the oesophageal

groove can carry liquids straight to the abomasum, so milk-fed calves behave more like monogastrics.

Rectal dosing is used when the animal is vomiting or unconscious, or for local effect. Part of the rectal blood flow bypasses the liver, so first-pass loss is reduced, but absorption is erratic and defaecation may expel the dose. It is rarely used in large animals, though enemas and suppositories are common in small animals.

Parenteral routes

Parenteral means outside the gut, and all these routes use a sterile needle or catheter. **Intravenous (IV)** gives the fastest effect and complete bioavailability, and suits emergencies, irritant drugs and large volumes. But a mistake cannot be recalled, so inject slowly, avoid perivascular leakage (irritants cause sloughing), and never give oil-based or suspension products IV unless the label allows it. Fast IV calcium in cattle can cause cardiac arrest.

Intramuscular (IM) is absorbed in minutes, faster from a well-perfused muscle and with watery solutions than with oily or suspension depots. In **food animals**, IM injections can cause abscesses, scars and tissue damage that persist to slaughter and spoil valuable cuts. Hence the usual advice is to use the neck muscle, with a small volume per site, or the subcutaneous route where the label permits. In horses, IM injection of irritant products can lead to clostridial myositis. Poor technique also risks nerve damage, as with the sciatic nerve in small animals.

Subcutaneous (SC) absorption is slower and more gradual, suiting vaccines, insulin and some fluids; large volumes can be given, though irritant drugs may cause local reactions. **Intraperitoneal (IP)** allows rapid absorption from the large, well-supplied peritoneal surface; it is used for fluids in neonates and exotic or laboratory animals and for euthanasia agents in some settings, but it carries a risk of injecting into organs, gut or bladder, and of peritonitis, so IV or SC is generally preferred in routine practice. **Intradermal** injection puts a very small volume into the skin and is used for allergy tests and tuberculin testing; a raised bleb confirms correct placement. Intra-articular, epidural and intrathecal routes need strict asepsis.

Topical, transdermal, inhalational and local routes

Topical products are applied to skin or mucous membranes for a local effect, such as ointments, sprays and dips for skin disease and ectoparasites. **Transdermal** products (patches, gels, spot-ons and pour-ons) are meant to cross the skin into the blood. Skin thickness, hair, blood flow and body site all change absorption, and animals may lick the product off, so cats given a topical drug can swallow it. Never apply a dog permethrin product to a cat.

Inhalation delivers drugs rapidly to the lungs and the large absorptive surface gives quick effect with lower systemic exposure. Nebulisers and metered-dose inhalers (with a spacer and mask for small animals) are used in feline asthma and equine airway disease; anaesthetic gases are also inhaled.

Intramammary infusion places antibiotics through the teat canal into the quarter, with lactating-cow tubes designed for short withdrawal and dry-cow tubes for prolonged retention. Clean the teat end first. **Intrauterine** products (boluses, infusions) are used for metritis and endometritis, but systemic absorption and milk or meat residues must be considered. **Ocular** drugs include drops (short contact), ointments (longer contact and blur vision briefly) and subconjunctival injections, and always keep the tip from touching the eye. **Otic** drops need an intact eardrum, so confirm integrity before using ototoxic drugs.

Dosage forms in veterinary practice

A dosage form is the drug plus excipients shaped for use. **Solids** include tablets, capsules, powders, granules, **boluses** (large tablets for ruminants and horses), and chewables made palatable for dogs. **Liquids** include solutions, syrups, suspensions (shake well), emulsions and **drenches**, which are liquids given orally to ruminants and horses. **Semisolids** include ointments, creams, gels and pastes, the last being useful for horses and cats because they are squirted into the mouth.

Injectables may be aqueous or oily solutions, suspensions, emulsions or freeze-dried powders reconstituted before use. They must be sterile and, if multi-dose, usually contain a preservative. **Premixes** are concentrated drug-plus-carrier mixtures blended into feed by a licensed feed mill to make **medicated feed**; **water medication** uses soluble powders or liquids dosed through drinkers. Both depend on animals eating or drinking enough, and sick animals eat and drink less. **Pour-ons** are poured along the topline of cattle and **spot-ons** are applied to a small spot of

skin in dogs and cats; both spread over the skin or are absorbed. Other forms include dips, sprays, collars, ear tags, and intravaginal devices for oestrus control.

Modified-release, novel delivery and avoiding errors

Modified-release products control how fast or where a drug is released. Oral examples are enteric-coated or osmotic tablets and ruminal boluses. **Long-acting injectables** use oily vehicles, poorly soluble salts, or polymer matrices (as in long-acting oxytetracycline products) to form a depot under the skin or in muscle. **Implants** (growth promoters or contraceptives in some species, depending on law) and pellets release drug over weeks or months. **Liposomes** are tiny lipid vesicles that carry a drug, reduce its toxicity and prolong its action; liposomal amphotericin B and liposomal bupivacaine are examples in practice. Microneedles and hydrogels are newer concepts. Advantages are fewer handlings and better compliance; drawbacks are a long residue or withdrawal period and no easy way to stop the drug if adverse effects occur.

Choosing: use IV for emergencies; oral for routine maintenance in a cooperative patient; SC or long-acting injection where handling is difficult; topical where the lesion is local; and the label-approved route for any food animal. **Common errors:** giving a drug by an unlabelled route, injecting an irritant perivascularly, using an oily depot IV, using the wrong species product, shaking too little for a suspension, drenching a struggling animal (risk of aspiration pneumonia), crushing modified-release tablets, and ignoring withdrawal periods.

Concept cleared

Concept cleared: Bioavailability

Think of posting a parcel. IV is hand delivery, so the full parcel arrives. Oral is courier through many offices: some is held up in the stomach, some is lost in the liver. Bioavailability is simply the share of the parcel that actually reaches the address, the blood.

Concept cleared: Depot injection

A depot works like a tap left slightly open instead of a bucket tipped at once. The drug is placed in a poorly soluble or oily form under the skin or in muscle, and it leaks into the blood slowly. That gives longer action but also longer residues.

Concept cleared: Rumen effect

The rumen is a giant cooking pot of microbes holding 100 litres or more of feed. A drug dropped into it gets diluted, delayed and sometimes eaten by the microbes before reaching the intestine. The same pot lets a heavy bolus sit and release drug for months.

Concept cleared: Pour-on versus spot-on

A pour-on is like spreading butter along a whole slice of bread: the dose is spread along the back of a large animal. A spot-on is a single dab of jam on one spot, in small animals, from where the drug spreads through skin oils or enters the blood.

Compare and contrast

Parenteral routes compared

Route	Onset and key features
Intravenous	Immediate; 100% bioavailability; for emergencies and irritants; risk of shock and perivascular damage
Intramuscular	Minutes; good for aqueous solutions and depots; risk of abscess, tissue damage and residues in food animals
Subcutaneous	Slower and steadier than IM; suits vaccines, insulin and fluids; irritants may cause local swelling
Intraperitoneal	Fast absorption from large surface; used in neonates and laboratory animals; risk of organ puncture and peritonitis
Intradermal	Very small volume into skin; used for skin tests such as tuberculin; local effect only

Common dosage forms and their typical use

Dosage form	Typical use
Bolus	Large oral tablet for cattle, sheep and horses; may be sustained-release in the rumen
Drench	Liquid given orally to ruminants and horses; aspiration risk if given badly
Premix	Drug concentrate blended into feed to produce medicated feed
Paste	Squirted into mouth of horses and cats; easy administration
Pour-on	Poured along topline of cattle for lice, flies and worms
Spot-on	Applied to a skin spot in dogs and cats, mainly for ecto- and endoparasites

Species notes

Cattle

Prefer neck IM or SC injections of small volumes to protect meat quality; oral drugs are diluted and delayed by the rumen, and intraruminal boluses can release drug for weeks to months.

Horse

Pastes and granules in feed are common; IM injections of irritants may cause clostridial myositis and oral bioavailability of some drugs is poor, partly because of feed binding.

Dog

Tablets, chewables and spot-ons are standard; check flavouring and avoid xylitol-containing human liquids.

Cat

Pastes and liquids are easier than tablets; tablets can stick in the oesophagus, so follow with water, and cats may lick off topical products.

Poultry

Flock treatment is by drinking water or feed, so intake falls in sick birds;

spray and drinking-water vaccines are routine.

Clinical pearls

Self-test: 10 questions

1. Which route gives 100 percent bioavailability by definition?

The drug is placed directly in the blood, so the whole dose reaches the circulation.

2. A heavy intraruminal bolus remains in the rumen mainly because of its:

Adequate density or an irregular shape prevents regurgitation and passage, so the bolus stays and releases drug slowly.

3. The main reason to avoid hindquarter IM injections in cattle is:

Abscesses and scarring in prime cuts reduce carcass value and can retain drug residues.

4. Which is a risk specific to the intraperitoneal route in small animals?

Blind needle placement may enter bowel, bladder or organs, and infection can cause peritonitis.

5. A product poured along the back of a cow to control ectoparasites is a:

Pour-ons are liquids applied along the topline for topical or transdermal action.

6. Medicated feed is made by blending feed with a:

A premix is a drug concentrate in a carrier that is mixed into the ration.

7. Which statement about oily depot injections is correct?

The oily vehicle slows absorption from the site, prolonging action and tissue persistence; IV use may cause embolism.

8. Liposomes are best described as:

Drug is enclosed in a lipid bilayer, which can reduce toxicity and prolong effect.

9. A raised skin bleb after injection indicates correct placement for which route?

Intradermal volumes are tiny and form a visible bleb in the dermis.

10. Which is a common handling error with drenches?

This can send liquid into the trachea and cause aspiration pneumonia.

Key points to revise

1. Bioavailability is 100% by the IV route and lower by other routes.
2. Onset order is roughly IV, inhalation, IM, SC, oral and transdermal.
3. Oral route is cheap and safe but slow, variable and subject to first-pass effect.
4. Rumen dilutes and delays oral drugs but allows long-acting intraruminal boluses.
5. IM injections in food animals can leave scars and residues, so use the neck and small volumes.
6. Premixes are blended into feed; medicated water depends on intake of sick animals.
7. Depot injections, implants and liposomes prolong action but also prolong residues.
8. Choose route by site of action, speed needed, species and label approval.

Go deeper on this site

- Ch 3. Pharmacokinetics: how the body handles a drug (in this book)
- Ch 10. Pharmacy basics: storage, stability and compounding (in this book)
- How to write a veterinary prescription in India
- Drug dose calculation guide

Sources

- MSD Veterinary Manual: Routes of Administration and Dosage Forms of Drugs
- PMC (NCBI): Advanced Strategies of Drug Delivery via Oral, Topical, and Parenteral Routes: Where Do Equine Medications Stand?
- Alabama Cooperative Extension: Beef Quality Assurance, Administering Cattle Health Products Properly

CHAPTER 9 OF 11

Prescription writing, calculations and records

A good prescription is a clear, complete instruction that another person can follow safely. This chapter covers prescription parts, dosage forms and routes, rational drug choice, label reading, a simple calculation, and storage and record-keeping.

After this chapter you can

- List the parts of a veterinary prescription and explain the purpose of each.
- Describe common dosage forms and routes: injectables, boluses, premixes, drenches and pour-ons.
- Apply the principles of rational drug choice.
- Read a label and convert between % w/v and mg/mL.
- Explain basic storage, cold chain, compounding and record-keeping practice.

Parts of a veterinary prescription

A prescription is a written order from a registered veterinarian to a pharmacist, dispenser or owner. Its job is to avoid errors. Practice in India broadly follows the

classical format, though your institution or State Veterinary Council may prefer its own layout.

1. **Heading:** name, qualification, registration number, address and contact of the veterinarian or clinic.
2. **Date** and serial number.
3. **Patient and owner details:** owner name and address, species, breed, age, sex, body weight, and identification such as ear tag number for farm animals.
4. **Diagnosis** or tentative diagnosis (helpful for audit and antimicrobial stewardship).
5. **Superscription:** the symbol Rx, meaning 'take' or 'recipe'.
6. **Inscription:** the drug name (preferably generic), strength and dosage form.
7. **Subscription:** instructions to the dispenser, such as the total quantity to supply.
8. **Signa (transcription):** directions for the owner: dose in practical units, route, frequency, duration, and relation to feed.
9. **Special advice:** withdrawal period for milk, meat or eggs, storage, warnings, and follow-up date.
10. **Signature** of the veterinarian.

Legal note (hedged). In India, medicines in Schedule H and Schedule H1 of the Drugs and Cosmetics Rules are meant to be sold only on a prescription, and a published analysis reports that H1 added requirements such as keeping prescription records for three years and a sales register. Whether and how these requirements apply to veterinary prescriptions can differ, so check the current Drugs and Cosmetics Rules, CDSCO notices and your State Veterinary Council rules rather than relying on this book.

Routes and dosage forms

A dosage form is the physical form in which the drug is made ready for use. The route is the path by which it enters the animal. Choose both to suit the species, disease and the person who will give the drug.

Form	Key points
Injectables (IV, IM, SC)	Sterile solutions or suspensions; IV acts fastest; depot forms give prolonged action; some are freeze-dried and reconstituted before use.
Tablets, capsules, pastes	Oral forms for individual animals; suitable for dogs and cats; paste is useful for horses.
Drenches	Liquid given by mouth with a dosing gun or bottle to cattle, sheep and goats; used for dewormers and tonics.
Boluses	Large oral solid units for ruminants, given with a balling gun; some are sustained-release and remain in the rumen for weeks or months.
Premixes	A drug blended with a carrier for uniform mixing into feed; used for flocks, herds and pigs; requires accurate mixing.
Pour-ons and spot-ons	Liquids applied to the skin along the back, absorbed through skin; used against ectoparasites and some worms; residue control matters.
Water-soluble powders	Dissolved in drinking water for poultry; intake depends on water consumption.

Each route has trade-offs. Oral dosing is convenient but slower and less predictable. Injections are reliable but need sterile technique and can cause injection-site damage in meat animals. Topical forms are easy but can be licked or washed off. Mass medication through feed or water is practical for flocks, but sick birds eat and drink less, so they may receive too little.

Rational drug choice

Rational use means the right drug, for the right patient, in the right form, at the right dose and time, for the right duration, at an acceptable cost. A simple step-by-step approach helps.

- **Make a diagnosis** first. Use laboratory tests where possible instead of treating every fever with an antibiotic.
- **Define the goal:** cure, relieve signs, or prevent disease.
- **Choose the drug** using efficacy, safety, species suitability, the route available, and local resistance patterns. Prefer a narrow-spectrum antibiotic when it works.
- **Consider the patient:** age, pregnancy, lactation, liver and kidney function, and other drugs given.

- **Consider food safety:** check withdrawal times if the animal gives milk, eggs or meat.
- **Consider the owner:** cost, ease of dosing and the chance of completing the course.
- **Review:** follow up, adjust, and stop the drug when it is no longer needed.

Avoid irrational combinations of many drugs in one visit. Every extra drug raises the risk of interactions and adds to cost.

Reading labels and a simple calculation

A label usually states the active ingredient (preferably by generic name), strength or concentration, volume or number of units, batch number, manufacture and expiry dates, storage conditions, withdrawal period, and the species the product is meant for. Read the unit carefully. A strength such as '5% w/v' means 5 g of drug in 100 mL of liquid, which equals 50 mg in 1 mL. In general, to convert % w/v to mg/mL, multiply the percentage by 10.

Illustration only (not a real dose): Suppose a made-up drug called Drug X is supplied as 10 mg/mL. A hypothetical order is 5 mg per kg body weight for an animal weighing 20 kg.

1. Total drug needed = 5 mg/kg x 20 kg = 100 mg.
2. Volume to give = 100 mg divided by 10 mg/mL = 10 mL.

The numbers are round on purpose. Never use these figures for treatment; always take the real dose from the product label or a trusted reference. Check the answer for common sense, and double-check units (mg versus g, mL versus L) before drawing up a syringe, because a decimal slip can cause a tenfold overdose.

Compounding, storage, cold chain and records

Compounding and stability. Compounding means altering a medicine beyond what the label provides, for example mixing or diluting it. Compounded products are not approved by regulators, may have poor quality control, and may be unstable or incompatible. Use a licensed product where one exists, never mix drugs in one syringe unless compatibility is known, and discard reconstituted products after the time stated on the label. Light, heat, moisture and air can all spoil drugs. Suspensions should be shaken before use.

Storage. Keep medicines in their original container, in a cool, dry place away from direct sun, children and feed. Keep disinfectants and pesticides apart from medicines. Observe expiry dates and use older stock first.

Cold chain. Vaccines and some heat-sensitive medicines are usually labelled for storage at 2 to 8 degrees Celsius. Freezing and heat can both destroy them. Keep them in a refrigerator or cold box with ice packs from supplier to point of use, place them away from the door and cooling element, record the temperature regularly, and never refreeze or return an exposed product to stock. Plan for power failure.

Records. Keep a treatment register with date, animal identity, diagnosis, drug, batch number, dose, route, duration, withdrawal period and the person who treated. Records support food safety, antimicrobial audit, follow-up and, where required by law, inspection.

Concept cleared

Concept cleared: Rx and the prescription as a recipe
A prescription is like a recipe handed to a cook. Rx means 'take', the inscription lists the ingredients, the subscription tells the cook how much to prepare, and the signa tells the family how to serve it. If any part is missing or unclear, the dish, and the patient, can go wrong.

Concept cleared: % w/v
Think of sugar dissolved in tea. A 5% w/v solution has 5 grams of sugar in every 100 mL of tea. Since 5 grams is 5000 mg, each single mL carries 50 mg. So multiply the percentage by 10 to get mg per mL.

Concept cleared: Cold chain
Think of ice cream on a long journey. If it melts even once on the way, refreezing does not restore it. Vaccines behave the same way: they must stay cold at every handover from factory to farm, or the dose may look normal but give no protection.

Concept cleared: Premix versus drench

A premix is like adding masala powder to the whole pot of curry: it is mixed into feed so every animal eating gets some. A drench is like giving each person a measured cup of medicine: one animal, one measured liquid dose by mouth.

Memory aid: Remember: Parts of a prescription (HDSIS)

Heading and patient details, Diagnosis, Superscription (Rx), Inscription (drug), Subscription (dispenser instructions), Signa (owner directions), then Signature.

Compare and contrast

Common veterinary dosage forms

Form	Typical species	Main advantage	Main limitation
Injectable	All species	Fast, reliable	Needs sterility; tissue residues
Bolus	Cattle, sheep, goat	Convenient; can be sustained-release	Needs a balling gun; risk of regurgitation
Premix in feed	Poultry, pigs, herds	Treats groups easily	Uneven mixing; sick animals eat less
Drench	Ruminants, horses	Measured oral dose	Risk of aspiration if given badly
Pour-on	Cattle, sheep	Easy, low stress	Variable absorption; licking; residues

Conversion practice for concentration

Label strength	Meaning	mg per mL
1% w/v	1 g in 100 mL	10 mg/mL
5% w/v	5 g in 100 mL	50 mg/mL
10% w/v	10 g in 100 mL	100 mg/mL
0.5% w/v	0.5 g in 100 mL	5 mg/mL

Species notes

Dog

Tablets and spot-ons are common; weigh the dog and write the dose in whole tablets or mL so the owner can follow it.

Cat

Pills and liquids can be hard to give, and dog-labelled products may be unsafe, so check the label for cat use.

Cattle

Boluses, drenches, pour-ons and injectables are all used; record the withdrawal period for milk and meat on every prescription.

Horse

Oral pastes are widely used; check that feed premixes made for other species are never given to horses.

Sheep/Goat

Drenches and boluses are common for worm control; weigh or estimate carefully because small animals are easily overdosed.

Poultry

Medication goes mostly through water or feed; check water intake and mixing accuracy, and respect egg and meat withdrawal times.

Clinical pearls

Self-test: 10 questions

1. The symbol Rx in a prescription is called the:

Rx, meaning 'take', is the superscription; the drug list is the inscription.

2. Directions to the owner about dose and frequency form the:

The signa (transcription) tells the owner how to use the drug.

3. A 5% w/v solution contains how much drug per mL?

5 g in 100 mL is 5000 mg per 100 mL, which is 50 mg per mL.

4. In the illustration only example, 100 mg of Drug X at 10 mg/mL needs what volume?

Volume equals amount divided by concentration: 100 mg divided by 10 mg/mL is 10 mL.

5. A bolus is mainly intended for:

Boluses are large oral solid units given to ruminants, some with sustained release in the rumen.

6. A premix is used for:

Premixes are drug-carrier blends designed for even mixing into feed.

7. A pour-on is best described as:

Pour-ons are topical liquids spread over the skin, used mainly in cattle and sheep.

8. The usual storage range written on vaccine labels is:

Vaccines are usually stored refrigerated at 2 to 8 degrees Celsius and must not be frozen.

9. Which statement about compounded medicines is most accurate?

Compounded products are not regulator-approved and may vary in quality or stability.

10. Which entry is essential on a prescription for a dairy cow?

The withdrawal period prevents residues in milk.

Key points to revise

1. A prescription has heading, date, patient and owner details, diagnosis, Rx, inscription, subscription, signa, advice and signature.
2. Check current Indian rules for Schedule H and H1 drugs rather than assuming they apply to veterinary practice.
3. Dosage forms include injectables, drenches, boluses, premixes, pour-ons and water-soluble powders.
4. Rational drug choice means right drug, patient, dose, route, duration and cost.
5. To convert % w/v to mg/mL, multiply the percentage by 10.
6. Compounded products are unapproved and may be unstable; use licensed products when available.
7. Vaccines are usually stored at 2 to 8 degrees Celsius; never freeze or refreeze them.
8. Keep a treatment register with drug, batch, dose, route and withdrawal period.

Go deeper on this site

- Ch 8. Dosage forms, routes and drug delivery (in this book)
- Ch 2. Drug regulation and the law in India (in this book)
- How to write a veterinary prescription in India
- Drug dose calculation guide
- Veterinary Drug Index

Sources

- Merck Veterinary Manual: Routes of Administration and Dosage Forms of Drugs
- Merck Veterinary Manual: New Animal Drugs, Extralabel Drug Use, Compounded Drugs, and Generic Drugs
- HPRA (Ireland): Supply of veterinary medicines that are heat sensitive
- JAC-Antimicrobial Resistance (PMC): The impact of stringent prescription-only antimicrobial sale regulation (Schedule H1) in India

Pharmacy basics: storage, stability and compounding

A good drug can fail if stored, mixed or discarded badly. This chapter covers storage and cold chain, expiry, incompatibilities, compounding basics, labelling, disposal and stock records.

After this chapter you can

- Describe correct storage and cold-chain practice for drugs and vaccines
- Distinguish expiry date from beyond-use date and explain reconstituted-product stability
- Classify incompatibilities as physical, chemical or therapeutic with examples
- State the cautions for mixing drugs in a syringe or fluid bag
- Outline reasons, risks and principles of compounding, and safe disposal and record-keeping

Storage conditions and the cold chain

Every drug label carries storage instructions, and they are part of the product, not decoration. Common wording is *store below 25 or 30 °C*, *store in a refrigerator (2 to 8 °C)*, *do not freeze*, *protect from light* and *keep in original container*. Heat and moisture speed up hydrolysis and oxidation, so a clinic cupboard near a hot wall, a vehicle dashboard or a damp store room will quietly destroy potency. Keep stock off the floor and away from sun, food and chemicals.

The **cold chain** is the unbroken series of cold storage and transport steps from manufacturer to animal. Vaccines are the key example. Most should be kept at 2 to 8 °C throughout, and surveys of farm refrigerators show that being too warm, especially in summer, is the commonest fault. Freezing is equally harmful for many products: adjuvanted inactivated vaccines and oil-emulsion vaccines can be damaged below 0 °C even when they look normal, and freeze-sensitive vaccines lose potency immediately. Live freeze-dried vaccines lose potency above 8 °C, and become even more heat-sensitive after reconstitution. Good practice includes a dedicated refrigerator without a freezer compartment, a minimum-maximum thermometer in the centre, no storage in the door, no food inside, a daily temperature log, and insulated boxes with conditioned ice packs in the field. After a suspected breach, isolate the stock and seek the manufacturer’s advice.

Controlled and scheduled drugs, pesticides and euthanasia agents should be stored locked. For India, check current rules for Schedule H, H1 and X drugs.

Expiry, beyond-use dates and reconstituted products

The **expiry date** is the last date up to which the manufacturer guarantees that the unopened product, stored as labelled, keeps its potency and safety. It is usually set by stability studies, often as the time when about 10 percent of the drug has degraded. Expired medicines should not be used, as potency is lost and some degradation products are harmful; degraded tetracycline is a classic example, linked with kidney injury.

A **beyond-use date (BUD)** is different. It is the date after which a product should not be used, assigned once the container is opened, reconstituted, diluted or compounded. It is always shorter than the original expiry. Some pharmacopoeial guides for non-sterile compounded products suggest, in general, about 14 days for water-containing preparations kept without preservative (cold storage), about 35 days with preservatives, about 90 days for non-water liquids, and about 180 days for solid forms, unless stability data support more. Check the current reference.

Many antibiotics come as dry powder and are mixed with the supplied diluent before use. **Reconstituted injectables** have a short life, ranging from hours to days depending on the drug, diluent and temperature, and often longer when refrigerated. Oral antibiotic suspensions such as amoxicillin-clavulanate last only about 10 to 14 days. Reconstituted vaccines are generally used within a short time stated on the leaflet. Use the supplied diluent and label the vial with date and time of mixing. Colour change, cloudiness or particles signal trouble, but potency can fall without any visible change.

Light, heat and moisture sensitivity

Light, especially ultraviolet, can cause **photodegradation** in drugs such as phenothiazines, some vitamins and many injectables, which is why they come in amber glass or opaque cartons. Keep them in the original package and out of the sun. Heat speeds nearly every reaction, and moisture promotes hydrolysis of esters and beta-lactam antibiotics, so keep tablets and powders in tightly closed containers. Freeze-thaw cycles can also damage suspensions and emulsions. Oxidation often causes darkening or a pink or amber tinge, an early visual clue.

Incompatibilities and mixing in a syringe or fluid bag

An **incompatibility** is an undesirable change when drugs are mixed. There are three kinds.

- **Physical:** a visible change without a chemical reaction, such as precipitation, cloudiness, colour change or gas. Diazepam, which is dissolved in organic solvents, can precipitate when diluted in saline or lactated Ringer's; calcium solutions can form a precipitate with bicarbonate or phosphate; some alkaline drugs (for example, thiopentone) precipitate with acidic ones.
- **Chemical:** a reaction that destroys or alters the drug, often with no visible sign. Aminoglycosides can be inactivated when mixed with beta-lactams in the same container, and some antibiotics are unstable in certain fluids or at the wrong pH. Tetracyclines bind calcium and other metals (chelation).
- **Therapeutic:** the drugs are compatible in the container but their effects clash in the animal, such as two drugs with additive toxicity (an aminoglycoside with another nephrotoxic drug) or antagonism, such as a bacteriostatic antibiotic given with a bactericidal beta-lactam in some infections.

Mixing cautions. Do not combine drugs in one syringe or bag unless the label, manufacturer or a trusted compatibility reference says it is safe. Use one drug per syringe by default. If mixing is approved, draw them up in the recommended order, use the recommended diluent, inspect for precipitates, label the syringe clearly and use quickly. Never add drugs to blood products. Never use a cloudy or discoloured mixture. Treat any added drug as shortening the fluid bag's shelf life: label it with drug, amount, date, time and your initials. Use aseptic technique, since fluid bags and open syringes support bacterial growth.

Compounding in veterinary practice

Compounding means preparing a customised drug from ingredients, for example turning a human tablet into a flavoured liquid, or mixing two products. Valid reasons include no approved product for the species or condition, an unsuitable strength or form for a very small or exotic animal, an animal that cannot take the available form (a cat that refuses tablets), or an allergy to an excipient.

The risks are real. Studies of compounded products show wide variation in potency; some preparations contained far less drug than labelled and some none at

all. Compounded drugs are not reviewed for safety and effectiveness in the way approved products are, so they carry no proof of efficacy, and adverse events may go unreported.

Principles in outline: use an approved product first where one exists; compound only for an individual animal under a valid veterinarian-client-patient relationship; use pharmaceutical-grade ingredients and a qualified pharmacist or a licensed facility rather than improvised mixing; define the BUD and storage; give clear labelling and client instructions; keep records; and take extra care in food animals, as residues and withdrawal periods may be unknown. Regulators such as the US FDA permit compounding from approved finished drugs in defined circumstances and have strict views on bulk substances and office stock. *Indian points: check current rules* under the Drugs and Cosmetics Act and its rules, the veterinary council's regulations and any state requirements before compounding or supplying any preparation.

Packaging, labelling, disposal and inventory

Packaging protects the drug from light, moisture, air and contamination, and keeps it identifiable. Dispense in clean, light-protecting containers where needed. A dispensed label should show the animal and owner, drug name and strength, directions, date, expiry or BUD, storage advice, the prescriber's details and a warning such as "for animal treatment only", with a withdrawal period for food animals.

Disposal. Never throw drugs into general rubbish, drains or open land. Expired and unwanted medicines, and especially antibiotics and cytotoxics, can harm the environment, spread resistance and poison scavengers and animals. Segregate them and send them for authorised treatment or take-back. **Sharps** (needles, scalpel blades, broken ampoules) go into a rigid, puncture-resistant, leak-proof container immediately after use; never recap or bend needles, and never overfill the container. India has Bio-Medical Waste Management Rules with colour-coded categories, and veterinary institutions may be covered; *check current rules* for colour codes, authorised handlers and record requirements.

Inventory and records. Keep a stock register or software record covering item, batch number, expiry, quantity received, used and balance. Apply **FEFO** (first expiry, first out), check expiry dates on a schedule, and remove expired stock to a

marked area. Record the batch of vaccines and injectables used on each patient, and keep purchase invoices from licensed suppliers. Order according to documented need, to reduce waste at source.

Concept cleared

Concept cleared: Cold chain
Think of carrying ice cream home from the shop. If it melts even once on the way, refreezing does not fix it. A vaccine is the same: one warm or frozen stretch between factory and animal can spoil it, even if it looks fine. The chain is only as strong as its weakest link.

Concept cleared: Expiry versus beyond-use date
Expiry is the date printed on a sealed packet of milk. Once you open it, the clock runs faster, and you use your own judgement. The beyond-use date is that second, shorter clock, which starts when a bottle is opened, mixed or compounded.

Concept cleared: Incompatibility
Mixing drugs is like mixing paints or cooking ingredients. Sometimes they curdle in front of you (physical), sometimes they react silently and lose their power (chemical), and sometimes they mix well but their effects fight inside the animal (therapeutic).

Concept cleared: Compounding risk
A home-made copy of a branded recipe may look similar, yet nobody has tested whether it tastes, mixes or works the same. Compounding is useful only when no tested product exists, because every change in vehicle or form may change dose delivered.

Memory aid: Safe mixing checklist

"CLEAR": Compatibility checked, Label the syringe or bag, Examine for particles, Aseptic technique, Record and use Right away.

Compare and contrast

Three types of incompatibility

Type	Example and key point
Physical	Diazepam precipitates in saline or lactated Ringer's; visible cloudiness or crystals
Chemical	Aminoglycoside inactivated by beta-lactam in same container; often invisible
Chelation (chemical)	Tetracycline binds calcium and metals, lowering absorption or activity
Therapeutic	Two nephrotoxic drugs together, or a bacteriostatic drug with a bactericidal beta-lactam

Expiry date versus beyond-use date

Feature	Expiry date vs beyond-use date
Set by	Expiry: manufacturer's stability data. BUD: prescriber or pharmacist for opened, mixed or compounded products
Applies to	Expiry: unopened product in original pack. BUD: after opening, reconstitution, dilution or compounding
Length	Expiry: months to years. BUD: usually hours to weeks
Where written	Expiry: on pack. BUD: on dispensed or prepared label

Species notes

Cattle

Field vaccines and injectables travel in insulated boxes and often sit in hot sheds, so keep them cool, keep opened multi-dose vials dated, and

Poultry

Freeze-dried live vaccines are heat-sensitive and must be reconstituted with the supplied diluent and used quickly; water-soluble medicines

record batch numbers and withdrawal periods.

need fresh preparation daily or as the label directs.

Cat

Compounded flavoured liquids and gels are popular because cats resist tablets, but potency and stability vary, so use an expiry or BUD and prefer tested products.

Horse

Compounded oral products such as pastes may lack proof of potency, and stability is affected by heat in tack rooms or trailers.

Clinical pearls

Self-test: 10 questions

1. The recommended storage range for most vaccines throughout the cold chain is:

Most vaccines are kept at 2 to 8 degrees Celsius; both warmer and freezing temperatures damage them.

2. Which vaccine type is most likely to be damaged by freezing?

Freezing can disturb the adjuvant structure, reducing the vaccine's effect, even if the product looks normal.

3. A beyond-use date is assigned:

It is a shorter limit for a product whose original packaging has been opened or altered.

4. Cloudiness when diazepam is diluted in saline is an example of:

The drug, dissolved in organic solvent, precipitates in the aqueous fluid, causing a visible physical change.

5. Aminoglycoside inactivated by mixing with a beta-lactam in the same container is an example of:

The drugs react and lose potency, often without any visible change.

6. Which practice for mixing drugs is most appropriate?

Unverified mixtures may precipitate or lose potency, so default to separate syringes and confirm from a reliable source.

7. A main concern about compounded drugs compared with approved products is:

Compounded drugs are not evaluated like approved products and studies have shown variable potency.

8. The best container for used needles is:

Sharps must be contained in puncture-proof, leak-proof containers immediately after use to prevent injury.

9. FEFO in inventory control means:

Stock closest to expiry is used first to reduce wastage.

10. Amber glass bottles are used mainly to protect drugs from:

Amber glass blocks ultraviolet and some visible light that cause photodegradation.

Key points to revise

1. Follow label storage: temperature, light and moisture protection, original container.

2. Vaccine cold chain is 2 to 8 degrees Celsius and many vaccines must never be frozen.
3. Expiry applies to unopened packs; beyond-use date applies once opened, mixed or compounded.
4. Reconstituted injectables and suspensions have short lives and need date labelling.
5. Incompatibilities may be physical, chemical or therapeutic; some chemical ones are invisible.
6. One drug per syringe is the default; mix only with documented compatibility.
7. Compound only when no suitable approved product exists, and check current legal rules in India.
8. Segregate expired drugs and sharps and dispose by authorised routes; keep batch-wise stock records using FEFO.

Go deeper on this site

- Ch 8. Dosage forms, routes and drug delivery (in this book)
- Ch 9. Prescription writing, calculations and records (in this book)
- How to write a veterinary prescription in India
- Veterinary Drug Index

Sources

- ACIAR: Veterinary Cold Chain Manual, Ensuring Effective Vaccines
- Veterinary Practice News: Best practices for storing pharmaceuticals
- dvm360: Drug compounding, issues affecting safety and efficacy
- US FDA: Animal Drug Compounding
- WHO: Health-care waste fact sheet

CHAPTER 11 OF 11

Experimental pharmacology: bioassay, screening and trials

How drugs are tested: bioassay principles, isolated tissues, screening, toxicity studies, veterinary clinical trials, animal ethics in India and the statistics needed to judge results.

> **After this chapter you can**

- Explain why animal experiments are used and state the 3Rs
- Describe direct, indirect, matching and bracketing bioassays and the parallel-line idea
- Outline screening, toxicity studies and veterinary clinical trials
- Know the role of CPCSEA and the IAEC in India
- Interpret mean, SD, SEM, p-value, t-test and confidence interval

Why animals are used and the 3Rs

A drug cannot be given to patients before we know what it does, how strong it is and how harmful it can be. Animal experiments let us study the **whole living system**: absorption, distribution, metabolism, excretion, effect on many organs, and toxicity. Cell cultures and computer models cannot yet reproduce all of this. In veterinary pharmacology, animals are also the *target patients*, so studies in dogs, cattle, poultry and others directly support product approval.

Animal use is accepted only with ethical limits, summarised as the **3Rs**, proposed by Russell and Burch in 1959:

- **Replacement**: use non-animal methods (cell cultures, computer simulation, isolated tissues from slaughter animals) when they can answer the question.
- **Reduction**: use the smallest number of animals that still gives a reliable result; good statistical design helps.
- **Refinement**: change procedures to cause the least pain and distress, for example anaesthesia, analgesia, humane end-points and good housing.

Too few animals gives a meaningless result, which is also wasteful, so reduction does not mean using as few as possible at any cost.

Principles of bioassay

Bioassay means estimating the potency of a substance by measuring its effect on living tissue or an animal, comparing it with a **standard preparation** of known potency. It is used when chemical assay is impossible or unsuitable, for example for digitalis, insulin, heparin, oxytocin, vaccines or vitamins in biological samples. The **test preparation** is the unknown sample.

The basic logic: the same tissue is given the standard and the test; if equal responses come from equal doses, potencies are equal. If the test needs a larger dose to give the same response, it is weaker.

- **Direct assay**: the dose needed to produce a fixed end-point (for example, the dose that stops the heart in a test animal) is measured for standard and test. Potency ratio equals the ratio of the doses needed.
- **Indirect assay**: fixed doses are given and the size of the response is measured. This is done in a quantal form (all-or-none, such as survival) or graded form (such as height of a muscle contraction).
- **Matching (interpolation) assay**: the dose of the test is adjusted until its response matches that of the standard. A simple example is matching the contraction of an isolated tissue.
- **Bracketing assay**: two doses of the standard, one giving a smaller and one a larger response, are chosen so that the response to the test falls between them (is bracketed). Test dose is then calculated by interpolation.
- **Multiple-point assays** (for example 2+2 or 3+3): several doses of each are used. Within the useful range, response is roughly a straight line against log dose. The standard and test lines should be **parallel**; parallel lines mean the two drugs act in the same way and differ only in potency. The horizontal gap between the lines gives the potency ratio.

Good design needs randomisation, a sensitive and stable preparation, doses spaced in a geometric series, and repeat tests with enough replicates to give a confidence interval around the potency.

Isolated preparations and drug screening

Isolated tissues are kept alive in an organ bath containing warm, oxygenated physiological salt solution, and their contraction or relaxation is recorded on a recorder or transducer. This removes reflexes, metabolism and other body influences, so drug action on the tissue is easy to see. At concept level, common ones include:

- **Guinea-pig ileum**: contracts to acetylcholine and histamine; used for cholinergic and antihistamine studies.

- **Rat or rabbit uterus**: used for oxytocin and other uterine stimulants and relaxants.
- **Rabbit jejunum**: spontaneous rhythmic movements; used for spasmolytics and cholinergic drugs.
- **Frog rectus abdominis**: contracts to acetylcholine; used for neuromuscular drugs.
- **Isolated heart (Langendorff type) and rat vas deferens**: for cardiac and adrenergic studies.
- **Rat fundus strip, aortic ring**: for amines and vascular drugs.

Drug screening is the stepwise search for a useful new compound. A typical path: choose a disease target; test many compounds in simple in vitro or cell tests; confirm with in vivo tests in animals that model the disease; study dose-response, mechanism and ADME; then pick a lead compound for safety testing. Many compounds drop out at each step.

Preclinical safety, clinical trials and Indian rules

Before human or target-animal clinical use, **toxicity studies** are done in outline as follows:

- **Acute toxicity**: single dose or several doses within 24 hours; shows toxic signs, target organs and the approximate lethal range. Modern methods (OECD guidelines) use fewer animals and stop at clear toxicity rather than aiming for a precise LD_{50}.
- **Sub-acute (repeated dose, about 28 to 90 days)**: looks at behaviour, body weight, blood tests, organ weights and histopathology, and helps identify a no-adverse-effect level.
- **Chronic**: months to a year or more in animals, for drugs meant for prolonged use; looks for organ damage and tumour formation.
- Special studies: reproductive and teratogenicity, mutagenicity and local tolerance.

Clinical trials in veterinary medicine test the product in the target species, usually under farm or clinic conditions, to prove efficacy and safety. In outline, early studies establish tolerance and dose in a few animals, then controlled studies in naturally affected animals compare the product with a placebo or an accepted drug, with

randomisation and blinding where possible. For food animals, residue and withdrawal period studies are essential. **VICH GL9 (Good Clinical Practice)** is the harmonised guideline for how such studies are designed, run, monitored and reported so that data are reliable and regulators in different regions can accept them, with animal welfare and food safety kept in view. Human-style Phase I to IV labels are used mostly in human drug development; veterinary programmes are organised by target-animal safety, dose determination and confirmation of efficacy.

In **India**, animal experiments are governed by the Prevention of Cruelty to Animals Act, 1960 and the rules made under it for breeding of and experiments on animals. The **CPCSEA** (Committee for the Purpose of Control and Supervision of Experiments on Animals) registers institutions and supervises them. Each registered institution must have an **Institutional Animal Ethics Committee (IAEC)** that reviews every protocol; proposals involving larger animals need CPCSEA involvement. Rules and forms are amended from time to time, so students must always check the current official CPCSEA/DAHD documents.

Basic statistics and reading a trial critically

Statistics tells us whether a difference is real or just chance.

- **Mean**: the average of the observations.
- **Standard deviation (SD)**: how widely individual values are scattered around the mean. It describes the sample.
- **Standard error of the mean (SEM)**: SD divided by the square root of n; it shows how precisely the mean itself is estimated. It becomes smaller when more animals are used.
- **p-value**: the chance of seeing a difference at least this large if the drug truly had no effect. A p below 0.05 is conventionally called significant. It does not tell the size or importance of the effect.
- **t-test**: compares the means of two groups relative to their scatter (unpaired for separate groups, paired for the same animals before and after). For three or more groups, ANOVA is used.
- **Confidence interval (CI)**: a range, usually 95%, likely to contain the true value; a narrow CI means a precise estimate, and a CI for a difference that includes zero means no clear effect.

Reading a trial critically: check whether animals were randomly allocated, whether there was a suitable control group, whether observers were blinded, whether sample size was enough, which end-points were chosen, whether all animals are accounted for, whether the effect is clinically meaningful and not just statistically significant, who funded the study, and whether results from one species can be applied to yours.

Concept cleared

Concept cleared: Bioassay
Imagine comparing two lots of chilli powder by how many people sneeze when each is sprinkled in the same room. You never measure the chemical, only the effect, and you compare with a lot of known strength. Bioassay does the same: a standard of known potency and a test sample are compared on one living tissue, and equal responses mean equal strength.

Concept cleared: Parallel lines
Think of two cyclists going up the same road at the same slope, one starting further back. Their paths are parallel and differ only by the distance between them. In a bioassay, parallel log dose-response lines show the standard and test act the same way; the gap between them is simply the potency difference.

Concept cleared: SD versus SEM
SD is like the spread of heights in a class: tall and short children differ a lot. SEM is like asking how accurately the class average height is known; measure more children and the average becomes more trustworthy even though the spread of heights stays the same. SD describes scatter, SEM describes precision of the mean.

Concept cleared: p-value

If a coin lands heads nine times in ten, you suspect it is biased, but a fair coin could do this by luck, rarely. The p-value is the chance of such a result if nothing is really happening. A small p makes luck unlikely, but it never says how big or useful the effect is.

Memory aid: 3Rs

Replace it, Reduce the number, Refine the procedure: Replacement, Reduction, Refinement.

Compare and contrast

Direct versus indirect bioassay

Feature	Direct assay	Indirect assay
What is measured	Dose needed for a fixed end-point	Response to fixed doses
Dose	Varied until end-point reached	Chosen in advance
Response type	End-point reached or not	Quantal or graded
Example idea	Dose stopping the heart of a test animal	Contraction height of isolated uterus
Potency ratio from	Ratio of doses needed	Dose-response lines or interpolation

SD, SEM and confidence interval

Measure	What it tells you
SD	Scatter of individual values around the mean
SEM	Precision of the sample mean (SD divided by square root of n)
Effect of larger n	SD stays about the same; SEM falls
95% CI	Range likely to hold the true value
p-value	Chance of such a difference if there were no true effect

Species notes

Dog

Dogs are common in veterinary clinical trials and are a standard non-rodent species for safety studies; breed differences such as MDR1 gene variants can change drug response.

Cat

Cats have limited glucuronidation, so results from other species may not predict their handling of drugs such as paracetamol; they need species-specific safety data.

Cattle

Cattle trials for food-animal drugs must include residue and withdrawal period studies, and rumen function can change oral drug behaviour.

Poultry

Poultry trials are done at flock level under farm conditions, and results are judged on group outcomes such as mortality and weight gain.

Sheep/Goat

Goats and sheep cannot be assumed to behave like cattle; many drugs have no label for them, so species-specific data matter.

Clinical pearls

Self-test: 10 questions

1. Bioassay is used to estimate the

Bioassay compares the biological effect of a test sample with a standard of known potency.

2. In a bracketing assay, the test response is

Two standard doses are chosen so the test response falls between them.

3. Parallel dose-response lines for standard and test indicate

Parallelism shows similar action; only the horizontal distance (potency) differs.

4. Which preparation is classically used to study oxytocin?

Isolated uterus contracts in response to oxytocin.

5. The 3Rs were proposed by

Russell and Burch described replacement, reduction and refinement in 1959.

6. Which statistic describes the precision of the sample mean?

SEM equals SD divided by the square root of n and shows how well the mean is estimated.

7. A p-value of 0.03 means

The p-value is the probability of such a result under no true effect; it says nothing of effect size.

8. Each registered Indian animal facility must have a

The IAEC reviews and monitors animal experiments at the institution under CPCSEA rules.

9. VICH GL9 deals with

GL9 is the harmonised guideline for design, conduct and reporting of veterinary clinical studies.

10. Which is a refinement measure?

Refinement reduces pain and distress; the other options are replacement or reduction.

Key points to revise

1. Bioassay measures potency by comparing test with a standard on living tissue.
2. Direct assay finds dose for fixed end-point; indirect assay measures response to set doses.
3. Bracketing places the test response between two standard doses.
4. Screening moves from in vitro tests to in vivo models to safety studies.
5. Toxicity studies are acute, sub-acute and chronic, plus special studies.
6. VICH GL9 sets good clinical practice for veterinary studies.
7. IAEC and CPCSEA oversee animal experiments in India under the PCA Act, 1960.
8. The 3Rs are replacement, reduction and refinement.

Go deeper on this site

- Ch 4. Pharmacodynamics: how a drug acts (in this book)
- Ch 1. Introduction, history and sources of drugs (in this book)
- How to study veterinary MCQs

Sources

- EMA: VICH GL9 Good clinical practices
- FDA CVM: GFI #85 (VICH GL9) Good Clinical Practice
- IISc: CPCSEA guidelines
- PubMed: Replacement, reduction and refinement

How to use Book 1: a short discussion

General pharmacology is the base on which every other drug topic stands. Before a student meets a single antibiotic, anaesthetic or poison, they need a working picture of what a drug is, where it comes from, how the body moves it around, how it produces an effect, and what the law and common sense say about using it. This book gathers those ideas in eleven chapters. It is designed so that each chapter can be read in about half an hour and tested straight away with ten questions.

The order of the chapters

The first two chapters set the scene: what pharmacology is, where drugs come from, and how veterinary drugs are regulated in India. The middle chapters are the scientific core. Pharmacokinetics describes what the body does to a drug. Pharmacodynamics describes what the drug does to the body. The chapter on receptors and signal transduction opens the box between a drug binding and a cell responding. The later chapters turn the science into practice: species differences and adverse reactions, special patients, dosage forms and routes, prescription writing, pharmacy basics, and finally how new drugs are studied. If you are short of time, read chapters three, four and six first, because the rest of the series leans on them.

Why species matter from the very start

A veterinary student cannot treat pharmacology as human pharmacology with different body weights. A cat, a dog, a cow and a hen handle the same molecule in different ways. Some species lack liver reactions that others rely on. Ruminants hold a drug in the rumen before it reaches the blood. Birds have a different kidney circulation. The species notes in every chapter are not decoration. They are the part most often tested in practice and in viva, and they are the part that prevents harm in the clinic.

Law, residues and responsibility

Drugs given to animals can affect people: through residues in milk, meat and eggs, through resistance spreading between animals and humans, and through misuse of controlled medicines. For that reason this book includes a chapter on the Indian legal framework. Rules change and some details in public reports differ from each other, so the chapter says where a point comes from and tells you to read the current official

notification before relying on it. Treat it as a map of the legal ground, not as legal advice.

A study routine that works

Read each chapter in three passes. On the first pass read the objectives and the "Concept cleared" boxes only. On the second pass read the Learn section and the comparison tables slowly. On the third pass attempt the quiz without looking back, and read every explanation, even for answers you got right. Two days later repeat only the quiz. This spacing improves recall far more than a single long reading session. Finish each chapter by reading the key points aloud and explaining one of them to a classmate.

What this book is not

This book teaches concepts. It contains no dose tables, because doses depend on the product, the species, the age and the clinical picture, and they belong on the product label and in your veterinarian's judgement. It does not replace your college textbook or a clinical examination. Each chapter lists the sources behind its main points, and a few statements rest on standard textbook knowledge rather than a single web page, so use the sources and your teachers to confirm anything that matters for an exam or for a patient.

What comes next

Book 1 is the first of seven. The following books cover systemic pharmacology, chemotherapy and antimicrobials, applied therapeutics, anaesthesiology and analgesia, toxicology, and species-wise therapeutics with revision tools. Links inside each chapter point to related chapters and to guides on this site.

Educational information only. It does not replace an examination by a licensed veterinarian. Written for DrblochVet by Dr. Rameez Bloch, BVSc & AH, MVSc (Gujarat Veterinary Council Reg. 3570). The book content is for reading on this site and may not be copied or redistributed.

BVSC & AH STUDY BOOK 2 OF 7

Systemic Pharmacology: Drugs by Body System

Thirty-three chapters on the drugs that act on the autonomic nervous system, brain, inflammation, heart, blood, kidney, lungs, gut and hormones. Each chapter explains the mechanism, the clinical meaning and the species cautions, and ends with a 10-question self-test.

33 chapters | **330** practice questions | **No** dose tables

By Dr. Rameez Bloch, BVSc & AH, MVSc

Start here

Pick a chapter from the list on the left (or the top bar on a phone). The chapters follow seven parts: autonomic and neuromuscular drugs, central nervous system, inflammation and joint drugs, cardiovascular, blood and renal drugs, respiratory and digestive drugs, and endocrine and reproductive drugs. Each chapter has six parts: Learn, Concepts, Compare, Species, Quiz and Revise. Your quiz progress is saved on this device only.

CHAPTER 1 OF 33

Autonomic nervous system and neurotransmission

The autonomic nervous system controls involuntary functions through two divisions that use acetylcholine and noradrenaline. This chapter explains how the two systems are organised, how each transmitter is made, released and removed, and which receptor subtypes sit on which organs.

After this chapter you can

- Compare the anatomical organisation of the sympathetic and parasympathetic divisions

- Describe synthesis, storage, release and removal of acetylcholine
- Describe synthesis, storage, release and removal of noradrenaline
- Match muscarinic, nicotinic and adrenergic receptor subtypes to their main organ effects
- Explain why knowing the transmitter and receptor predicts drug effects and side effects

Why the autonomic system matters in pharmacology

The autonomic nervous system (ANS) runs the body's involuntary functions: heart rate, blood pressure, gut motility, glandular secretion, pupil size, bronchial tone and bladder emptying. A very large number of veterinary drugs work by copying, blocking or prolonging the action of its two main transmitters, **acetylcholine (ACh)** and **noradrenaline (NA, norepinephrine)**.

If you understand the pathway, you can predict both the intended effect and the side effects of drugs such as atropine, xylazine, neostigmine, phenylephrine and propranolol without memorising them one by one.

Sympathetic and parasympathetic organisation

Both divisions use a **two-neuron chain**: a preganglionic neuron from the central nervous system synapses in a ganglion with a postganglionic neuron, which then reaches the effector organ. The divisions differ in where they leave the cord and where the ganglia lie.

- **Sympathetic (thoracolumbar outflow).** Preganglionic fibres leave the thoracic and anterior lumbar cord. Ganglia lie close to the spinal cord (paravertebral chain and prevertebral ganglia), so preganglionic fibres are short and postganglionic fibres long. One preganglionic fibre contacts many postganglionic neurons, so the response is widespread, the so-called fight or flight pattern.
- **Parasympathetic (craniosacral outflow).** Fibres leave with cranial nerves III, VII, IX and X and with the sacral segments. Ganglia lie near or within the target organ, so preganglionic fibres are long and postganglionic fibres short. The response is more discrete, the rest and digest pattern. The vagus carries most of the parasympathetic supply to the thorax and abdomen.

Two exceptions are worth remembering. The **adrenal medulla** behaves like a modified sympathetic ganglion: preganglionic fibres act directly on it and it releases mainly adrenaline into the blood. **Sweat glands** in many species receive sympathetic fibres that release ACh rather than NA. Sweating is prominent in the horse, but in that species it is driven largely by circulating adrenaline acting on the glands, so do not over-generalise.

Most organs receive both supplies and the two usually oppose each other, which is why a drug that blocks one division unmasks the other.

Acetylcholine: synthesis, release and removal

ACh is the transmitter at all autonomic ganglia, at parasympathetic postganglionic endings, at the skeletal neuromuscular junction, and at sympathetic endings to sweat glands.

1. **Synthesis.** Choline is taken up into the nerve terminal by a transporter (the rate-limiting step) and combined with acetyl-CoA by *choline acetyltransferase*.
2. **Storage.** ACh is packed into synaptic vesicles.
3. **Release.** An action potential opens voltage-gated calcium channels. Calcium entry triggers vesicle fusion and exocytosis. Botulinum toxin acts here by preventing release.
4. **Receptor action.** ACh binds nicotinic or muscarinic receptors on the target cell.
5. **Removal.** *Acetylcholinesterase* splits ACh into choline and acetate within milliseconds. Much of the choline is recycled into the terminal. There is no significant reuptake of intact ACh.

Because removal is by enzyme and not by reuptake, **anticholinesterase drugs** and organophosphate insecticides cause ACh to accumulate, which is the basis of cholinergic poisoning (see the next chapter).

Noradrenaline: synthesis, release and removal

NA is the transmitter at most sympathetic postganglionic endings. The adrenal medulla also releases adrenaline and some NA.

1. **Synthesis.** Tyrosine is converted to DOPA by *tyrosine hydroxylase* (the rate-limiting step), then to dopamine. Dopamine is taken into vesicles and converted

to NA by *dopamine beta-hydroxylase*. In the adrenal medulla NA is further methylated to adrenaline.

2. **Storage.** NA is held in vesicles together with ATP.
3. **Release.** As with ACh, calcium-dependent exocytosis follows the action potential.
4. **Feedback.** NA acts on presynaptic alpha-2 receptors on the same terminal and reduces further release. This is why alpha-2 agonists such as xylazine and dexmedetomidine lower sympathetic outflow and cause sedation and bradycardia.
5. **Removal.** The main route is **reuptake into the nerve terminal** by the noradrenaline transporter (uptake-1). Smaller roles are played by uptake into other tissues, diffusion away, and breakdown by monoamine oxidase (MAO) and catechol-O-methyltransferase (COMT).

A common confusion: ACh is destroyed at the synapse, whereas NA is mostly *recycled*. Drugs that block reuptake therefore potentiate NA but not ACh.

Receptor subtypes and organ effects

The transmitter does not decide the response; the **receptor on the organ** does.

Cholinergic receptors

- **Nicotinic.** Ligand-gated ion channels. Muscle type (N_M) at the neuromuscular junction; neuronal type (N_N) in autonomic ganglia and the adrenal medulla.
- **Muscarinic (M_1 to M_5).** G-protein-coupled receptors on effector organs. M_2 in the heart slows the rate and conduction. M_3 in smooth muscle and glands causes contraction, secretion, bronchoconstriction, increased gut motility, bladder emptying and miosis. M_1 is found in ganglia and the CNS.

Adrenergic receptors

- **Alpha-1.** Vascular smooth muscle constriction (raises blood pressure), contraction of sphincters, dilation of the pupil.
- **Alpha-2.** Mostly presynaptic inhibition of transmitter release; also central sedation and some vasoconstriction.
- **Beta-1.** Heart: faster rate, stronger contraction, faster conduction; renin release from the kidney.

- **Beta-2.** Bronchodilation, vasodilation in skeletal muscle, relaxation of uterus and gut smooth muscle.
- **Beta-3.** Lipolysis; some role in bladder relaxation.

Clinical link: a bronchodilator such as salbutamol is chosen for its beta-2 selectivity so that heart rate is affected less, and a non-selective beta blocker can worsen airway narrowing for the same reason.

Putting it together and common confusions

To predict a drug's action, ask three questions: which transmitter pathway does it touch, at which step (synthesis, release, receptor, removal), and which receptor subtype is involved.

- Ganglionic drugs affect both divisions because ACh at ganglia is nicotinic in both.
- Nicotinic receptors in muscle and ganglia are different subtypes, which is why neuromuscular blockers do not usually cause autonomic effects at clinical concentrations.
- Most vascular beds are controlled by sympathetic tone alone; there is little parasympathetic supply to them, so vessel diameter is changed mainly by altering sympathetic activity.
- Receptor effects can vary by species and organ, so always check the actual response in the animal in front of you.

Concept cleared

Two-neuron chain
Both divisions have a preganglionic and a postganglionic neuron joined at a ganglion. ACh is the ganglionic transmitter in both.

Transmitter versus receptor
Effects depend on the receptor subtype in the organ. ACh excites the gut through muscarinic receptors but slows the heart through the same family acting on M2.

Removal differs

ACh is hydrolysed by acetylcholinesterase; NA is mainly taken back up by the nerve terminal. This explains why anticholinesterases and reuptake blockers behave differently.

Presynaptic alpha-2 brake

Alpha-2 receptors on sympathetic terminals reduce NA release. Alpha-2 agonists exploit this for sedation and analgesia.

Memory aid: Remembering the outflows

Sympathetic = Thoracolumbar (T before P in the alphabet pairs with S: 'SympaTHetic = THoracic'). Parasympathetic = Craniosacral ('Para = cranial and sacral, the two ends'). Receptor shortcut: alpha-1 constricts, beta-1 speeds the heart, beta-2 relaxes airways.

Compare and contrast

Sympathetic versus parasympathetic

Feature	Sympathetic	Parasympathetic
Outflow	Thoracolumbar	Craniosacral
Ganglia	Near spinal cord	Near or in target organ
Preganglionic fibre	Short	Long
Postganglionic transmitter	Mostly NA	ACh
Typical effect	Fight or flight, widespread	Rest and digest, discrete

ACh versus NA handling

Step	Acetylcholine	Noradrenaline
Precursor	Choline + acetyl-CoA	Tyrosine
Rate-limiting step	Choline uptake	Tyrosine hydroxylase
Release trigger	Calcium-dependent exocytosis	Calcium-dependent exocytosis
Main removal	Acetylcholinesterase	Neuronal reuptake
Receptors	Nicotinic, muscarinic	Alpha and beta

Species notes

Dog and cat

Vagal tone at rest is high, especially in athletic dogs, so sinus arrhythmia and slow resting rates can be normal. Cats are sensitive to the effects of alpha-2 agonists on heart rate and vomiting.

Horse

The gut is very sensitive to autonomic balance; drugs that reduce parasympathetic activity can slow motility and predispose to colic. Sweating is mainly under adrenaline influence.

Ruminants

Rumen motility depends on vagal activity, so drugs that block or mimic the parasympathetic system have marked effects on rumen function. Ruminants are very sensitive to alpha-2 agonists.

Pig and poultry

Autonomic principles are the same, but drug responses and sensitivity differ; avoid extrapolating dose or response from other species and use the label or data sheet.

Clinical pearls

Self-test: 10 questions

1. Which statement correctly describes the parasympathetic division?

Parasympathetic outflow is craniosacral, with ganglia close to the effector so postganglionic fibres are short.

2. The rate-limiting step in noradrenaline synthesis is catalysed by:

Tyrosine hydroxylase converts tyrosine to DOPA and limits the pathway.

3. The main mechanism terminating the synaptic action of noradrenaline is:

Neuronal reuptake (uptake-1) is the principal route; MAO and COMT are minor.

4. Acetylcholine at the synapse is removed mainly by:

Acetylcholinesterase splits ACh into choline and acetate, and choline is recycled.

5. Which receptor mediates slowing of the heart by the vagus?

Cardiac M2 receptors reduce rate and AV conduction.

6. Bronchodilation is mainly produced by stimulation of:

Beta-2 receptors relax airway smooth muscle, while M3 causes bronchoconstriction.

7. Presynaptic alpha-2 receptors on sympathetic terminals:

They provide negative feedback, which is exploited by alpha-2 agonists.

8. The adrenal medulla is best described as:

It is innervated by preganglionic sympathetic fibres and releases adrenaline into the blood.

9. The transmitter in all autonomic ganglia is:

Both divisions use ACh at the ganglion, acting on neuronal nicotinic receptors.

10. Alpha-1 stimulation in vascular smooth muscle causes:

Alpha-1 receptors constrict vessels and raise blood pressure.

Key points to revise

1. The ANS uses a two-neuron chain with a ganglion between neurons.
2. Sympathetic outflow is thoracolumbar; parasympathetic is craniosacral.
3. ACh is made from choline and acetyl-CoA by choline acetyltransferase.
4. Acetylcholinesterase removes ACh at the synapse.
5. NA is made from tyrosine; tyrosine hydroxylase is rate-limiting.
6. NA is removed mainly by neuronal reuptake, with MAO and COMT playing minor roles.
7. Muscarinic M2 slows the heart; M3 causes secretion and smooth muscle contraction.
8. Beta-1 acts on the heart and beta-2 on airways and some vessels.

Go deeper on this site

- Ch 2. Cholinergic drugs (in this book)
- Ch 3. Anticholinergic drugs (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Lecture notes: Drugs acting on the autonomic nervous system (BASU)
- Merck Manual Consumer Version: Overview of the Autonomic Nervous System
- Vetscraft: Cholinergic drugs

CHAPTER 2 OF 33

Cholinergic drugs

Drugs that mimic or prolong the action of acetylcholine: direct agonists, reversible and irreversible anticholinesterases, their place in ruminant and equine practice, and how cholinergic toxicity (organophosphate and carbamate poisoning) is recognised and understood.

After this chapter you can

- Distinguish direct-acting cholinergic agonists from anticholinesterases
- Explain why bethanechol, pilocarpine and carbachol act where they do, using muscarinic receptor distribution
- Compare reversible and irreversible anticholinesterases, including the idea of enzyme aging
- Describe uses of cholinergic drugs in ruminant, equine and small animal practice and the cautions that go with them
- Recognise the muscarinic, nicotinic and central signs of cholinergic toxicity and the logic of treatment

The cholinergic synapse in brief

Acetylcholine (ACh) is released by all preganglionic autonomic neurons, by postganglionic parasympathetic neurons, by motor neurons at the neuromuscular junction, and by some neurons in the brain. It acts on two receptor types. **Muscarinic** receptors (M1 to M5) are G-protein-coupled and sit on effector organs: heart, smooth muscle, glands and eye. **Nicotinic** receptors are ligand-gated ion channels found in autonomic ganglia and at the skeletal muscle end plate.

ACh is destroyed within milliseconds by **acetylcholinesterase** (AChE) at the synapse. A cholinergic drug therefore has two ways to raise cholinergic activity: copy ACh at the receptor (a *direct agonist*) or stop the enzyme from destroying it (an *anticholinesterase*). The anticholinesterase is an indirect agonist, because it only works where ACh is already being released.

A common confusion is to treat cholinergic and parasympathomimetic as the same thing. They overlap, but nicotinic effects at ganglia and muscle are cholinergic and

are not parasympathetic.

Direct-acting agonists

Natural ACh is useless as a drug because AChE and plasma cholinesterases destroy it almost at once and it acts on every cholinergic receptor. Useful agonists are made resistant to these enzymes and are more selective.

- **Bethanechol** is an ester of choline that resists breakdown and acts almost only on muscarinic receptors. Its main target is the detrusor muscle of the bladder and gastrointestinal smooth muscle. It is used for bladder atony and detrusor hyporeflexia, and has been suggested in horses with urine retention from neurological disease. Current veterinary references describe it as promoting detrusor contraction, so it should only be used when the outflow is not obstructed. Giving it against a blocked urethra raises bladder pressure and risks rupture.
- **Carbachol** acts on both muscarinic and nicotinic receptors and resists hydrolysis. It is used as an intraocular miotic in surgery. Its systemic use is limited by widespread effects, and in horses it can provoke colic.
- **Pilocarpine** is a plant alkaloid with muscarinic action. Its classical uses are as a miotic in glaucoma and as a sialogogue. Because it is a tertiary amine, it enters the brain, and systemic overdose causes central effects.

The expected effects of a muscarinic agonist are easy to predict: slow heart rate, bronchoconstriction, salivation, lacrimation, sweating, increased gut motility and secretion, bladder contraction and miosis. Every contraindication follows from these effects: asthma-like airway disease, bradycardia, intestinal or urinary obstruction and peptic ulcer.

Reversible anticholinesterases

These drugs bind AChE and temporarily block it, so ACh survives longer and its effects are amplified at every site where it is released. Three drugs are used often enough to be worth separating by how they bind.

- **Edrophonium** binds by weak, purely reversible forces. Its effect lasts only minutes. It is used for the diagnostic test for myasthenia gravis and for brief reversal of neuromuscular block.

- **Neostigmine** and **pyridostigmine** transfer a carbamyl group to the enzyme. This carbamylated enzyme recovers slowly (minutes to hours), so the effect lasts longer. Both are quaternary ammonium compounds, so they do not enter the brain well. Pyridostigmine is the usual long-term treatment for acquired myasthenia gravis in dogs.
- **Physostigmine** is a tertiary amine. It crosses the blood-brain barrier, which is why it is used to reverse central anticholinergic poisoning in some situations.

Neostigmine also has a small direct effect at the skeletal muscle end plate, and it is the standard reversal agent for non-depolarising muscle relaxants. Because it enhances muscarinic effects everywhere, an anticholinergic such as atropine or glycopyrrolate is given with it to stop bradycardia, salivation and bronchospasm.

Irreversible anticholinesterases and enzyme aging

Organophosphates (OPs) phosphorylate the serine in the active site of AChE. The bond is so stable that the enzyme is effectively lost until new enzyme is made. Some OP compounds are also used as ectoparasiticides and as insecticides, which is where most clinical cases come from. Carbamate insecticides, in contrast, inhibit AChE by carbamylation, which is reversible. Carbamates generally give a shorter and less severe illness for that reason, though poisoning can still be fatal.

The key concept is **aging**. After a time that depends on the compound, the phosphorylated enzyme loses a chemical group and becomes resistant to oxime reactivators such as pralidoxime. Oximes work only on non-aged enzyme, so they are most useful early after exposure.

Beyond the acute cholinergic crisis, veterinary references describe an **intermediate syndrome** in dogs and cats, appearing one to four days after a large exposure, with weakness of neck, limb and respiratory muscles and without the salivation and fasciculations of the acute phase. Delayed neuropathy is a separate entity described for some OPs. Details are in the sources listed below.

Ecothiopate and similar long-acting agents have been used as eye drops in glaucoma in humans, but have little place in Indian veterinary practice.

Uses in ruminant, equine and small animal practice

Clinical use of cholinergic stimulants is narrower than the pharmacology suggests, because the side effects are widespread and the conditions treated usually have a cause that should be corrected first.

- **Ruminants.** Neostigmine has traditionally been used to stimulate forestomach motility in atony, but only after the underlying cause (metabolic disease, indigestion, hypocalcaemia and similar) is dealt with. Stimulating a paralysed gut against a mechanical obstruction is harmful. Ruminants are also very sensitive to cholinergic drugs and to organophosphate poisoning through sprayed forage, dips and misused pesticides.
- **Horses.** The equine gut is prone to colic when stimulated. Neostigmine and other cholinomimetics can cause abdominal pain, and a primary use of neostigmine in horses is therefore reversal of neuromuscular block under anaesthesia, with an anticholinergic to guard against bradycardia. Bethanechol may be considered for bladder atony, with the injectable form only available through compounding in some countries.
- **Dogs and cats.** Bethanechol for detrusor atony after the outflow has been confirmed open; pyridostigmine for myasthenia gravis; edrophonium for diagnosis of myasthenia.

The theme to teach students is simple: first find out whether the gut or bladder is obstructed, then decide whether a stimulant is safe.

Cholinergic toxicity

Cholinergic toxicity can come from overdose of a cholinomimetic, from anticholinesterase drugs, or most often from organophosphate and carbamate insecticide exposure. The signs can be grouped by receptor.

- **Muscarinic:** salivation, lacrimation, urination, diarrhoea (the SLUD group), vomiting, colic, sweating, miosis, bronchoconstriction with excess bronchial secretion, and slow heart rate.
- **Nicotinic:** muscle fasciculations, then weakness and paralysis. Respiratory muscle failure is a main cause of death.
- **Central:** restlessness, ataxia and seizures. Cattle and sheep more often show depression, while dogs and cats more often show convulsions.

Treatment logic. Atropine blocks the muscarinic effects, and is given to effect and repeated. It does not touch nicotinic signs such as fasciculations and muscle paralysis, which is why large OP exposures can still kill an animal whose secretions are dry. Pralidoxime reactivates non-aged enzyme and is therefore most helpful early and in organophosphate poisoning; veterinary references advise against using it alone in carbamate poisoning. Decontamination of skin and gut and supportive ventilation matter as much as the antidotes. Morphine, barbiturates and phenothiazines are listed as contraindicated in these references.

A common trap: with carbamates, blood cholinesterase may look near normal in the laboratory because the inhibition reverses quickly. Treat the animal, not the test.

For any local rules on withdrawal periods or banned pesticides in India, check the current notification.

Concept cleared

Concept cleared: Direct versus indirect
A direct agonist is like a person who walks in and sits on the chair. An anticholinesterase is like someone who stops the cleaners from removing the chairs. The second only works when chairs (ACh) are already being put out, so its effect follows the natural pattern of nerve activity.

Concept cleared: Why bethanechol is selective
Bethanechol carries a chemical group that protects it from cholinesterase and also makes it fit muscarinic sites far better than nicotinic ones. That is why it can empty a bladder without producing muscle twitching.

Concept cleared: Enzyme aging
Think of an organophosphate as glue holding a door shut. For a short time a solvent (pralidoxime) can dissolve the glue. After aging the glue has set hard and the solvent no longer works, so the enzyme is lost until the body makes more.

Concept cleared: Atropine and the nicotinic gap

Atropine is a muscarinic blocker only. In organophosphate poisoning it dries secretions and corrects slow heart rate, but muscle weakness and paralysis are nicotinic, so an animal can still stop breathing even with a dry mouth and dilated pupils.

Memory aid: SLUD and the nicotinic extras

SLUD = Salivation, Lacrimation, Urination, Diarrhoea (muscarinic). Add miosis, bradycardia, bronchospasm. Then Nicotinic = muscle twitch, then paralysis. Atropine fixes SLUD but not the twitch.

Compare and contrast

Direct agonists

Drug	Receptors	Resists cholinesterase	Main use
Bethanechol	Muscarinic	Yes	Bladder atony, detrusor hyporeflexia
Carbachol	Muscarinic and nicotinic	Yes	Intraocular miosis in surgery; limited systemic use
Pilocarpine	Muscarinic	Not an ester, not hydrolysed	Miotic in glaucoma, sialogogue
Acetylcholine	Both	No	Not used clinically

Anticholinesterases

Drug	Binding	Duration	Notes
Edrophonium	Reversible, non-covalent	Minutes	Myasthenia test; brief reversal
Neostigmine, pyridostigmine	Carbamylation, reversible	Hours	Reversal of relaxants; myasthenia; quaternary, poor brain entry
Physostigmine	Carbamylation, reversible	Hours	Tertiary, enters brain
Organophosphates	Phosphorylation, aging	Days or longer	Poisoning; oxime reactivation early only
Carbamate insecticides	Carbamylation, reversible	Shorter	Poisoning; atropine main antidote

Species notes

Cattle and sheep

Often show depression rather than convulsions in OP poisoning; rumen contents can prolong absorption, so activated charcoal is especially recommended in cattle. Poisoning is usually accidental, for example from sprayed forage or dips.

Horse

Cholinomimetics can provoke colic, so neostigmine is used mainly to reverse relaxants, together with an anticholinergic. Bethanechol has been suggested for bladder atony after neurological disease.

Dog

Pyridostigmine is used for acquired myasthenia gravis; bethanechol for detrusor atony once obstruction is excluded. Intermediate syndrome after massive OP exposure is reported mainly in dogs and cats.

Cat

Cats are sensitive to organophosphates, and the low end of the atropine range is used in treatment. Dichlorvos collars have been linked to an ataxia and depression syndrome.

Pig

Pigs can be poisoned by contaminated drinking water; treatment follows the same atropine-first logic as other species.

Clinical pearls

Self-test: 10 questions

1. Which drug is a direct-acting, muscarinic-selective agonist used for bladder atony?

Bethanechol resists cholinesterase and acts on muscarinic receptors in the detrusor. The others are anticholinesterases.

2. Why is acetylcholine not used as a drug?

AChE and plasma cholinesterases destroy it within moments, and it has no receptor selectivity.

3. Which anticholinesterase has the shortest duration of action?

Edrophonium binds by weak reversible forces and acts for minutes.

4. Which anticholinesterase can enter the brain?

Physostigmine is a tertiary amine. Neostigmine and pyridostigmine are quaternary and poorly cross the blood-brain barrier.

5. Enzyme aging in organophosphate poisoning means that

After aging, the phosphorylated enzyme is resistant to oximes, so they are most useful early.

6. Which sign of OP poisoning is NOT corrected by atropine?

Fasciculations and paralysis are nicotinic effects; atropine blocks only muscarinic receptors.

7. Why is an anticholinergic given with neostigmine when reversing a muscle relaxant?

Neostigmine raises ACh at muscarinic sites too; the anticholinergic blocks those unwanted effects.

8. Why should bethanechol be used cautiously in a urinary retention case?

It stimulates the detrusor, so the outflow must be open first.

9. Which statement about carbamate poisoning is correct?

Reversible inhibition may recover during sampling or transport; atropine is the mainstay, and oximes alone are not advised.

10. In horses, the main caution with neostigmine is

Equine gut is sensitive to cholinergic stimulation; this limits clinical use other than relaxant reversal.

Key points to revise

1. Cholinergic drugs act directly on receptors or indirectly by inhibiting acetylcholinesterase.
2. Bethanechol is muscarinic selective and acts on bladder and gut smooth muscle.

3. Neostigmine and pyridostigmine are quaternary and act peripherally; physostigmine is tertiary and acts centrally.
4. Edrophonium is the shortest acting anticholinesterase.
5. Organophosphates bind irreversibly; aging makes the enzyme resistant to oximes.
6. Carbamates inhibit reversibly and cause shorter illness.
7. Cholinergic toxicity has muscarinic, nicotinic and central signs.
8. Atropine is the antidote for muscarinic signs; pralidoxime reactivates enzyme early in OP poisoning.

Go deeper on this site

- Ch 3. Anticholinergic drugs (in this book)
- Ch 1. Autonomic nervous system and neurotransmission (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Organophosphate toxicosis in animals
- Merck Veterinary Manual: Carbamate insecticides toxicity
- Merck Veterinary Manual: Pharmacotherapeutics in urine retention in animals

CHAPTER 3 OF 33

Anticholinergic drugs

Muscarinic antagonists: how atropine, glycopyrrolate and hyoscine block parasympathetic effects, their use in premedication, bradycardia and smooth muscle spasm, and the cautions that differ between species.

After this chapter you can

- Explain the mechanism of muscarinic receptor blockade and predict the organ effects
- Compare atropine, glycopyrrolate and hyoscine by structure, brain entry and duration

- Describe indications in premedication, vagal bradycardia, spasm and organophosphate poisoning
- Recognise atropine toxicity and its management in principle
- State species-specific cautions for ruminants, horses, rabbits, cats and dogs

Mechanism and the effects you can predict

Anticholinergic drugs in this chapter are **competitive muscarinic antagonists**. They occupy the receptor so acetylcholine cannot act. They do not stop release of acetylcholine, and they do not block nicotinic receptors at the neuromuscular junction in ordinary doses.

Since muscarinic receptors are on the heart, glands, smooth muscle and eye, the effects can be worked out from the parasympathetic system in reverse:

- **Heart:** block of M2 receptors at the sinoatrial node raises heart rate and speeds atrioventricular conduction.
- **Glands:** less saliva, bronchial, and sweat secretion. Gastric acid falls only a little.
- **Smooth muscle:** bronchodilation, reduced gut motility and tone, and relaxation of the bladder detrusor.
- **Eye:** mydriasis and loss of accommodation (cycloplegia).
- **Brain:** tertiary amines such as atropine and hyoscine enter the central nervous system and can cause sedation or, at higher doses, excitement.

Every cautionary statement about these drugs is a result of one of these effects. Glaucoma, tachycardia, intestinal ileus and urinary retention all worsen.

Atropine

Atropine is a plant alkaloid (from Atropa belladonna and related plants). It is a tertiary amine, so it is well absorbed and crosses the blood-brain and placental barriers. Veterinary notes put its vagal-blocking action at roughly an hour to an hour and a half, which is shorter than glycopyrrolate.

A well-known point is the **initial slowing of heart rate** that can occur after rapid intravenous injection, before the rise in heart rate. This is attributed to a brief central vagal effect. It is a reason to give the drug slowly and not to panic when the first change is a lower rate.

Atropine is also the antidote for muscarinic signs of cholinesterase-inhibitor poisoning and for overdose of neostigmine or edrophonium. In that use it is given to effect, and the endpoint is not a fixed amount but dry secretions, a clear chest and a heart rate that has recovered.

Atropine causes mydriasis, so it is avoided in glaucoma and when the iris is stuck to the lens. Used in the eye, it is a long-acting mydriatic and cycloplegic, helpful in uveitis to relieve ciliary spasm.

Glycopyrrolate and hyoscine

Glycopyrrolate is a synthetic quaternary ammonium compound. Because it carries a permanent charge, it passes poorly across the blood-brain barrier and the placenta. Compared with atropine it has little central effect, produces less tachycardia, and its action lasts longer, around two to three hours in the teaching material used here. It is often chosen for patients with central nervous system disease and for pregnant animals, and it is the standard partner for neostigmine. It is usually more expensive than atropine, which matters in many Indian practices.

Hyoscine (scopolamine) is another belladonna alkaloid. The two forms behave very differently:

- **Hyoscine hydrobromide** is a tertiary amine with prominent central effects: sedation, amnesia and antiemetic action, which is why it is used for motion sickness in people.
- **Hyoscine butylbromide** is quaternary. It does not enter the brain much, and its main use is as a **spasmolytic** for smooth muscle cramps in gut, bile and urinary tracts. It is used in horses with spasmodic colic and to relax the rectum for examination, and in other species for colic or spasm. Check the product label for the species it is registered for in India.

Other synthetic muscarinic antagonists include ipratropium for airways and tropicamide for eye examination. Their selection depends on route and desired site of action, not on a new mechanism.

Uses: premedication, bradycardia and spasm

Premedication. In the past anticholinergics were given routinely before anaesthesia to dry secretions and to prevent vagal reflexes. Current teaching is that routine use

is not advised. They are used when there is a reason, such as procedures that provoke vagal stimulation (for example, traction on the eye) or when a drug that slows the heart is given. A rise in heart rate also raises myocardial oxygen demand, so a healthy animal with a normal heart rate gains little.

Bradycardia. Anticholinergics treat bradycardia that is due to vagal tone, for instance with opioids, with surgical traction, or during reversal of neuromuscular block with neostigmine. They do not treat every slow heart rate. For example, the slow rate after an alpha-2 agonist comes with raised vascular tone and is a response to hypertension. Whether to give an anticholinergic in that case is debated, and many clinicians prefer reversing the alpha-2 drug.

Spasm. Hyoscine butylbromide and atropine relax smooth muscle in gut and urinary spasm. Spasmolytic action is only symptomatic, and the cause of pain still has to be found.

Poisoning. Atropine is the principal antidote for the muscarinic signs of organophosphate and carbamate poisoning. It is repeated as needed and does not reverse nicotinic muscle effects.

Atropine toxicity

Overdose or plant poisoning produces the opposite picture to cholinergic toxicity: dry mouth, dilated unresponsive pupils, fast heart rate, hot dry skin with raised body temperature, restlessness or delirium, urinary retention and ileus. The old human saying is dry as a bone, red as a beet, mad as a hatter, blind as a bat.

In animals, management is supportive: cooling, sedation of agitation, fluids and watching for gut stasis and urinary retention. Physostigmine can reverse the central and peripheral effects of anticholinergics in selected cases, but it carries its own risks and should be used on professional guidance.

Atropine used to treat organophosphate poisoning can also be overdone. The aim is to dry secretions and restore heart rate, not to produce full atropinisation with a fast heart rate and ileus. Veterinary references advise avoiding overtreatment.

Cautions by species

- **Horses.** Atropine is not routinely used in anaesthesia. It can cause ileus and colic, and a long-lasting depression of gut motility is dangerous in a species with a sensitive gut. If it is needed for a slow heart rate, some practitioners give mineral oil or take other precautions. Glycopyrrolate is seen as the more suitable drug in some situations. Heavy sweating is part of equine thermoregulation, so reduced sweating matters in hot climates.
- **Ruminants.** Atropine is not very good at drying oral secretions in ruminants and some authors say it makes saliva thicker, which impairs clearance and may raise the risk of bloat. Rumen motility is also reduced. Low doses and careful monitoring of the rumen are advised.
- **Rabbits and rats.** Many rabbits have an enzyme, atropinesterase, in the liver that destroys atropine, so doses that work in dogs may fail. Veterinary notes say they need higher doses, and glycopyrrolate is often preferred in practice.
- **Cats.** Cats are sensitive to the effects of xylazine, and atropine may be given with alpha-2 drugs by some practitioners. Check for cardiopulmonary disease before using any combination.
- **Dogs.** Avoid anticholinergics in animals that already have a fast heart rate, and in those with glaucoma. In brachycephalic dogs, the thickened secretions can obstruct the airway.

Concept cleared

Concept cleared: Tertiary versus quaternary
A quaternary drug carries a permanent charge, so it cannot easily slip through the lipid wall of the brain capillary. Glycopyrrolate and hyoscine butylbromide are quaternary and stay in the body. Atropine and hyoscine hydrobromide are tertiary and walk into the brain.

Concept cleared: Competitive block
Atropine sits on the receptor like a person holding a seat. If acetylcholine rises a lot, as in organophosphate poisoning, it can push the blocker away, so large amounts of atropine may be needed to maintain the block.

Concept cleared: Why heart rate first falls

Fast intravenous atropine can briefly stimulate vagal centres or act on some receptors before blocking the heart. It is a short effect, and slow injection reduces it.

Concept cleared: Not all bradycardia is vagal

Atropine corrects bradycardia caused by high vagal tone. A slow heart rate caused by an alpha-2 agonist is a baroreflex response to raised vascular resistance, so blocking the vagus may add workload to the heart.

Memory aid: Atropine in reverse

Cholinergic is SLUD (wet). Anticholinergic is the opposite: dry mouth, big pupils, fast heart, hot skin, slow gut, no urine. If you know SLUD, say the opposite for atropine.

Compare and contrast

Atropine, glycopyrrolate and hyoscine

Drug	Structure	Brain entry	Duration (teaching notes)	Main points
Atropine	Tertiary	Yes	About 1 hour or somewhat more	Antidote; mydriasis; first dip in heart rate if given fast
Glycopyrrolate	Quaternary	Poor	About 2 to 3 hours	Less tachycardia; suits CNS disease and pregnancy
Hyoscine hydrobromide	Tertiary	Yes	Variable	Sedative and antiemetic effects
Hyoscine butylbromide	Quaternary	Poor	Variable	Spasmolytic for gut and urinary tract

Anticholinergic versus cholinergic toxicity

Feature	Anticholinergic toxicity	Cholinergic toxicity
Pupils	Dilated	Constricted
Secretions	Dry	Excessive
Heart rate	Fast	Slow
Gut	Ileus	Hypermotility, diarrhoea
Skin	Hot, dry	Sweating
Antidote	Supportive; physostigmine in selected cases	Atropine, and an oxime for OP

Species notes

Horse

Atropine can cause ileus and colic, so it is not used routinely; glycopyrrolate is considered when an anticholinergic is needed. Hyoscine butylbromide is used for spasmodic colic.

Cattle and sheep

Atropine is poor at drying secretions in ruminants and may thicken saliva; watch for bloat and impaired rumen function. Drug doses are lower per body weight than in small animals.

Rabbit

Atropinesterase in the liver destroys atropine in many rabbits, so the response is unreliable. Glycopyrrolate is often used instead.

Cat

Atropine is used for vagal bradycardia and as the OP antidote at the low end of the range. Cats given xylazine often vomit; check heart and lung health first.

Dog

Use only when indicated; avoid in tachycardia and glaucoma. Glycopyrrolate gives longer action and less heart rate increase than atropine.

Clinical pearls

Self-test: 10 questions

1. Which drug is a quaternary ammonium compound with little CNS effect?

Glycopyrrolate carries a permanent charge and passes poorly across the blood-brain barrier.

2. Atropine acts by

It competes with acetylcholine at muscarinic receptors.

3. Which effect is NOT expected from atropine?

Atropine causes mydriasis; miosis is a cholinergic effect.

4. The main reason atropine is not routinely used in horses is

Reduced gut motility is dangerous in horses.

5. Why may atropine fail in some rabbits?

Hepatic atropinase breaks down atropine in many rabbits.

6. Hyoscine butylbromide is mainly used as

It is quaternary and acts peripherally on smooth muscle.

7. In organophosphate poisoning, atropine does NOT treat

Those are nicotinic effects.

8. Why give glycopyrrolate with neostigmine?

Neostigmine raises acetylcholine at muscarinic sites; the anticholinergic blocks those effects.

9. Which sign suggests anticholinergic toxicity?

Anticholinergic toxicity is the reverse of cholinergic toxicity.

10. Why is atropine avoided in glaucoma?

Pupil dilation may worsen drainage and raise intraocular pressure.

Key points to revise

1. Anticholinergics are competitive muscarinic antagonists.
2. Effects: tachycardia, dry secretions, bronchodilation, reduced gut motility, mydriasis.
3. Atropine is tertiary and enters the brain; glycopyrrolate is quaternary and does not.
4. Glycopyrrolate acts longer than atropine and gives less tachycardia.
5. Hyoscine butylbromide is used for smooth muscle spasm.
6. Atropine is the antidote for muscarinic signs of OP and carbamate poisoning, but not nicotinic signs.
7. Atropine toxicity is the reverse of SLUD.
8. Species cautions: ileus in horses, thick secretions in ruminants, atropinesterase in rabbits.

Go deeper on this site

- Ch 4. Adrenergic agonists and antagonists (in this book)
- Ch 2. Cholinergic drugs (in this book)

- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Hill Agricultural / COVAS teaching material: Preanaesthetics
- Western University of Health Sciences: Pharmacology of premedication
- Merck Veterinary Manual: Organophosphate toxicosis in animals

CHAPTER 4 OF 33

Adrenergic agonists and antagonists

Adrenergic drugs mimic or block noradrenaline and adrenaline at alpha and beta receptors. This chapter links receptor selectivity to the effects you see in shock, cardiac arrest, anaphylaxis, sedation, asthma and heart disease.

After this chapter you can

- Name the adrenergic receptor subtypes and the main effect of each
- Compare the catecholamines (adrenaline, noradrenaline, dopamine, dobutamine, isoprenaline) by receptor selectivity
- Explain why adrenaline is the drug of choice in anaphylaxis and cardiac arrest
- Distinguish selective and non-selective alpha and beta blockers and their clinical uses
- Predict adverse effects and cautions from receptor pharmacology

Adrenergic receptors in brief

Sympathetic nerves release **noradrenaline**, and the adrenal medulla releases mainly **adrenaline**. Both act on G-protein-coupled receptors. Almost every adrenergic drug effect can be predicted if you remember four receptor types.

Selectivity is the key idea of this chapter. A drug that is selective for one receptor gives a narrower, more predictable effect. A drug that acts on several gives a broad effect, which can be useful in an emergency but causes more side effects.

- **Alpha-1**: smooth muscle contraction. Vasoconstriction (raises blood pressure), mydriasis, contraction of the bladder neck and urethral sphincter.
- **Alpha-2**: mostly presynaptic and central. Reduce noradrenaline release and sympathetic outflow, causing sedation, analgesia and muscle relaxation. Peripherally they can cause vasoconstriction.
- **Beta-1**: heart. Raise heart rate and force of contraction and speed conduction. Also stimulate renin release.
- **Beta-2**: bronchodilation, vasodilation in skeletal muscle, uterine relaxation, and glycogenolysis.

Catecholamines and their selectivity

Catecholamines have a catechol ring and act quickly. They are destroyed in the gut and by enzymes (MAO and COMT), so they are given by injection or infusion and last only minutes. This is useful because the effect can be titrated and stopped quickly.

- **Adrenaline (epinephrine)**: acts on alpha-1, beta-1 and beta-2. The result depends on dose and tissue. It strongly increases cardiac work and oxygen demand.
- **Noradrenaline (norepinephrine)**: mainly alpha-1 and beta-1, with little beta-2. It is a potent vasopressor, used when the problem is low vascular tone.
- **Dopamine**: the precursor of noradrenaline. Acts on dopamine receptors, beta-1, and at higher rates alpha-1, partly by releasing noradrenaline.
- **Dobutamine**: synthetic, mainly beta-1. It increases contractility more than heart rate and does not release noradrenaline.
- **Isoprenaline**: non-selective beta agonist with no alpha action. It causes tachycardia and arrhythmias, so its use is limited, for example in short-term treatment of bradyarrhythmias.

A common confusion: dopamine is often called the 'renal dose' drug. Low rates act on renal dopamine receptors and increase renal blood flow and urine output, but this has not been shown to protect kidneys, so do not treat it as a kidney-saving drug.

Uses in shock, cardiac arrest and anaphylaxis

In **shock** the aim is to restore tissue perfusion. First correct the cause and the fluid deficit. Adrenergic drugs are added when blood pressure or cardiac output remain poor after fluids. Match the drug to the problem: a weak pump (cardiogenic shock) responds to beta-1 agents such as dobutamine or dopamine. Vasodilatory shock (for example sepsis) needs a vasopressor such as noradrenaline. Using a pure inotrope in a vasodilated patient will not fix pressure.

In **cardiac arrest**, adrenaline is the standard drug. Its alpha-1 action raises aortic diastolic pressure and so coronary and cerebral perfusion during compressions. Beta effects add little and may increase myocardial oxygen demand.

In **anaphylaxis**, adrenaline is the first-line drug. It is a physiological antagonist of the mediators released: alpha-1 reverses vasodilation and oedema, beta-1 supports the heart, and beta-2 relaxes bronchial muscle and reduces further mediator release from mast cells. Antihistamines and corticosteroids act too slowly and do not replace it.

Caution: adrenaline can cause ventricular arrhythmias, particularly when the myocardium is already sensitised, for example by some inhalant anaesthetics. Extravasation of vasoconstrictor infusions can cause local tissue necrosis, so give them through a secure intravenous line.

Other agonists: alpha-2 and beta-2 drugs

Alpha-2 agonists (xylazine, medetomidine, dexmedetomidine, detomidine, romifidine) are widely used as sedative-analgesics in animals. Their cardiovascular effects follow from the receptor: initial vasoconstriction and hypertension, then bradycardia and reduced cardiac output. Ruminants are very sensitive to xylazine. These effects can be reversed by an alpha-2 antagonist such as atipamezole or yohimbine.

Beta-2 agonists (salbutamol, terbutaline, clenbuterol) relax bronchial and uterine smooth muscle. They are used for airway disease and, in some species, for tocolysis. Higher doses lose selectivity, causing tachycardia and tremor.

Alpha-1 agonists such as phenylephrine are vasopressors and nasal or ocular decongestants. Phenylpropanolamine and pseudoephedrine act mainly by releasing noradrenaline and have been used to raise urethral tone in urinary incontinence in dogs.

Regulation: beta-2 agonists have been misused as growth promoters in food animals. Check the current notification on the status of such use in India.

Alpha and beta blockers

Blockers occupy the receptor without activating it, so their effect depends on how much sympathetic tone is present.

- **Alpha-1 blockers** (prazosin, phenoxybenzamine): cause vasodilation and relax the urethral sphincter. Phenoxybenzamine binds irreversibly and is used to prepare patients with phaeochromocytoma and sometimes for urethral spasm. Main adverse effect is hypotension.
- **Alpha-2 antagonists** (atipamezole, yohimbine): reverse sedation from alpha-2 agonists.
- **Non-selective beta blockers** (propranolol): block beta-1 and beta-2. They slow the heart and reduce arrhythmias, but beta-2 blockade can cause bronchospasm, so they are risky in asthmatic or feline airway disease.
- **Beta-1 selective blockers** (atenolol, metoprolol, esmolol): preferred when the airways matter. Esmolol is very short acting and is given by infusion for supraventricular tachyarrhythmias.
- **Carvedilol** blocks beta and alpha-1 receptors and is used in some cardiac patients.

Cautions for beta blockers: they can precipitate decompensation in animals with severe heart failure that depend on sympathetic drive, they can mask signs of hypoglycaemia, and stopping them abruptly can cause rebound tachycardia. Selectivity is relative and is lost at higher doses.

Putting it together: predicting effects

When you meet an adrenergic drug, ask three questions. Which receptors does it act on? Is it an agonist or a blocker? How fast is it removed? From these answers you can predict heart rate, blood pressure, airway tone and likely adverse effects without memorising lists.

Examples: a beta-1 selective agonist should raise contractility with less effect on the airways. A pure alpha-1 agonist should raise pressure and may cause a reflex

slowing of the heart. A non-selective beta blocker should slow the heart and tighten the airways.

Drug interactions follow the same logic. Monoamine oxidase inhibitors increase the effect of indirectly acting amines and of dopamine. Alpha-2 agonists combined with other sedatives deepen cardiovascular depression. Alpha blockers given with a beta agonist can leave beta-2 vasodilation unopposed, causing hypotension, which is the reason adrenaline's pressor effect can reverse in the presence of an alpha blocker.

Concept cleared

Selectivity is relative
Receptor selectivity falls as dose rises. A beta-1 selective drug at a high dose also acts on beta-2.

Dose-dependent adrenaline effects
Adrenaline has alpha and beta actions at once. Which one dominates depends on dose, route and the tissue involved.

Match drug to the haemodynamic problem
Pump failure needs an inotrope, vasodilatory shock needs a vasopressor, and both need volume and the underlying cause treated.

Physiological antagonism
Adrenaline reverses anaphylaxis by producing opposite effects to the mediators, not by blocking them.

Memory aid: Receptors: 1, 2, 1, 2
Alpha-1 constricts, alpha-2 calms. Beta-1 beats the heart, beta-2 breathes (opens the airways).

Compare and contrast

Catecholamines at a glance

Drug	Main receptors	Main effect	Typical use
Adrenaline	Alpha-1, beta-1, beta-2	Vasoconstriction, cardiac stimulation, bronchodilation	Cardiac arrest, anaphylaxis
Noradrenaline	Alpha-1, beta-1	Strong vasoconstriction	Vasodilatory shock
Dopamine	Dopamine, beta-1, alpha-1 at higher rate	Inotropy, then pressor effect	Cardiogenic or endotoxic shock
Dobutamine	Beta-1	Increased contractility	Low output heart failure
Isoprenaline	Beta-1, beta-2	Tachycardia, vasodilation	Short-term bradyarrhythmia

Adrenergic blockers

Drug	Selectivity	Main effect	Key caution
Prazosin	Alpha-1	Vasodilation, lower urethral tone	Hypotension
Phenoxybenzamine	Alpha, irreversible	Prolonged alpha block	Hypotension, slow offset
Atipamezole	Alpha-2	Reverses sedation	Sudden arousal, vasodilation
Propranolol	Beta-1 and beta-2	Slows heart, reduces arrhythmia	Bronchospasm
Atenolol	Beta-1	Slows heart	Decompensated heart failure

Species notes

Dogs

Dobutamine and dopamine are used by infusion in low output states. Phenylpropanolamine is used for urethral sphincter incompetence.

Cats

Cats are sensitive to beta-2 blockade of airways. Dobutamine has a longer half-life and can stimulate the central

Atenolol and similar drugs are used in selected cardiac cases.

nervous system, so it is used cautiously and rarely.

Horses

Clenbuterol is used for airway disease, and detomidine and romifidine are common alpha-2 sedatives. Check competition rules on prohibited substances.

Ruminants

Cattle are highly sensitive to xylazine, and sedation can come with salivation, bloat risk and, in pregnancy, uterine effects. Use of adrenergic drugs in food animals needs a withdrawal and regulatory check.

Birds and exotics

Alpha-2 agonists are used with care because of cardiovascular depression. Atipamezole reversal is common.

Clinical pearls

Self-test: 10 questions

1. Which receptor mainly mediates bronchodilation?

Beta-2 receptors relax bronchial smooth muscle, which is why beta-2 agonists are used for airway disease.

2. First-line drug for anaphylaxis is

Adrenaline reverses vasodilation, oedema and bronchospasm quickly. Antihistamines and steroids are slower and adjunctive.

3. Which catecholamine is mainly a beta-1 agonist that raises contractility with little noradrenaline release?

Dobutamine acts mainly on beta-1 receptors and does not release noradrenaline.

4. Why is adrenaline given in cardiac arrest?

The alpha-1 effect increases aortic diastolic pressure and hence coronary and cerebral perfusion during compressions.

5. Atipamezole reverses the effects of

Atipamezole is an alpha-2 antagonist and reverses alpha-2 agonist sedation.

6. A non-selective beta blocker is most hazardous in an animal with

Beta-2 blockade can tighten the airways and worsen bronchospasm.

7. Phenoxybenzamine differs from prazosin because it

Phenoxybenzamine binds alpha receptors irreversibly, so its effect is prolonged.

8. A patient in vasodilatory shock after adequate fluids most needs

The problem is low vascular tone, so an alpha-1 vasopressor is appropriate.

9. Common early effect of alpha-2 agonists on the cardiovascular system is

Peripheral vasoconstriction raises pressure initially, then reflex bradycardia and reduced output follow.

10. Which statement about selectivity is correct?

At higher doses selective drugs act on other receptor subtypes too.

Key points to revise

1. Four receptor types: alpha-1, alpha-2, beta-1, beta-2.
2. Catecholamines are short acting and given by infusion or injection.
3. Adrenaline acts on alpha-1, beta-1 and beta-2.
4. Noradrenaline is mainly a vasopressor.
5. Dobutamine is mainly beta-1 and increases contractility.
6. Adrenaline treats anaphylaxis by reversing its effects physiologically.
7. Alpha-2 agonists sedate and are reversed by atipamezole or yohimbine.
8. Selectivity is lost at higher doses.

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- Ch 5. Ganglion and neuromuscular blocking drugs (in this book)
- Ch 3. Anticholinergic drugs (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Positive Inotropes for Use in Animals

CHAPTER 5 OF 33

Ganglion and neuromuscular blocking drugs

Drugs that block nicotinic transmission at autonomic ganglia and at the skeletal muscle end plate. The chapter covers depolarising and non-depolarising relaxants, reversal, monitoring and the drug interactions that matter during anaesthesia.

After this chapter you can

- Explain why ganglion blockers have almost no clinical use while neuromuscular blockers are important in anaesthesia
- Compare depolarising and non-depolarising block in mechanism, early signs and reversibility
- Describe how neostigmine, anticholinergics and sugammadex reverse block
- State what must be monitored when a relaxant is used and why
- List drugs and conditions that prolong neuromuscular block

Two nicotinic targets, two very different outcomes

The nicotinic acetylcholine receptor is a ligand-gated ion channel. There are different subtypes: one in autonomic ganglia (neuronal type) and one at the skeletal muscle end plate (muscle type). Drugs that block them are therefore separated into **ganglion blockers** and **neuromuscular blockers**.

Neuromuscular blockers paralyse skeletal muscle so that surgery, intubation and controlled ventilation are easier. They are used only in animals that are already unconscious, because they have **no sedative, analgesic or anaesthetic action**. An animal that is paralysed but not anaesthetised is fully aware and in pain, and cannot show it.

A common confusion is to think that a relaxant makes the animal unconscious or pain free. It does not. Another is to treat the loss of movement as proof of adequate anaesthesia. After a relaxant, a rise in heart rate or blood pressure to a surgical stimulus may be the only warning that depth is too light, so cardiovascular trends must be watched closely.

Ganglion blocking drugs

Ganglion blockers such as hexamethonium, mecamylamine and the older trimetaphan occupy neuronal nicotinic receptors, or the channel they form, in both sympathetic and parasympathetic ganglia. They block all autonomic outflow at once.

The effect in a given organ depends on which branch dominates at rest. This is the key idea. In blood vessels, sympathetic tone dominates, so the result is vasodilation and a fall in blood pressure, with orthostatic hypotension. In the heart, vagal tone

dominates, so heart rate rises. In the gut and bladder, parasympathetic tone dominates, so there is constipation, ileus and urinary retention. In the eye, the pupil dilates and accommodation is lost. Salivation is reduced.

Because they affect everything, are hard to control and give rise to these effects, ganglion blockers are not used in routine veterinary practice. They remain important in teaching because they illustrate how organs are under dual control, and because some drugs have ganglion-blocking effects as a side action. The details of any use in a specific species should be checked in a current formulary.

Non-depolarising (competitive) blockers

Atracurium, cisatracurium, rocuronium, vecuronium and pancuronium bind to the nicotinic receptor at the end plate without opening it. They compete with acetylcholine, and when enough receptors are blocked the end plate cannot reach threshold, so the muscle relaxes. Because the block is competitive, it can be overcome by raising acetylcholine, which is the basis of reversal.

Muscles go weak in a progressive way and then become flaccid. Small, fast muscles of the eye and face are affected earliest, then limbs and trunk, and the diaphragm last. Recovery happens in reverse, with the diaphragm returning first. Good breathing does not prove that the muscles of the larynx and pharynx are safe, so swallowing and airway protection may still be impaired.

The agents differ in how they are cleared. Steroidal agents (rocuronium, vecuronium, pancuronium) depend on organ function. Atracurium and cisatracurium are broken down by enzymatic hydrolysis and by Hofmann elimination in plasma, so they are less affected by liver and kidney disease and are often chosen in sick animals. Atracurium can release histamine at higher doses, and slow injection reduces this. Pancuronium can raise heart rate through muscarinic blocking effects.

Depolarising blocker: succinylcholine

Succinylcholine (suxamethonium) is the only depolarising relaxant in common use. It attaches to the nicotinic receptor and opens it, like acetylcholine does, but it is not removed quickly by acetylcholinesterase. The end plate stays depolarised and

cannot respond to further stimulation. The first sign is **fasciculation**, followed by flaccid paralysis.

Its action is ended by plasma pseudocholinesterase (butyrylcholinesterase), which breaks it down before it reaches the junction, and by diffusion away from the end plate. Anything that lowers pseudocholinesterase, including liver disease, malnutrition, pregnancy and some drugs, prolongs the effect.

The block has two phases. **Phase I** is the depolarising block just described. With large, repeated or infused doses it may change to **phase II**, which resembles a non-depolarising block.

Succinylcholine is rarely used in current veterinary practice. Reasons listed by current references include arrhythmias, potassium release that can be dangerous in animals with muscle disease, myoglobinuria after recovery, a possible link with malignant hyperthermia, and the absence of a specific antagonist. In the past it was used for restraint of large animals and wildlife, but because it paralyses without analgesia or sedation, this is now considered unacceptable.

Reversal and monitoring

Reversal of non-depolarising block. Anticholinesterases such as neostigmine, pyridostigmine and edrophonium raise acetylcholine at the junction so it can win the competition. Because they raise acetylcholine at muscarinic receptors too, they cause bradycardia, bronchospasm, salivation and hypermotility, so atropine or glycopyrrolate is given with them. Neostigmine takes several minutes and cannot reverse a very deep block. Reversal should be started only when some recovery is already present.

Sugammadex is a different kind of drug. It is a cyclodextrin that wraps around rocuronium and vecuronium, removing them from the junction. It acts quickly, has no muscarinic effects and can reverse a deep block, but it does not work for atracurium and cisatracurium.

Succinylcholine. Phase I block should not be reversed with an anticholinesterase, because it will deepen the block. Phase II block may respond, so the type of block must be known.

Monitoring. Because paralysis removes the usual signs of anaesthetic depth (jaw tone, palpebral reflex, movement), depth has to be judged from cardiovascular responses and other monitors. Ventilation must be supported until function returns. A peripheral nerve stimulator is used to judge the degree of block and its recovery, and full recovery should be confirmed before extubation to avoid hypoventilation, hypoxia and aspiration.

Drug interactions and patient factors

A relaxant rarely acts alone, and its duration depends on what else the patient receives and on the patient's condition.

- **Inhalant anaesthetics** (isoflurane, sevoflurane) increase the potency of non-depolarising blockers, so less drug is needed.
- **Antibiotics:** aminoglycosides, polymyxins, tetracyclines and lincosamides can enhance block. A dog given gentamicin and a relaxant may recover slowly.
- **Other drugs:** quinidine, procaine, lidocaine, diazepam and barbiturates can enhance block in some circumstances.
- **Physiological factors:** hypermagnesaemia, hypokalaemia, acidosis and hypothermia prolong block. Correct these before reversing.
- **Disease:** myasthenia gravis makes animals very sensitive to non-depolarising agents. Liver, kidney and low pseudocholinesterase states change how long certain agents last.
- **Anticholinesterase drugs and organophosphates** prolong succinylcholine, since they inhibit cholinesterase.

The practical rule is to review every drug the patient has received, including recent dips or pesticide exposure, before using a relaxant, and to use a nerve stimulator where possible.

Concept cleared

Concept cleared: Ganglion block depends on tone
A ganglion blocker removes both autonomic brakes and accelerators. What you see is whichever branch was winning at rest: vessels lose sympathetic tone and dilate, while the heart loses vagal tone and speeds up.

Concept cleared: Competitive versus depolarising

A competitive blocker is a key stuck in the lock that does not turn: the door cannot open. Succinylcholine is a key that turns and then jams: the door opens once, then stays unresponsive. More acetylcholine can push out the first key, but it only worsens the jam.

Concept cleared: Why reversal needs an anticholinergic

Neostigmine does not know where the acetylcholine is. It protects it at muscle and also at heart, gut and glands. The anticholinergic protects those other sites.

Concept cleared: Sugammadex is a chemical trap

It does not act on receptors. It captures rocuronium or vecuronium molecules like a cup, so the relaxant leaves the junction and the muscle recovers. That is why it does not work for drugs that do not fit the cup.

Memory aid: Which block to reverse

Competitive block: Compete back with neostigmine (plus atropine or glycopyrrolate). Depolarising phase I: Do not reverse, wait. Rocuronium and vecuronium only: Sugammadex.

Compare and contrast

Depolarising and non-depolarising block

Feature	Succinylcholine (depolarising)	Atracurium, rocuronium, vecuronium (non-depolarising)
Action at receptor	Activates, holds end plate depolarised	Occupies without activating
Early sign	Fasciculations	Progressive weakness
Termination	Plasma pseudocholinesterase and diffusion	Redistribution, metabolism or excretion depending on drug
Effect of anticholinesterase	Phase I prolonged; phase II may be reversed	Reversed
Veterinary use	Rare; important adverse effects	Standard choice with ventilation

Reversal agents

Agent	Mechanism	Works on	Notes
Neostigmine	Anticholinesterase	Non-depolarising block	Slow; muscarinic effects; give with anticholinergic
Edrophonium	Short anticholinesterase	Non-depolarising block	Brief; also an anticholinergic beforehand
Pyridostigmine	Anticholinesterase	Non-depolarising block	Longer acting
Sugammadex	Encapsulates drug	Rocuronium, vecuronium	Fast; no muscarinic effects; not for atracurium or cisatracurium

Species notes

Dog

Succinylcholine lasts longer in dogs than in cats according to veterinary references. Atracurium and

Cat

Succinylcholine action is shorter than in dogs. Intubation and laryngospasm have been studied

cisatracurium are useful in animals with liver or kidney disease.

with rocuronium and sugammadex in cats.

Horse
Atracurium and rocuronium are used with ventilation. Anticholinesterases can cause bradycardia, hypotension and colic, so an anticholinergic may be needed.

Cattle
Succinylcholine was historically used for restraint. Paralysis without analgesia is unacceptable, and reliable airway and ventilation support is needed.

Pig
Pigs of some breeds are susceptible to malignant hyperthermia triggered by succinylcholine and some inhalants; avoid known triggers.

Clinical pearls

Self-test: 10 questions

1. Why can ganglion blockers cause hypotension?

Blood vessels are mainly under sympathetic tone, so ganglion block causes vasodilation.

2. A neuromuscular blocker used alone in a conscious animal would

These drugs act at the end plate and have no central effect.

3. The first sign after succinylcholine is

Initial depolarisation causes muscle twitching before paralysis.

4. Which drug terminates succinylcholine action?

It is broken down by plasma cholinesterase before reaching the junction.

5. Which relaxant is cleared mainly by Hofmann elimination and ester hydrolysis?

Atracurium and cisatracurium do not depend much on liver or kidney function.

6. Sugammadex will NOT reverse

It encapsulates steroidal agents only.

7. Why is glycopyrrolate or atropine given with neostigmine?

Neostigmine raises ACh at muscarinic sites and causes bradycardia and secretions.

8. Which muscle usually recovers first from non-depolarising block?

The diaphragm is relatively resistant, but airway protection may still be impaired.

9. Which of these prolongs non-depolarising block?

Aminoglycosides, hypothermia, acidosis, hypermagnesaemia and hypokalaemia prolong block.

10. A phase I succinylcholine block should be

Anticholinesterases prolong phase I block.

Key points to revise

1. Ganglion blockers affect all autonomic outflow and are not used clinically; effects depend on dominant tone.
2. Neuromuscular blockers act at the muscle-type nicotinic receptor and give no sedation or analgesia.
3. Non-depolarising agents compete with acetylcholine and can be reversed.
4. Succinylcholine depolarises the end plate and causes fasciculations first.
5. Succinylcholine is ended by pseudocholinesterase and has no antagonist.
6. Neostigmine reversal needs an anticholinergic.
7. Sugammadex encapsulates rocuronium and vecuronium.
8. Monitoring with a nerve stimulator and ventilation support are essential.

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- Ch 6. Anticonvulsants and drugs for epilepsy (in this book)
- Ch 4. Adrenergic agonists and antagonists (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Neuromuscular blocking agents for animals
- Cornell: Neuromuscular blockade, Essentials of Small Animal Anesthesia and Analgesia
- Merck Veterinary Manual: Competitive nondepolarizing agents and antagonists

CHAPTER 6 OF 33

Anticonvulsants and drugs for epilepsy

How anticonvulsant drugs calm an over-excitable brain, with the concepts behind phenobarbital, bromide, levetiracetam and other drugs, a stepwise approach to status epilepticus, and the species cautions that matter in practice.

> **After this chapter you can**

- Explain the three broad mechanisms by which anticonvulsants reduce seizure activity
- Describe why phenobarbital needs monitoring and causes drug interactions
- Explain why bromide has a very long half-life and why it is avoided in cats
- State the role of levetiracetam and other add-on drugs
- Outline the stepwise approach to status epilepticus and the main species cautions

Seizures, epilepsy and the aim of treatment

A **seizure** is a sudden, abnormal and excessive electrical discharge of brain neurons that shows as a change in behaviour, movement or consciousness. **Epilepsy** means recurrent seizures that arise from the brain itself. A seizure can also be a symptom of another problem, such as hypoglycaemia, hypocalcaemia, a liver shunt, toxins or a brain tumour. These are called reactive or structural causes, and treating the cause matters more than giving an anticonvulsant.

Anticonvulsants do not cure epilepsy. They raise the seizure threshold so that fewer and milder seizures occur. The usual goal is fewer seizures with acceptable side effects, not zero seizures at any cost. Treatment is usually started when seizures are frequent, are in clusters, last long, or cause severe post-ictal signs, and the owner must understand that it is lifelong in most dogs.

Most drugs work in one or more of three ways. They **enhance inhibition** (more GABA effect), they **block excitation** (block sodium or calcium channels, or reduce glutamate), or they **change neurotransmitter release** at the nerve terminal.

Phenobarbital

Phenobarbital is a barbiturate and remains a first-choice drug in dogs and an option in cats and horses. It binds the $GABA_A$ receptor and prolongs the opening of the chloride channel, so the neuron becomes harder to fire. It also reduces excitatory glutamate effects at higher concentrations.

Three ideas make it easy to understand.

- **Slow onset.** A steady blood level takes some days to build up, because the half-life is long. It is therefore not a drug for stopping a seizure that is happening now.

- **Enzyme induction.** Phenobarbital induces liver microsomal enzymes. Over weeks it speeds up its own breakdown (so the blood level can fall on the same dose) and the breakdown of other drugs such as some other anticonvulsants, corticosteroids and many others. Stopping it reverses this and can make other drugs suddenly stronger.
- **Liver effects.** Mild enzyme rises are common and often harmless, but long use at high blood levels can cause real liver injury. Serum levels and liver tests are therefore checked from time to time.

Common early side effects are sedation, ataxia, increased appetite, thirst and urination. These often fade over a few weeks. Rarely, blood cell changes occur. Doses are never stopped suddenly, because withdrawal can provoke seizures, including status epilepticus.

Bromide

Potassium or sodium bromide is an old drug that is still very useful. Bromide ions compete with chloride ions and enter neurons through chloride channels, which makes the cell membrane hyperpolarised and harder to excite.

The key concept is the **very long half-life**, measured in weeks. Because of this, a steady-state level takes several months to reach, and the drug is cleared by the kidney, not the liver. This is why it is a good partner for phenobarbital in dogs with liver trouble or when phenobarbital alone is not enough, and why a missed dose matters little once at steady state.

Bromide handling follows chloride handling by the kidney. If the dog eats a high-salt (high-chloride) diet, bromide is excreted faster and the level falls. If salt intake is cut, the level rises. A sudden change in diet can therefore cause breakthrough seizures or toxicity. Typical side effects are sedation, ataxia, thirst, appetite increase and sometimes pancreatitis or skin reactions.

Cats are different. A good proportion of cats given bromide develop a cough or an asthma-like airway disease, so it is generally avoided in this species.

Levetiracetam, imepitoin and other drugs

Levetiracetam binds synaptic vesicle protein SV2A and reduces abnormal neurotransmitter release. It has few drug interactions and little liver metabolism, and

it is generally well tolerated, with mild sedation or ataxia the commonest effects. Its weakness in dogs is a short half-life, so it needs frequent dosing or an extended-release form. It is used as an add-on in dogs with poor control, and in cats and horses. It is also a useful drug in animals with liver disease because it is not heavily metabolised there.

Zonisamide blocks sodium and calcium channels and is used as an add-on in dogs. **Imepitoin** is a partial agonist at the benzodiazepine site of the $GABA_A$ receptor. It is licensed for idiopathic epilepsy in dogs in some countries; check whether it is marketed in India. **Gabapentin** and **pregabalin** act on calcium channels and are used as add-ons, and gabapentin is also an analgesic. **Phenytoin** is a sodium channel blocker that is poorly suited to dogs because it is cleared quickly there.

The general rule: start with one drug, give it time and measure the blood level when possible, then add a second drug with a different mechanism if control is poor. Combining two drugs that act in the same way adds side effects more than benefit.

Status epilepticus and cluster seizures

Status epilepticus means a seizure lasting more than a few minutes, or seizures repeating without recovery between them. It is an emergency because prolonged seizures cause hyperthermia, hypoxia, brain swelling and death. **Cluster seizures** are several seizures within a short period.

The approach is by steps.

1. **Stabilise.** Secure the airway, give oxygen, and place an intravenous catheter. Check blood glucose, calcium and body temperature. Hypoglycaemia and hypocalcaemia are quickly corrected and treat the cause.
2. **Stop the seizure with a benzodiazepine.** Diazepam or midazolam acts within a minute or two on $GABA_A$ receptors. If there is no vein, rectal diazepam or intranasal or intramuscular midazolam can be used. The effect is short, so the next drug must follow.
3. **Give a long-acting drug.** Intravenous phenobarbital or levetiracetam is used to hold the control. Levetiracetam is useful when liver disease or sedation is a concern.

4. **If seizures continue,** a constant rate infusion of midazolam or propofol, or general anaesthesia, is used under monitoring with ventilatory support.

Cool the animal if the temperature is high, and look for the underlying cause once stable. Owners of epileptic dogs may be taught to give rectal diazepam at home for clusters.

Common confusions and species cautions

Seizure is not the same as epilepsy, and a first seizure does not always need a drug. **Phenobarbital is both an anticonvulsant and a sedative,** so early sedation does not mean the dose is too high. **Blood levels are a guide, not a target.** The animal is treated, not the number.

Species points matter. **Dogs** metabolise many anticonvulsants quickly, so drugs such as phenytoin are poor choices. **Cats** are sensitive to many drugs; bromide is avoided, and oral diazepam has been linked to rare, severe liver failure, so liver tests are advised if it is used. Cats also clear drugs slowly because of limited glucuronidation, which is a reason to take care with dosing. **Horses and foals** have seizures from trauma, hypoxic injury or infection, and diazepam, phenobarbital or other drugs are used under veterinary advice. **Cattle, sheep and goats** rarely have true epilepsy. Seizures in these species usually signal a cause such as polioencephalomalacia, hypomagnesaemia, lead poisoning or listeriosis, and treating the cause is the key step. **Food animals** need attention to drug residues and withdrawal periods; check the current rules for any extra-label drug use.

Finally, never stop an anticonvulsant suddenly, and warn owners about the sedation that appears in the first weeks.

Concept cleared

Concept cleared: Raising the seizure threshold

Think of a brake on a car going downhill. Seizure drugs do not remove the hill (the cause of the over-excitable brain); they add brakes. GABA drugs press the brake pedal, sodium channel blockers slow the engine, and SV2A drugs cut the fuel supply. More than one brake can be used together.

Concept cleared: Enzyme induction by phenobarbital
Phenobarbital is like a worker who trains the factory to make more machines. The liver builds more drug-metabolising enzymes, so phenobarbital itself and other drugs are cleared faster. When the worker leaves, the extra machines remain for a while and then fade, so other drugs can suddenly become stronger.

Concept cleared: Bromide and chloride
Bromide enters the body like a guest using chloride's ticket. The kidney cannot easily tell them apart, so a salty diet pushes bromide out, and a low-salt diet keeps it. Because the guest stays for weeks, a steady level takes months and the diet must stay constant.

Concept cleared: Why benzodiazepines are used first in an emergency
A benzodiazepine opens the GABA door wider within a minute, so it stops the seizure quickly. But it leaves quickly too, like a fire extinguisher. A long-acting drug is then needed to keep the fire from restarting.

Memory aid: Phenobarbital side effects: 'SAPPP'
Sedation, Ataxia, Polyphagia, Polydipsia, Polyuria. Also remember Liver and Interactions (induction). For the status epilepticus order, remember 'Safe, Stop, Sustain': Stabilise the animal, Stop with a benzodiazepine, Sustain with a long-acting drug.

Compare and contrast

Main anticonvulsants compared

Drug	Main action	Key strength	Key caution
Phenobarbital	Enhances GABA-A chloride channel	Effective, cheap, widely used	Slow onset, enzyme induction, liver effects, sedation
Bromide	Chloride-channel entry, hyperpolarisation	Not liver metabolised; useful add-on	Weeks to steady state; diet chloride; avoid in cats
Levetiracetam	Binds SV2A, reduces release	Few interactions, well tolerated	Short half-life in dogs; add-on use
Zonisamide	Blocks Na and Ca channels	Add-on in dogs	Check species and availability
Diazepam or midazolam	Enhances GABA-A	Fast emergency control	Short effect; oral diazepam in cats risks liver injury

Emergency step versus maintenance

Feature	Emergency drugs	Maintenance drugs
Examples	Diazepam, midazolam, propofol	Phenobarbital, bromide, levetiracetam
Onset	Seconds to minutes	Days to months
Duration	Short	Long
Purpose	Stop an ongoing seizure	Reduce future seizures
Route	Intravenous, rectal, intranasal	Mostly oral

Species notes

Dog

Idiopathic epilepsy is common. Phenobarbital and bromide are classic drugs, and levetiracetam and others are add-ons. Phenytoin is a poor choice because it is cleared quickly.

Cat

Phenobarbital is commonly used, and levetiracetam is a good add-on. Bromide is generally avoided because of airway disease, and oral diazepam has been linked to rare severe liver failure.

Horse and foal
Seizures in foals often follow hypoxic injury or infection. Diazepam and phenobarbital are used under veterinary advice, and the cause is investigated.

Cattle, sheep and goat
True epilepsy is rare. Seizures usually point to polioencephalomalacia, hypomagnesaemia, lead poisoning or listeriosis, so treating the cause is the key step.

Food-producing animals
Anticonvulsant use is extra-label. Withdrawal periods and residue rules must be checked in the current Indian guidance before any use.

Clinical pearls

Self-test: 10 questions

1. Which is the main action of phenobarbital?

Phenobarbital prolongs chloride channel opening at the GABA-A receptor and makes the neuron harder to fire.

2. Why can phenobarbital blood levels fall on a constant dose over several weeks?

Phenobarbital induces liver enzymes that speed up its own metabolism.

3. Why is bromide avoided in cats?

A good proportion of cats develop cough or asthma-like disease on bromide.

4. A dog on bromide is moved to a high-salt diet. What is expected?

More chloride intake increases bromide excretion by the kidney.

5. Which drug binds SV2A?

Levetiracetam acts at synaptic vesicle protein SV2A to reduce abnormal transmitter release.

6. First drug class for stopping an ongoing seizure in status epilepticus?

Benzodiazepines act within minutes on GABA-A receptors.

7. Which should be checked early in a seizing animal?

Hypoglycaemia and hypocalcaemia are fast, correctable causes.

8. Why is bromide useful in a dog with liver disease?

Bromide is excreted unchanged by the kidney.

9. Seizures in a goat kid are most likely to need which approach?

True epilepsy is rare in ruminants, and causes such as polioencephalomalacia are treatable.

10. What is the risk of sudden withdrawal of an anticonvulsant?

The brain has adapted to the drug, and abrupt removal can provoke severe seizures.

Key points to revise

1. Anticonvulsants raise the seizure threshold; they do not cure epilepsy.
2. Main mechanisms are enhancing GABA inhibition, blocking Na or Ca channels and altering neurotransmitter release.
3. Phenobarbital enhances GABA-A chloride channel opening and is slow to reach steady state.
4. Phenobarbital causes enzyme induction, sedation, polyphagia, polyuria and possible liver injury.
5. Bromide has a half-life of weeks, is cleared by the kidney and is avoided in cats.
6. Levetiracetam binds SV2A and has few interactions and little liver metabolism.
7. Status epilepticus is treated by stabilising, giving a benzodiazepine, then a long-acting drug.
8. Ruminant seizures usually signal a cause that must be treated.

Go deeper on this site

- Ch 7. Behaviour-modifying drugs (in this book)
- Ch 8. CNS stimulants, analeptics and respiratory stimulants (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- BMC Veterinary Research: International Veterinary Epilepsy Task Force consensus on antiepileptic drug treatment in dogs
- Wikipedia: Phenobarbital
- Wikipedia: Status epilepticus

CHAPTER 7 OF 33

Behaviour-modifying drugs

How anxiolytics and antidepressants change fear, anxiety and compulsive behaviour in dogs and cats, when drugs actually help, and the safety points and interactions, especially serotonin syndrome, that students must know.

> **After this chapter you can**

- Explain why behaviour drugs are an aid to behaviour modification and not a replacement
- Describe the actions of benzodiazepines, buspirone, trazodone and gabapentin as anxiolytics
- Describe the actions of SSRIs, tricyclic antidepressants and MAO-B inhibitors
- Explain serotonin syndrome and the drug combinations that cause it
- State the main cautions in cats and dogs

When drugs help and when they do not

Fear, anxiety and aggression are common reasons why dogs and cats are surrendered or abandoned. Drugs can help, but they do not teach an animal what to do instead. A **behaviour modification plan** (training, management of the environment, and a calmer routine) is the base, and the drug is a helper that lowers the anxiety enough for the animal to learn.

The first step is always to look for a **medical cause**. Pain, thyroid disease, urinary problems, itching or cognitive decline can all present as a behaviour problem. A cat that urinates outside the box may have cystitis, not a behaviour disorder.

Drugs are most useful in three situations: a **situational** fear, such as thunder, fireworks, travel or a vet visit; a **chronic anxiety** disorder, such as separation anxiety or generalised anxiety; and **compulsive disorders**, such as tail chasing or over-grooming. Drugs are less useful for a normal behaviour that the owner finds unwelcome. Pheromone products (for example, dog or cat appeasing pheromones) are not drugs in the usual sense and can be used alongside.

Anxiolytics: benzodiazepines, buspirone, trazodone and gabapentin

Anxiolytics work fast or work slowly. This difference decides how they are used.

- **Benzodiazepines** (diazepam, alprazolam, lorazepam) enhance $GABA_A$ receptor action and act in an hour or less. They suit predictable events such as thunderstorms. Cautions: sedation, ataxia, and **disinhibition**, in which an anxious animal becomes more bold and may bite. They may also impair learning and can be habit forming. In cats, oral diazepam has been reported to cause rare, serious liver injury.

- **Buspirone** is a partial agonist at serotonin 5-HT_{1A} receptors. It takes weeks to work, has little sedation and does not cause dependence. It has been used in cats with fear or social anxiety and spraying.
- **Trazodone** blocks 5-HT_{2A} receptors and weakly blocks serotonin reuptake. It is used for situational anxiety, for example before a vet visit or during confinement after surgery. It can cause sedation and, with other serotonergic drugs, serotonin syndrome.
- **Gabapentin** acts on calcium channels and is calming in cats before a vet visit. Sedation is its main side effect.
- **Alpha-2 agonists** such as dexmedetomidine given through the cheek are used for noise aversion in some countries. Check what is marketed locally.

Antidepressants: SSRIs, tricyclics and MAO-B inhibitors

Antidepressants are used for long-term anxiety and compulsive behaviour. They do not work at once. Benefit takes **several weeks**, so owners must be told to give them daily and to avoid giving up early.

Selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine and sertraline, block the serotonin transporter, so more serotonin stays in the synapse. Over time the receptors adapt, and this slow adaptation is why the effect is delayed. Common effects are reduced appetite, mild lethargy, gastrointestinal upset and, in some animals, an early increase in restlessness.

Tricyclic antidepressants (TCAs), such as clomipramine and amitriptyline, block reuptake of serotonin and noradrenaline. They also block muscarinic, histamine and alpha-1 receptors, which causes dry mouth, constipation, urine retention, sedation and low blood pressure. They can affect heart rhythm, so a heart check is wise in older animals or those with heart disease. Clomipramine is licensed for separation anxiety in dogs in some countries; check the current Indian status.

Selegiline inhibits monoamine oxidase B and is used in some countries for canine cognitive dysfunction and sometimes for anxiety. It must never be combined carelessly with other serotonergic drugs.

Safety, interactions and serotonin syndrome

Serotonin syndrome is a toxic excess of serotonin, most often caused by combining two or more drugs that raise serotonin. Signs include agitation, tremor, hyperthermia, sweating or panting, diarrhoea, fast heart rate and, in severe cases, seizures. It is treated by stopping the drugs, supportive care and cooling, with a benzodiazepine for tremor and seizures, under veterinary advice.

Drug combinations to be careful about include:

- SSRI or TCA with **selegiline** or other MAO inhibitors.
- SSRI or TCA with **tramadol**, which also affects serotonin, and with **trazodone** or buspirone.
- **Amitraz** (a tick treatment) has MAO-inhibiting effects, so caution is advised in dogs on these drugs.
- Cough preparations or other products containing serotonergic ingredients.

Other points: an SSRI or TCA is stopped by gradual withdrawal, not suddenly. These drugs can lower the seizure threshold, so use caution in epileptic animals. Liver and kidney function influence how they are cleared. Blood tests before and during long-term therapy are usual practice. Never give human preparations without veterinary advice, because the formulations may contain xylitol or other unsafe additives, and the effective amount differs by species. Check the current notifications on controlled drugs, because some of these drugs, such as benzodiazepines, may be regulated.

Dogs and cats in practice

In **dogs**, SSRIs and clomipramine are used for separation anxiety, generalised anxiety and compulsive disorders. Benzodiazepines, trazodone, gabapentin or a cheek-applied alpha-2 agonist are chosen for noise phobias and travel, often started before the event, because they work better when given early than after the fear has set in. Some dogs need a combination, such as a daily SSRI plus a situational drug.

In **cats**, fluoxetine or clomipramine can be used for urine spraying, over-grooming and some anxiety disorders after medical causes are excluded. Buspirone is also used. Cats are sensitive to many drugs, and tablets can be hard to give, so it is important to choose a form the owner can manage. Cats clear many drugs slowly,

so dosing is individual and the veterinarian's advice must be followed. Over-grooming may be itch, not anxiety, so check the skin first.

Follow up is part of the treatment. Review the animal after a few weeks, record appetite, sleep, activity and the target behaviour, and plan a slow reduction after a long period of good control. Do not assume the drug has failed before several weeks have passed.

Common confusions

Sedation is not the same as calming. A drug that makes the animal sleepy may leave the fear unchanged, and it can make learning harder. **Fast drugs and slow drugs are not interchangeable.** A daily SSRI will not help a dog on the day of a thunderstorm unless it has already been given for weeks, and a benzodiazepine does not treat chronic anxiety well.

Antidepressants are used in animals for anxiety and compulsion, not depression. The word describes the drug class, not the problem being treated.

A paradoxical reaction is a known effect. If an animal becomes more excited or aggressive after a benzodiazepine, the drug should be stopped. **Pheromones and nutraceuticals** have a limited evidence base compared with drugs but are safe companions to behaviour work.

Finally, remember the limits of a veterinarian's role in India: many of these drugs are human products used extra-label, so the owner should be told this, and the responsibility for monitoring remains with the veterinarian.

Concept cleared

Concept cleared: Drug as a helper to training
A drug is like training wheels on a bicycle. It keeps the animal steady enough to practise a new skill, but it does not ride the bicycle for it. When training stops, the benefit may fade.

Concept cleared: Why SSRIs take weeks

Raising serotonin in the synapse happens within hours, but the brain's receptors and nerve connections adapt slowly. Think of turning up the volume on a radio at once, but the room taking weeks to get used to the sound.

Concept cleared: Serotonin syndrome

Each serotonergic drug adds water to the same bucket. One drug may keep it below the brim, but two or three can overflow. That overflow is hyperthermia, tremor, agitation and seizures.

Concept cleared: Disinhibition

An anxious animal is held back by fear, like a car with the handbrake on. Some benzodiazepines release the handbrake before the animal has learned to behave calmly, so a fearful animal can become bold or aggressive.

Memory aid: Behaviour drug plan: 'MBD'

Medical cause first, Behaviour modification second, Drug third. For antidepressants remember 'Weeks, not days', and for serotonin syndrome remember 'too much serotonin: hot, shaky, agitated'.

Compare and contrast

Fast and slow behaviour drugs

Group	Examples	Onset	Best use
Benzodiazepines	Diazepam, alprazolam	Minutes to an hour	Predictable events such as storms
Trazodone, gabapentin	Trazodone, gabapentin	About an hour	Vet visits, travel, confinement
Buspirone	Buspirone	Weeks	Mild anxiety, cats
SSRIs	Fluoxetine, sertraline	Weeks	Chronic anxiety, compulsive disorders
TCAs	Clomipramine, amitriptyline	Weeks	Separation anxiety, compulsive behaviour

SSRIs and TCAs compared

Feature	SSRI	TCA
Main action	Blocks serotonin reuptake	Blocks serotonin and noradrenaline reuptake
Other receptor effects	Few	Muscarinic, histamine, alpha-1 blockade
Typical side effects	Reduced appetite, GI upset, restlessness	Dry mouth, constipation, sedation, heart effects
Special caution	Serotonin syndrome with MAO-B inhibitors	Heart disease, urine retention, seizures

Species notes

Dog

SSRIs and clomipramine are used for chronic anxiety and compulsive behaviour. Benzodiazepines, trazodone and gabapentin are used for situational fear. Give situational drugs before the trigger.

Cat

Fluoxetine, clomipramine, buspirone and gabapentin are used. Oral diazepam has been linked to rare severe liver injury. Exclude cystitis and skin disease before treating behaviour.

Horse

Farm animals

Behaviour drugs are rarely used. If used, check the rules for competition animals, because many of these drugs are prohibited substances.

Behaviour-modifying drugs are rarely used, and residue rules apply to food animals. Check the current guidance before any use.

Birds and exotics
Feather plucking has many medical causes, so look for disease and husbandry faults before drugs.

Clinical pearls

Self-test: 10 questions

1. What should be done first in an animal with a new behaviour problem?

Pain, endocrine and urinary disease can all appear as behaviour change.

2. Which drug is a 5-HT1A partial agonist?

Buspirone acts at serotonin 5-HT1A receptors and takes weeks to work.

3. Why do SSRIs take weeks to work?

The delayed effect is due to slow adaptive changes after serotonin rises.

4. Which problem may occur with benzodiazepines in an anxious dog?

Release of inhibition can make a fearful animal bold or aggressive.

5. A drug combination at risk of serotonin syndrome is:

An SSRI plus an MAO inhibitor increases serotonin excessively.

6. A drug that blocks muscarinic and histamine receptors as well as reuptake pumps is:

TCAs have anticholinergic and antihistamine effects.

7. For a dog with storm phobia, the best timing of a situational drug is:

Early dosing prevents the fear response from building up.

8. Selegiline is an inhibitor of which enzyme?

It inhibits MAO-B and is used for canine cognitive dysfunction in some countries.

9. Which cat problem was linked to oral diazepam?

Idiosyncratic hepatic failure has been reported.

10. Which statement about antidepressants in animals is correct?

The name is a class label; the usual targets are anxiety and compulsion.

Key points to revise

1. Behaviour drugs support behaviour modification and do not replace it.
2. Benzodiazepines are fast but may cause disinhibition and sedation.
3. Buspirone is a 5-HT1A partial agonist with a slow onset.
4. Trazodone and gabapentin are used for situational anxiety.
5. SSRIs block the serotonin transporter and take weeks to work.
6. TCAs have extra anticholinergic, antihistamine and heart effects.
7. Serotonin syndrome follows combinations of serotonergic drugs.

8. Check current Indian regulation for controlled drugs and extra-label use.

Go deeper on this site

- Ch 8. CNS stimulants, analeptics and respiratory stimulants (in this book)
- Ch 6. Anticonvulsants and drugs for epilepsy (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Wikipedia: Fluoxetine
- Wikipedia: Serotonin syndrome
- Wikipedia: Buspirone

CHAPTER 8 OF 33

CNS stimulants, analeptics and respiratory stimulants

How doxapram and the xanthines stimulate breathing and the brain, why analeptics are used less today, strychnine as a toxicant, and the practical approach to neonatal resuscitation and drug reversal.

After this chapter you can

- Define analeptics and respiratory stimulants and explain why their use has declined
- Describe the mechanism, uses and cautions of doxapram
- Describe the actions, toxicity and species points of xanthines such as theophylline, caffeine and theobromine
- Explain strychnine toxicity and its treatment
- Outline neonatal resuscitation and the role of specific reversal drugs

What are CNS stimulants and analeptics

CNS stimulants raise the activity of the brain and spinal cord. They work in three broad ways: they **block inhibition** (for example strychnine at glycine receptors and

picrotoxin at GABA channels), they **increase excitatory transmission or release of amines** (amphetamines), or they **block adenosine** (xanthines such as caffeine). **Analeptics** are stimulants used to reverse CNS and respiratory depression, for example after anaesthesia or overdose.

Older analeptics such as nikethamide, pentylenetetrazol and picrotoxin have a very narrow gap between stimulation and convulsion and are no longer used in modern practice. Today the useful drugs are few: doxapram, the xanthines, and, more importantly, **specific antagonists** for the depressant that was given.

The main idea: a stimulant does not replace oxygen or ventilation. A breathing animal that is hypoxic is helped first by airway care, oxygen and ventilation. A stimulant increases oxygen demand of the brain and heart, so it can make a bad situation worse.

Doxapram

Doxapram is the main respiratory stimulant in veterinary use. It acts mainly on the **peripheral chemoreceptors** in the carotid and aortic bodies, which tell the brain that oxygen is low. At larger amounts it also stimulates the respiratory centre in the medulla. Breathing becomes deeper and faster. It is given intravenously and acts within a minute or so, but the effect is short, so it may wear off before the depressant drug does.

Uses include stimulating breathing and wakefulness after anaesthesia, and speeding recovery of respiratory drive in animals depressed by some drugs. It is also used in practice to stimulate newborn animals (see below), although this is debated.

Cautions are important.

- Margin of safety is narrow. Higher exposure causes excitement, tremor, hyperventilation and seizures.
- It raises blood pressure and heart rate and can cause arrhythmias. It is risky in animals with heart disease, hypertension, head injury or a seizure history.
- It increases oxygen use by the brain and heart. If the animal is hypoxic, giving doxapram without oxygen can worsen cell injury.

- It does not reverse the depressant drug. It only masks it, so the animal can slip back into depression.
- It is not a substitute for a patent airway and mechanical ventilation.

Doxapram can also change the interpretation of anaesthetic depth tests, because it temporarily raises respiratory rate. Do not use it as a cover for over-dosed anaesthesia.

Xanthines: caffeine, theophylline and theobromine

Xanthines are plant-derived compounds found in coffee, tea, cocoa and kola. They have two main actions: they **block adenosine receptors** and they **inhibit phosphodiesterase**, which keeps cAMP high. Adenosine normally has a calming effect, so blocking it leads to stimulation.

The effects can be remembered by organ. **CNS:** alertness, restlessness, tremor and, at high levels, seizures. **Heart:** faster rate and stronger contraction, with arrhythmias at high levels. **Smooth muscle:** bronchial relaxation, which is why theophylline and aminophylline are used as bronchodilators in dogs, cats and horses. **Kidney:** mild diuresis. **Respiratory centre:** stimulation of breathing, which is why caffeine is used for apnoea of prematurity in human infants.

Theophylline has a narrow therapeutic range. Its clearance differs between species, individuals and with other drugs, so doses are not copied between species. Some drugs, such as certain fluoroquinolones and cimetidine, can slow its metabolism and raise levels, and this must be considered. Signs of excess are vomiting, restlessness, tachycardia and tremor.

Aminophylline is a water-soluble salt of theophylline. Bronchodilator use has declined because safer drugs exist, but the concept is a common exam question.

Methylxanthine toxicosis and strychnine

Chocolate toxicosis is a common emergency in dogs. The toxic agent is mainly **theobromine**, with some caffeine. Dark chocolate and cocoa powder contain much more than milk chocolate. Dogs clear theobromine slowly, and it is recirculated in the bile, so signs can persist. Signs are vomiting, restlessness, tremor, fast heart rate and seizures. Treatment is decontamination if early, supportive care, control of tremors and seizures, and monitoring of the heart.

Strychnine comes from the seeds of *Strychnos nux-vomica* and has been used in rodent and pest baits. Check the current Indian regulations on its use, because many such products are restricted. It acts by **blocking glycine receptors** in the spinal cord. Glycine normally inhibits motor neurons, so without it the animal has exaggerated reflexes and sudden, violent extensor spasms triggered by light, sound or touch. The animal remains conscious, which makes the signs very distressing. Death results from respiratory muscle spasm and exhaustion.

There is no specific antidote. Treatment is by **control of spasms** with sedation or anaesthesia, a quiet dark environment, a muscle relaxant such as methocarbamol, and support of breathing and temperature, plus decontamination if early. Stimulants are never given. Because strychnine is a spinal stimulant and not a seizure of cortical origin, the pattern is different from epilepsy.

Neonatal resuscitation and specific reversal drugs

A newborn that fails to breathe needs a stepwise approach: **clear the airway**, dry and rub the body to stimulate, keep warm, and give **oxygen and ventilation** as needed. These physical steps are the most important. Many current guidelines favour them over drugs. In calves, foals, puppies and kittens, the most common causes of poor breathing are hypoxia during birth, fluid in the airway, cold and drug depression from the dam's caesarean anaesthesia.

Drugs have a limited role. Doxapram is sometimes used as a stimulant, but its value in newborns is debated and it should not replace ventilation. If the dam was given an opioid, the newborn can be treated with a specific antagonist. **Naloxone** reverses opioid depression. Epinephrine is used for cardiac arrest during resuscitation. Blood sugar and body temperature must also be supported.

Specific antagonists are better than analeptics because they act at the receptor that was blocked: **naloxone** for opioids, **atipamezole** or yohimbine for alpha-2 agonists such as xylazine and medetomidine, and **flumazenil** for benzodiazepines. Remember that the antagonist may wear off before the depressant, so the animal must be watched for re-sedation. In ruminants, xylazine is also reversed by specific agents but sensitivity is high, so reversal is used with care.

Common confusions

Analeptic is not the same as respiratory stimulant. All analeptics stimulate the CNS, and some stimulate breathing, but the term is broader than doxapram. **A stimulant is not an antidote.** Doxapram does not remove the depressant drug, it only temporarily opposes its effect. **Strychnine is a toxicant, not a therapeutic drug,** and it is a spinal glycine antagonist, not a respiratory stimulant used in practice.

Caffeine and theophylline have the same mechanism, but differ in potency on organs. Caffeine is stronger on the CNS, and theophylline is stronger on smooth muscle and the heart. **Strychnine convulsions are reflex driven,** so touching or loudly approaching the animal can trigger a spasm.

In food animals, any extra-label use of these drugs needs attention to residues and the current rules.

Concept cleared

Concept cleared: Stimulant is not oxygen
Whipping a tired horse makes it run for a moment but does not feed it. A stimulant makes a depressed animal breathe harder for a short time, but it does not supply oxygen. Airway and ventilation come first.

Concept cleared: Doxapram acts on the oxygen sensors
The carotid and aortic bodies are like smoke detectors for low oxygen. Doxapram tricks the detectors into ringing louder, so the brain makes the animal breathe more. It does not fix the fire.

Concept cleared: Caffeine blocks the brake of adenosine
Adenosine is a natural calming signal. Xanthines sit on its receptor and stop it from working, so the brain, heart and breathing speed up.

Concept cleared: Strychnine removes a brake

Glycine is the brake on spinal motor neurons. Strychnine cuts the brake cable, so any small stimulus sets off a full muscle spasm while the animal stays awake.

Memory aid: Newborn resuscitation: 'ABC then drug'

Airway clear, Breathing supported with oxygen, Circulation checked, and only then drugs. For reversal agents remember 'N-A-F': Naloxone for opioids, Atipamezole for alpha-2 agonists, Flumazenil for benzodiazepines.

Compare and contrast

Stimulant drugs compared

Drug	Mechanism	Main use or concern	Key caution
Doxapram	Stimulates peripheral chemoreceptors and medulla	Respiratory stimulation after anaesthesia	Narrow margin, raises oxygen demand, short effect
Caffeine	Adenosine block, PDE inhibition	CNS and respiratory stimulation	Tremor, tachycardia, seizures
Theophylline	Adenosine block, PDE inhibition	Bronchodilator	Narrow therapeutic range, varies by species
Theobromine	Same mechanism as xanthines	Cause of chocolate toxicosis in dogs	Slow clearance in dogs
Strychnine	Blocks glycine receptors in the spinal cord	Toxicant, not a therapeutic drug	Convulsions triggered by stimuli; no antidote

Specific antagonists versus analeptics

Feature	Specific antagonist	Analeptic
Examples	Naloxone, atipamezole, flumazenil	Doxapram
Target	The receptor of the depressant drug	General CNS or chemoreceptor stimulation
Risk of seizures	Low	Present at high exposure
Preferred when	The depressant is known	Cause is unknown or antagonist unavailable

Species notes

Dog

Chocolate toxicosis from theobromine is common. Strychnine and other baits are a danger, and signs are triggered by stimuli.

Cat

Sensitive to many stimulants and slow to clear drugs. Use reversal agents with care, and avoid giving human products.

Horse

Theophylline and aminophylline have been used as bronchodilators. Caffeine and theobromine are prohibited substances in competition, so check the current rules.

Cattle and small ruminants

Neonatal calves and lambs depend on clearing fluid, drying and warming. Strychnine and baits can poison livestock, and residue rules apply to any drug used.

Newborn puppy, kitten and foal

Physical resuscitation comes first. Naloxone is useful when the dam received an opioid, and doxapram has a debated role.

Clinical pearls

Self-test: 10 questions

1. Doxapram mainly stimulates breathing through:

It acts on the carotid and aortic bodies and, at higher doses, on the medulla.

2. A main risk of giving doxapram to a hypoxic animal without oxygen is:

It raises oxygen use by the brain and heart.

3. Xanthines act by:

These two actions explain CNS, cardiac and bronchial effects.

4. The main toxin in chocolate poisoning in dogs is:

Theobromine is cleared slowly in dogs and is present in cocoa.

5. Strychnine acts by blocking:

Loss of glycine inhibition leads to reflex spasms.

6. A characteristic of strychnine poisoning is:

The animal stays aware and spasms are reflex driven.

7. Best reversal drug for opioid depression in a newborn after caesarean is:

Naloxone is an opioid antagonist.

8. Atipamezole reverses:

It is an alpha-2 antagonist.

9. The first step in neonatal resuscitation is:

Physical steps are the most important.

10. Why has the clinical use of older analeptics such as nikethamide declined?

They provoke seizures with little margin of safety.

Key points to revise

1. Analeptics reverse CNS depression, but most older ones are obsolete.
2. Doxapram stimulates peripheral chemoreceptors and the medullary respiratory centre.
3. Doxapram has a narrow margin and raises oxygen demand.
4. Xanthines block adenosine receptors and inhibit phosphodiesterase.
5. Theophylline has a narrow therapeutic range and species variation.
6. Strychnine blocks glycine receptors in the spinal cord and causes reflex convulsions.
7. Strychnine has no specific antidote; control spasms and support breathing.
8. Neonatal resuscitation relies mainly on airway, drying, warmth and ventilation.

Go deeper on this site

- Ch 9. Euthanasia agents and humane methods (in this book)
- Ch 7. Behaviour-modifying drugs (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Wikipedia: Doxapram

- Wikipedia: Aminophylline
- Wikipedia: Strychnine poisoning

CHAPTER 9 OF 33

Euthanasia agents and humane methods

Euthanasia means a death with minimal pain and distress. This chapter covers the guiding principles, why barbiturate overdose is the standard agent, species-appropriate methods, how death is confirmed and the legal and ethical points relevant to Indian practice.

After this chapter you can

- State the principles that make a method of euthanasia humane
- Explain how a barbiturate overdose causes unconsciousness, respiratory arrest and cardiac arrest
- Choose an appropriate approach for companion animals, horses, ruminants and other species in concept
- List the signs used to confirm death
- Describe the legal and ethical duties of the veterinarian in India, and the need to check current rules

What makes euthanasia humane

The word means a good death. A method is judged humane when it causes **rapid loss of consciousness** followed by death, with as little pain, fear and distress as possible. Two things matter most: how quickly the animal becomes unconscious, and whether the animal is aware of anything unpleasant before that moment.

Other points that guide the choice are reliability and irreversibility, safety of the people present, emotional effect on the owner and staff, suitability for the species and age, and the ability to confirm death. Euthanasia is a clinical procedure and needs the same planning as anaesthesia.

A common confusion is to mix up *euthanasia* with *slaughter* or *humane killing* in a herd emergency. The aim is similar, but the setting, the restraint and the permitted methods differ.

Planning also includes the place and the people. A quiet area, a non-slip surface, a calm handler and all drugs and equipment ready beforehand reduce stress for the animal and the owner. Owners should be told what to expect, including that the eyes may stay open, and should be offered the choice to be present. Good communication is part of humane practice, not an extra.

Another common confusion is between sedation and euthanasia. A sedated animal is still alive and can recover, so the euthanasia agent must still be given and death confirmed. Likewise, loss of consciousness alone is not death.

Barbiturate overdose: mechanism

An overdose of an injectable barbiturate, usually pentobarbital or a related agent, is the standard method for most species. Barbiturates enhance the action of GABA at the $GABA_A$ receptor, prolonging chloride channel opening. At anaesthetic levels they depress the cerebral cortex. Given in overdose, they go on to depress the brainstem respiratory and cardiovascular centres, and finally the heart.

The sequence is predictable. The animal loses consciousness first, then breathing stops, then the heart stops. Because **unconsciousness comes before the vital centres fail**, the animal does not feel the dying process if the drug is delivered properly.

The best route is **intravenous**, because onset is fastest. A calm animal and a clean vein help. Sedation beforehand makes the process gentler in fractious, fearful or aggressive animals and makes venous access easier.

Practical problems with barbiturates

Barbiturate euthanasia has some well known issues that students should be able to explain.

- **Perivascular injection** is painful because the solution is strongly alkaline. This is the main reason to confirm the needle is in the vein, and to sedate or use an alternative route when veins cannot be found.
- **Excitement stage.** If the drug is given slowly or into a poorly perfused vein, the animal may pass through a phase of excitement before unconsciousness. Fast, complete delivery avoids this.

- **Agonal breaths and muscle twitching** can occur after the heart has stopped or as consciousness is lost. They are reflexes and do not mean the animal is suffering, but owners should be warned beforehand.
- **Carcass hazard.** The drug persists in the body. Scavengers, dogs fed meat, or wildlife can be poisoned. Carcasses must be buried deeply or incinerated and never fed to other animals.

Combination products containing a barbiturate with a local anaesthetic or another agent exist in some countries. Availability and legal status in India vary, so check the current notification and local drug-control rules.

Species-appropriate methods and other agents

Dogs and cats. Sedate, place an intravenous catheter if possible, then give the overdose intravenously. In very small or collapsed patients, other routes such as intraperitoneal or intracardiac may be used only when the animal is already deeply unconscious or anaesthetised.

Horses and large ruminants. Sedation is important for safety and calm. A large volume of barbiturate is needed, which is costly, and the horse may collapse suddenly, so the setting and footing must be planned.

Rabbits, rodents, birds and reptiles. Injectable overdose after sedation or anaesthesia is preferred where veins or other routes are reachable. Inhaled anaesthetic overdose is also used for small mammals and birds, with attention to the induction phase being free of irritation.

Other chemical agents. Potassium chloride is acceptable *only* in an animal already under deep general anaesthesia, since it stops the heart but does nothing for consciousness. Used in a conscious animal it would be extremely cruel. Neuromuscular blockers alone are never acceptable, because they paralyse the animal while leaving it aware.

Physical methods. Properly performed captive bolt or gunshot can be conditionally acceptable in large animals and in field emergencies when the operator is trained and the animal is correctly restrained. They are not a casual substitute for drugs.

Confirming death

Never assume death on one sign. Confirm with several, and allow enough time for the effect of the agent.

- No heartbeat on auscultation, for a sufficient period.
- No respiration.
- No corneal or palpebral reflex, with fixed dilated pupils.
- No response to a firm toe pinch.
- Loss of mucous membrane colour and, later, rigor mortis, which is the final proof.

Muscle twitches or a few gasps after the heart has stopped do not mean the animal is alive. A veterinarian should still re-check after a short interval before releasing the body to the owner.

Time of observation matters. After an intravenous overdose the heart usually stops within a short period, but in cold, shocked or very large animals it may take longer. If any sign of life returns, give more agent. Wait until all signs are absent before declaring death, and before the owner or staff handle the body for disposal.

Legal and ethical notes for India

Veterinarians in India work under the Prevention of Cruelty to Animals Act, 1960 and its rules, and under state veterinary council codes. Rules on euthanasia of stray dogs, incurably ill or suffering animals, and on animal birth control programmes are set by notification and have been amended. **Check the current notification** before acting, and follow the written protocol of the institution, municipal body or animal welfare organisation involved.

Controlled drugs also matter. Barbiturates are regulated, and the supply, storage and record keeping must follow current drug-control law. Locally approved agents and their availability may differ from textbook descriptions from other countries.

Ethical practice includes a clear clinical reason, informed owner consent, a quiet place, a trained person to restrain, and respect for the owner's grief. Staff compassion fatigue is real, and a team should be able to talk about it. The decision should be documented, including the agent used and how death was confirmed.

Concept cleared

Concept cleared: Why unconsciousness comes first

Think of a house where the lights are switched off room by room. The brain's higher centres (the lights that give awareness) go dark before the basic engine rooms for breathing and heartbeat. A barbiturate overdose follows this order, so the animal is unaware by the time breathing and the heart stop.

Concept cleared: Why potassium chloride needs anaesthesia

Potassium chloride is like cutting the power to the pump without telling the person at the desk. It stops the heart but does not remove awareness. So it is acceptable only after the animal has been made fully unconscious by a general anaesthetic.

Concept cleared: Perivascular injection

The barbiturate solution is strongly alkaline, like a mild chemical irritant. If it leaks outside the vein, the tissue stings. Checking the catheter and giving sedation first protect the animal from this pain.

Concept cleared: Secondary poisoning

A barbiturate remains active in the body after death. A carcass left in the open is like a poisoned bait for dogs, vultures and wildlife that feed on it, so disposal must be by deep burial or incineration.

Memory aid: Humane euthanasia checklist

S-I-C-D: Sedate, Intravenous overdose, Confirm death with several signs, Dispose of the carcass safely. Remember that unconsciousness must come before anything that stops the heart.

Compare and contrast

Agents and their acceptability

Agent or method	Acts on	Acceptable when	Key caution
Intravenous barbiturate	Brain then heart	First choice for most species	Perivascular injection is painful; carcass hazard
Inhaled anaesthetic overdose	Brain	Small mammals, birds, reptiles	Choose agent without irritation; time to effect
Potassium chloride	Heart only	Only after deep general anaesthesia	No effect on consciousness
Neuromuscular blocker alone	Muscle	Never acceptable alone	Paralyses an aware animal
Captive bolt or gunshot	Brain physically	Trained operator, large animals, field emergencies	Correct placement and restraint essential

Signs for confirming death

Sign	What to check	Common confusion
Heartbeat	Auscultate for adequate time	Weak heart sounds in a collapsed animal
Respiration	Watch chest, no breaths	Agonal gasps after cardiac arrest are reflex
Corneal and palpebral reflex	Touch gently, no blink	Reflexes can persist briefly at deep anaesthesia
Pupils	Fixed and dilated	Some agents change pupil size early
Rigor mortis	Stiffening of muscle	Appears late, not immediate

Species notes

Dog

Sedation then intravenous barbiturate is the usual approach. Warn owners that twitching, a last breath or loss of bladder control can occur after death.

Cat

Small veins and fear make sedation especially useful. Handle gently and in a quiet place, and confirm the injection is truly intravenous.

Horse
Sedate first and plan the collapse and the body removal. Large volumes of drug are needed, and the carcass must be disposed of safely.

Cattle and small ruminants
Sedation and restraint are needed. In herd emergencies or where drugs are not available, trained operators may use accepted physical methods. Follow current rules.

Birds and small mammals
Anaesthetic overdose by inhalation or injection after sedation is preferred. Avoid methods that cause fear or irritation during induction.

Clinical pearls

Self-test: 10 questions

1. Which sequence best describes death after an intravenous barbiturate overdose?

The cortex is depressed first, so awareness is lost before the brainstem centres and heart fail.

2. The main reason barbiturate solutions are painful if injected outside the vein is that they are

The strongly alkaline solution irritates perivascular tissue.

3. Potassium chloride may be used for euthanasia only when the animal is

It stops the heart but does not cause unconsciousness, so awareness must already be abolished.

4. Why is a neuromuscular blocking agent alone unacceptable for euthanasia?

It does not cause unconsciousness or analgesia, so the animal may feel distress while unable to move.

5. A dog's chest moves in a gasp a few seconds after the heart has stopped. This is best explained as

Agonal breaths are reflex activity of a dying brainstem and do not indicate awareness.

6. Which statement about disposal of a carcass after barbiturate euthanasia is correct?

The drug persists and can poison animals that eat the carcass.

7. Which is the best sign sequence to confirm death?

Several signs are needed, because single signs can mislead.

8. Why is sedation before euthanasia useful in a fractious cat?

Sedation lowers distress and makes a clean intravenous injection more likely.

9. Before euthanising stray animals or for legal questions in India, the veterinarian should

Rules and notifications are amended, so current ones must be consulted.

10. For a small bird or rodent, which approach is commonly accepted?

Anaesthetic overdose gives unconsciousness before death, if induction is free of irritation.

Key points to revise

1. Euthanasia means rapid unconsciousness and death with minimal pain and distress.
2. Barbiturate overdose depresses cortex, then brainstem, then heart.
3. Intravenous route gives the fastest and gentlest result.
4. Sedation helps fearful, aggressive and difficult patients.
5. Agonal breaths and twitching are reflexes and not evidence of suffering, but owners should be told.
6. Potassium chloride is acceptable only in an animal under deep general anaesthesia.
7. Death is confirmed by absent heartbeat, breathing and reflexes, with rigor as final proof.
8. Indian rules and drug availability change, so always check the current notification.

Go deeper on this site

- Ch 10. Histamine and antihistamines (in this book)
- Ch 8. CNS stimulants, analeptics and respiratory stimulants (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- AVMA: Guidelines for the Euthanasia of Animals
- University of Minnesota Libraries: Principles of Pharmacology study guide
- Merck Veterinary Manual: Overview of Anti-inflammatory Agents (general pharmacology reference)

CHAPTER 10 OF 33

Histamine and antihistamines

Histamine is a tissue autacoid released from mast cells and basophils that acts on H1 to H4 receptors. This chapter explains H1 and H2 effects, how anaphylaxis

develops, the antihistamine classes, and why sedation and species differences matter in practice.

After this chapter you can

- Describe where histamine is stored and what triggers its release
- Contrast the actions of H1 and H2 receptors and name the main antagonists for each
- Explain the mechanism of anaphylaxis and why adrenaline, not an antihistamine, is the first-line drug
- Distinguish first-generation from second-generation H1 antihistamines
- State the sedation, anticholinergic and species cautions that apply to antihistamines

Histamine: source, release and receptors

Histamine is a small amine made from the amino acid histidine by the enzyme histidine decarboxylase. It is stored in granules of **mast cells** and **basophils**, and in enterocytochromaffin-like cells of the stomach and in some neurons. In most species mast cells are the main reservoir, found close to skin, gut, airway and blood vessels.

Release happens in two broad ways. The *immunological* route follows cross-linking of IgE on the mast cell surface by antigen, as in allergy and anaphylaxis. The *non-immunological* route follows direct drug or physical action; some drugs such as certain opioids, muscle relaxants and contrast agents can degranulate mast cells without any antibody.

Histamine acts on four G-protein-coupled receptors. **H1** works through Gq and the IP3/DAG pathway. **H2** works through Gs and raises cAMP. **H3** is mainly a presynaptic receptor in the nervous system, and **H4** is found on immune cells. For day-to-day veterinary pharmacology, H1 and H2 matter most.

H1 and H2 actions

The effects of histamine depend on which receptor is stimulated and where.

- **H1:** contraction of bronchial and intestinal smooth muscle, increased capillary permeability (oedema, wheal), vasodilation of small vessels, and itch through sensory nerve endings. In the brain, H1 stimulation promotes wakefulness, which is why blocking it causes drowsiness.
- **H2:** stimulation of gastric acid secretion from parietal cells, plus some cardiac stimulation and vasodilation.

The classic skin response, the "triple response", shows local redness, spread of flare through an axon reflex, and a wheal from leaky capillaries. This is the picture of urticaria seen in a dog after a vaccine reaction or insect sting.

A common confusion is to think histamine alone drives all allergic signs. It does not. Mast cells also release leukotrienes, prostaglandins, platelet-activating factor and proteases, which is why an antihistamine may relieve itch but not fully reverse bronchospasm or shock.

Anaphylaxis

Anaphylaxis is an acute, severe, systemic type I hypersensitivity reaction. A sensitised animal meets the antigen again, IgE on mast cells and basophils is cross-linked, and a sudden mass release of mediators follows. Common triggers in practice include injectable antibiotics (especially penicillins), vaccines, antisera, iron dextran, and insect stings.

The target organ differs between species, and this is a favourite exam point. In the **dog** the liver and gut are the main shock organs, with vomiting, diarrhoea, collapse and hepatic venous pooling. In the **cat** and **horse** the lung is prominent, with bronchospasm and respiratory distress. In **cattle** the lungs and also the udder and skin are involved, and in sheep and pigs respiratory and circulatory signs predominate.

Treatment rests on **adrenaline (epinephrine)** given promptly, together with fluids, oxygen and airway support. Adrenaline acts as a physiological antagonist: through beta and alpha receptors it reverses bronchospasm and vasodilation and stabilises mast cells. An H1 antihistamine is only an *adjunct*. It blocks further histamine action on receptors but does not displace histamine already bound, nor does it counter the other mediators. Corticosteroids are slow and also adjunctive.

Prevention matters too: keep the animal under observation after vaccination or injection, and record previous reactions.

H1 antihistamine classes

H1 antagonists are better described as **inverse agonists**: they stabilise the inactive receptor, and they compete with histamine at the receptor. They are grouped into generations.

First-generation drugs include diphenhydramine, chlorpheniramine, promethazine, pheniramine, hydroxyzine and cyproheptadine. They are lipid soluble and cross the blood-brain barrier easily. They cause sedation, and because they also block muscarinic receptors they cause dry mouth, urinary retention, tachycardia and reduced gut motility. Some, such as promethazine and dimenhydrinate, are used for motion sickness and vomiting through central and vestibular effects. Cyproheptadine also blocks 5-HT receptors, which is why it is used as an appetite stimulant in cats.

Second-generation drugs include cetirizine, loratadine, fexofenadine and levocetirizine. They are less lipophilic or are pumped out of the brain by P-glycoprotein, so sedation and anticholinergic effects are weaker. Their duration of action is generally longer.

Pharmacokinetics differ widely between species, so a human product cannot simply be assumed to work in an animal. Evidence for antihistamine benefit in canine atopic dermatitis is modest, and they are more useful as preventive or mild-case agents than for acute severe itch.

H2 blockers and other antihistaminic drugs

H2 antagonists such as ranitidine, famotidine and cimetidine block the histamine receptor on the parietal cell and reduce gastric acid output. They are used in gastric ulcer, gastritis and oesophagitis, though proton pump inhibitors suppress acid more strongly. Famotidine is generally preferred over cimetidine because cimetidine inhibits hepatic cytochrome P450 enzymes and causes more drug interactions. Check the current availability of ranitidine in India, as regulatory changes have affected it in several countries.

Mast cell stabilisers such as sodium cromoglycate prevent degranulation rather than block receptors. **Functional antagonists** such as adrenaline oppose histamine effects through other receptors. This three-way grouping (receptor blockers, release inhibitors, physiological antagonists) is a useful way to remember how histamine action can be countered.

Do not confuse H1 antihistamines, which give relief from allergy, with H2 blockers, which are used for acid disorders. They are not interchangeable.

Sedation and species cautions

Sedation is the commonest adverse effect of first-generation H1 drugs and is sometimes used on purpose, for example in anxious or itchy animals at night. It adds to the effect of other sedatives, opioids and anaesthetics, so combined use needs care.

Anticholinergic effects make these drugs unsuitable in animals with glaucoma, urinary outflow obstruction, severe cardiac arrhythmia or paralytic ileus. In pregnant or lactating animals, use only when the benefit is clear.

Cats are sensitive to some antihistamine preparations, and chlorpheniramine is one of the few commonly used for pruritus. Avoid human combination products containing decongestants or paracetamol, which are dangerous in cats. **Horses** may show excitement rather than sedation with first-generation drugs. In **food animals**, antihistamines used in anaphylaxis are given under veterinary advice and withdrawal periods and MRLs should be checked in the current notification. Competition horses may also face prohibited-substance rules.

Always weigh the benefit of an antihistamine against what else the animal is receiving. Most serious problems come from drug combinations or from ignoring the anticholinergic burden.

Concept cleared

Histamine is stored, not made on demand
Preformed histamine sits in mast cell granules and is released within seconds. This explains the speed of anaphylaxis.

Two main receptors, two main jobs

H1 mediates allergy, itch, bronchoconstriction and wakefulness. H2 mediates gastric acid secretion. Blockers are receptor specific.

Antihistamines prevent, they do not reverse

H1 blockers compete with free histamine, so they work best given early. In established anaphylaxis, adrenaline is the lifesaving drug.

Generation predicts side effects

First-generation drugs cross the brain and block muscarinic receptors. Second-generation drugs are far less sedating.

Memory aid: H1 and H2 in one line

H1 = 'Hives, Hissing airways, Hypnotic when blocked'. H2 = 'Hydrochloric acid, Two parietal cells'. Adrenaline is the answer to anaphylaxis, not an antihistamine.

Compare and contrast

H1 versus H2 receptors

Feature	H1	H2
G protein / messenger	Gq, IP3 and DAG	Gs, cAMP
Main effects	Bronchoconstriction, vascular leak, itch, wakefulness	Gastric acid secretion
Antagonists	Chlorpheniramine, cetirizine	Famotidine, ranitidine
Main use	Allergy, pruritus, motion sickness	Ulcer, gastritis, reflux

First versus second-generation H1 blockers

Feature	First generation	Second generation
Examples	Diphenhydramine, chlorpheniramine, promethazine	Cetirizine, loratadine, fexofenadine
Brain entry	High	Low
Sedation	Common	Mild or absent
Anticholinergic effects	Marked	Minimal
Duration	Shorter	Generally longer

Species notes

Dog

Liver and gut are the shock organs in anaphylaxis. Urticaria and facial swelling are common after stings and vaccines.

Cat

Respiratory distress is prominent in anaphylaxis. Avoid human combination cold products, which may contain paracetamol.

Horse

Lung involvement is typical in anaphylaxis. First-generation antihistamines may cause excitement in some animals.

Cattle and small ruminants

Anaphylaxis after injectables or feed allergens can show as respiratory and circulatory collapse. Check withdrawal periods and MRLs in the current notification.

Pig and poultry

Reactions to injectables and vaccines occur; treatment relies on adrenaline and supportive care under veterinary advice.

Clinical pearls

Self-test: 10 questions

1. Histamine is mainly stored in:

Preformed histamine sits in granules of mast cells and basophils and is released on degranulation.

2. Which receptor mediates gastric acid secretion?

H2 on parietal cells raises cAMP and promotes acid secretion.

3. First-line drug in anaphylaxis is:

Adrenaline reverses bronchospasm and vasodilation; antihistamines and steroids are adjuncts.

4. The H1 receptor signals through:

H1 is Gq coupled, activating phospholipase C.

5. Which is a second-generation antihistamine?

Cetirizine is poorly sedating because of limited brain penetration.

6. The main shock organ in canine anaphylaxis is typically the:

Dogs show hepatic and gastrointestinal involvement, unlike cats and horses where the lung predominates.

7. Why is cimetidine less preferred than famotidine?

Enzyme inhibition causes more drug interactions.

8. Cyproheptadine is used as an appetite stimulant because it:

Its serotonin antagonism is responsible for the appetite effect.

9. Sodium cromoglycate acts by:

It prevents degranulation instead of blocking receptors.

10. An important anticholinergic caution with first-generation antihistamines is:

Muscarinic blockade raises intraocular pressure and impairs bladder emptying.

Key points to revise

1. Histamine is stored in mast cells and basophils and released on IgE cross-linking or direct drug action.
2. H1 and H2 are G-protein-coupled receptors with different messengers and effects.
3. H1 stimulation causes bronchospasm, vascular leak and itch.
4. H2 stimulation drives gastric acid secretion.
5. Anaphylaxis is a type I hypersensitivity; the shock organ varies by species.
6. Adrenaline is the first-line drug in anaphylaxis.
7. First-generation H1 blockers are sedating and anticholinergic; second-generation drugs are less so.
8. Cats and horses need specific cautions with antihistamines.

Go deeper on this site

- Ch 11. Eicosanoids, serotonin and kinins (in this book)
- Ch 12. NSAIDs and antipyretics (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Antihistamines in animals
- Merck Veterinary Manual: NSAIDs in animals (for COX and adverse-effect context)
- Wikipedia: 5-HT receptor

CHAPTER 11 OF 33

Eicosanoids, serotonin and kinins

These local chemical messengers (autacoids) shape pain, inflammation, vascular tone, smooth muscle activity and vomiting. The chapter follows the arachidonic acid pathways, the 5-HT receptor subtypes and the kinin system, and links each to NSAIDs and anti-nausea drugs.

After this chapter you can

- Trace arachidonic acid through the cyclooxygenase and lipoxygenase pathways
- Name the main prostaglandins, thromboxane and leukotrienes and their effects
- Explain how corticosteroids and NSAIDs act at different points of the pathway
- Describe the main 5-HT receptor subtypes and drugs that act on them
- Explain how kinins are formed and how they link to pain and to ACE inhibitors

Autacoids: local messengers

Autacoids are substances made in tissues and acting close to where they are made. They are not stored like hormones in a gland, and they act briefly. Histamine, serotonin, kinins and eicosanoids belong to this group. Many drugs in this book work by blocking their synthesis or their receptors, which is why this chapter sits before the NSAID chapter.

A useful way to organise the group is by origin. Histamine and serotonin are amines stored in cells and released on stimulation. Kinins are peptides made from plasma proteins. Eicosanoids are lipids made on demand from membrane fat. Different origins explain why they are blocked by different drugs: antihistamines, 5-HT antagonists, ACE-related drugs and NSAIDs or steroids respectively.

Students often confuse autacoids with hormones. Hormones travel in blood to distant targets, while autacoids act locally and are destroyed within seconds to minutes. That brief life is why their effects are intense at the site of injury but do not spread through the whole body in health.

The arachidonic acid cascade

Eicosanoids come from **arachidonic acid**, a fatty acid held in cell membrane phospholipids. When a cell is injured or stimulated, the enzyme **phospholipase A_2** releases arachidonic acid. From there the road splits in two.

- The **cyclooxygenase (COX)** path makes prostaglandins, prostacyclin and thromboxane.
- The **5-lipoxygenase (5-LOX)** path makes leukotrienes.

Corticosteroids act high in the pathway. They induce proteins that inhibit phospholipase A_2 and also reduce COX-2 expression, so both branches fall.

NSAIDs act lower down and block COX only. This is why steroids have broader anti-inflammatory effects, and also why blocking COX may push more substrate towards the lipoxygenase path.

Prostaglandins and thromboxane

The COX enzymes convert arachidonic acid to an unstable intermediate, and tissue-specific enzymes then make the final product. The effect of each product depends on the cell.

- **PGE_2**: vasodilation, sensitises pain nerve endings, raises the hypothalamic temperature set point in fever, and protects the stomach by increasing mucus and bicarbonate and reducing acid.
- **PGI_2 (prostacyclin)**: vasodilation and inhibition of platelet aggregation. It protects the vessel wall.
- **TXA_2 (thromboxane)**: made in platelets, causes platelet aggregation and vasoconstriction. It opposes prostacyclin.
- **$PGF_{2\alpha}$**: contracts uterine and other smooth muscle, and causes regression of the corpus luteum in many species.

Prostaglandins in the kidney keep blood flow to the glomerulus when circulation is poor. This single idea explains why NSAIDs cause stomach and kidney effects while they treat pain.

Synthetic analogues are used clinically. A $PGF_{2\alpha}$ analogue is used to bring on luteolysis and to manage reproductive problems in cattle and other species, and a PGE analogue such as misoprostol is used to protect the stomach from NSAID injury. Exact products and uses should be taken from current labels.

Clinical meaning: because PGE_2 both causes pain and protects the stomach, no single drug can remove the first and keep the second. The best an NSAID can do is shift the balance. Prostaglandins also keep the ductus and uterine tone in the right state in pregnancy, so NSAIDs near parturition need caution and a check of the label.

COX-1, COX-2 and leukotrienes

COX-1 is present in most tissues all the time and supports normal functions: gastric protection, kidney perfusion and platelet function. COX-2 is mainly induced at sites of inflammation, but it is also present constitutively in some tissues such as kidney. So the split of *COX-1 is bad, COX-2 is good* is too simple. The chapter on NSAIDs takes this forward.

Leukotrienes are made by 5-lipoxygenase in white blood cells. **LTB_4** is a strong chemotactic agent attracting neutrophils. The cysteinyl leukotrienes (**LTC_4, LTD_4, LTE_4)** cause bronchoconstriction, mucus secretion and increased vascular permeability. They are important in allergic airway disease. Leukotriene pathways are not blocked by standard NSAIDs.

Clinical meaning: a drug that blocks COX may reduce pain without stopping leukotriene-driven airway constriction. In a coughing or allergic animal, an NSAID therefore does not replace an anti-inflammatory steroid or bronchodilator. In some sensitive individuals, shifting substrate to the lipoxygenase route may worsen airway signs, so caution is advised in animals with airway disease.

Serotonin (5-HT) and its receptors

Serotonin is made from tryptophan. Much of the body's store is in enterochromaffin cells of the gut, with the rest in platelets and in the brain. It acts through many receptor subtypes, and each has a different drug link.

- **5-HT_3** is a ligand-gated ion channel, unlike the other subtypes, which are G-protein-coupled. It is present in the gut and in the vomiting centre pathways. Antagonists such as ondansetron are anti-nausea drugs, and the appetite stimulant mirtazapine also blocks this receptor.
- **5-HT_4** stimulation increases gut motility. Prokinetics such as cisapride act this way where available.
- **5-HT_{2A}** on platelets and vascular smooth muscle promotes aggregation and vasoconstriction.
- **5-HT_{1A}** in the brain is linked to anxiety and mood, and is a target of some behaviour drugs.

Link to anti-nausea drugs: vomiting is triggered through several pathways, including serotonin, substance P (blocked by maropitant at NK_1 receptors), dopamine and histamine. Different drugs block different inputs, which is why one drug may work in one patient and not another.

Excess serotonergic stimulation, for example by combining certain drugs that raise serotonin, can lead to **serotonin syndrome**, with tremor, agitation and hyperthermia.

Common confusion: serotonin in the gut is not mainly the same pool as in the brain. Gut serotonin does not cross into the brain, so drugs that act on gut receptors can change motility or vomiting without changing mood.

Kinins

Kinins are small peptides. **Bradykinin** is formed when the enzyme kallikrein acts on kininogen in plasma and tissues, for example after tissue injury or contact activation. It acts on B_2 receptors to cause vasodilation, increased vascular permeability, smooth muscle contraction in the gut and airway, and pain by direct stimulation of nociceptors. It also stimulates release of prostaglandins, which then amplify pain, so kinins and eicosanoids work together in inflammation.

Bradykinin is broken down by **angiotensin-converting enzyme (ACE)**, the same enzyme that makes angiotensin II. Therefore ACE inhibitors, widely used in heart failure, raise kinin levels as well as lowering angiotensin II. In some species this is linked to cough or other effects, and this is a reason to know the shared enzyme. No kinin-blocking drug is routine in veterinary practice, so the main teaching value is understanding inflammation and the ACE link.

Concept cleared

Concept cleared: Where steroids and NSAIDs act
Imagine a river that starts at a lake (membrane phospholipid) and splits into two channels (COX and lipoxygenase). Steroids close the gate at the lake, so both channels run dry. NSAIDs block only one channel, the COX one.

Concept cleared: Why NSAIDs affect stomach and kidney
Prostaglandins act like quiet maintenance staff in the stomach and kidney, keeping mucus up and blood flowing. NSAIDs send these staff home along with the pain staff. The same drug that relieves pain also removes protection.

Concept cleared: Thromboxane versus prostacyclin
These two are a tug of war. Thromboxane from platelets pulls towards clotting and narrowing, while prostacyclin from the vessel wall pulls towards opening and preventing clots. Drugs that tilt the balance change bleeding and clotting tendencies.

Concept cleared: Why 5-HT3 is different
Most serotonin receptors act through slower G proteins like a thermostat. The 5-HT3 receptor is a channel, like a door that opens at once. That is why blocking it gives a fast anti-nausea effect.

Memory aid: Arachidonic acid fork
COX makes the Calm-and-Clot group (prostaglandins, prostacyclin, thromboxane); LOX makes the Leukotrienes. Steroids block the start, NSAIDs

block COX. For serotonin: 5-HT3 is the Three-letter 'channel' that is the Throw-up (vomiting) target.

Compare and contrast

Main eicosanoids

Mediator	Pathway	Main effects	Clinical link
PGE2	COX	Pain sensitisation, fever, vasodilation, gastric protection	NSAIDs reduce pain and fever but lessen protection
PGI2	COX	Vasodilation, anti-platelet	Vessel wall protection
TXA2	COX	Platelet aggregation, vasoconstriction	Platelet effect of aspirin-type drugs
PGF2 alpha	COX	Uterine contraction, luteolysis	Analogues used in reproduction
LTB4	5-LOX	Neutrophil chemotaxis	Not blocked by standard NSAIDs
LTC4, LTD4, LTE4	5-LOX	Bronchoconstriction, permeability	Allergic airway disease

5-HT receptor subtypes of clinical interest

Receptor	Type	Site	Drug link
5-HT1A	G-protein-coupled	Brain	Behaviour-modifying drugs
5-HT2A	G-protein-coupled	Platelets, vessels, brain	Aggregation and vasoconstriction
5-HT3	Ligand-gated ion channel	Gut, vomiting pathways	Ondansetron, mirtazapine as antagonists
5-HT4	G-protein-coupled	Gut	Prokinetics such as cisapride where available

Species notes

Dog

Cat

Dogs commonly receive 5-HT3 antagonists or maropitant for vomiting. NSAIDs can cause gastric injury because of reduced protective prostaglandins.

Cats have slow glucuronidation of many drugs, which affects NSAID choice. Platelet serotonin and thromboxane are thought to contribute to vasoconstriction in feline thromboembolic disease.

Cattle

PGF2 alpha analogues cause luteolysis and can end pregnancy, so pregnant animals must not be exposed unintentionally, and handlers should follow label safety advice.

Horse

Horses release eicosanoids in endotoxaemia and colic. NSAIDs such as flunixin are used for this reason, and the gut and kidney are watched for adverse effects.

Pigs and small ruminants

PGF2 alpha analogues are used to manage reproduction in some herds. Follow current label instructions and local regulation.

Clinical pearls

Self-test: 10 questions

1. Which enzyme releases arachidonic acid from membrane phospholipids?

Phospholipase A2 liberates arachidonic acid, the substrate for both COX and lipoxygenase.

2. Which pathway is NOT blocked by standard NSAIDs?

NSAIDs block cyclooxygenase. Leukotrienes come from the lipoxygenase route.

3. Corticosteroids reduce eicosanoids mainly by

They act high in the pathway, reducing both branches.

4. Which mediator promotes platelet aggregation?

Thromboxane from platelets causes aggregation and vasoconstriction.

5. Which leukotriene is strongly chemotactic for neutrophils?

LTB4 attracts neutrophils, while the cysteinyl leukotrienes act on airways and vessels.

6. Which serotonin receptor is a ligand-gated ion channel?

5-HT3 is a channel. The others are G-protein-coupled.

7. Ondansetron relieves nausea by blocking

It is a 5-HT3 antagonist. Maropitant blocks NK1.

8. Bradykinin is mainly broken down by

ACE degrades bradykinin, so ACE inhibitors raise kinin levels.

9. Why do NSAIDs cause stomach and kidney effects?

Prostaglandins support gastric mucus and renal blood flow, so reducing them removes protection.

10. A PGF2 alpha analogue given to a pregnant animal may

PGF2 alpha causes regression of the corpus luteum and can end pregnancy.

Key points to revise

1. Eicosanoids are made from arachidonic acid released by phospholipase A2.
2. COX makes prostaglandins and thromboxane, 5-LOX makes leukotrienes.
3. PGE2 causes pain sensitisation, fever and gastric protection.
4. TXA2 promotes platelet aggregation, PGI2 inhibits it.
5. LTB4 attracts neutrophils and cysteinyl leukotrienes constrict airways.
6. 5-HT3 antagonists are anti-nausea drugs, 5-HT4 agonists are prokinetics.
7. Bradykinin causes pain, vasodilation and permeability via B2 receptors.
8. Different anti-nausea drugs block different pathways: serotonin, substance P, dopamine and histamine.

Go deeper on this site

- Ch 12. NSAIDs and antipyretics (in this book)
- Ch 10. Histamine and antihistamines (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Nonsteroidal Anti-inflammatory Drugs in Animals
- Merck Veterinary Manual: Corticosteroids in Animals
- University of Minnesota Libraries: Principles of Pharmacology study guide

CHAPTER 12 OF 33

NSAIDs and antipyretics

NSAIDs relieve pain, inflammation and fever by blocking cyclooxygenase. This chapter explains COX-1 and COX-2, why stomach and kidney effects occur, why paracetamol is dangerous in cats, how food-animal use and withdrawal apply, and the vulture-related restrictions in India.

After this chapter you can

- Explain how NSAIDs produce analgesic, anti-inflammatory and antipyretic effects
- Compare COX-1 and COX-2 and the idea of COX-selective drugs
- Explain gastric and renal adverse effects and who is at risk
- Explain why paracetamol is toxic to cats
- Describe the food-animal and vulture-related issues for NSAIDs in India, and the need to check current rules

Mechanism of action

Non-steroidal anti-inflammatory drugs (NSAIDs) inhibit the **cyclooxygenase (COX)** enzymes, so less arachidonic acid is turned into prostaglandins and thromboxane. The previous chapter described these mediators.

- **Analgesia:** less PGE_2 means nerve endings are less sensitised to bradykinin and other pain signals. The effect is strongest in inflammatory pain.
- **Anti-inflammatory:** less vasodilation, swelling and prostaglandin-driven signalling at the site of injury.
- **Antipyretic:** during fever, cytokines raise PGE_2 in the hypothalamus and reset the temperature set point upwards. NSAIDs lower PGE_2 and the set point returns. They do not lower normal body temperature, and they do not help heat stroke, where the set point is unchanged.

Most NSAIDs block COX by competing with arachidonic acid. **Aspirin** is different, because it irreversibly acetylates COX. This is why its effect on platelets lasts for the life of the platelet.

Common confusion: students think NSAIDs work on the pain nerve itself like an opioid. They do not. They act at the site of injury by reducing the chemical that sensitises the nerve, which is why they work best in inflammatory pain and have no sedative or addictive effect. Their effect also has a ceiling, so giving more drug does not give more pain relief but does add more risk.

COX-1, COX-2 and selectivity

COX-1 is present all the time and supports stomach lining, kidney blood flow and platelet function. COX-2 rises at sites of inflammation and is the main target for pain relief. Drugs with more activity against COX-2 than COX-1 were developed to give pain relief with fewer stomach problems. Several veterinary drugs, such as meloxicam, carprofen and others, are described as preferentially COX-2 inhibitors in some species.

Do not oversimplify. COX-2 is also present in normal kidney, and in healing tissue, and selectivity differs between species and between laboratory tests. A COX-2 preferring drug is *safer for the stomach in many patients*, but it is not free of kidney, liver or other adverse effects. Some drugs are also described as dual inhibitors, because they affect both COX and lipoxygenase pathways. Learn the principle and check product labels for current claims.

Stomach and kidney effects

Stomach. Prostaglandins increase mucus, bicarbonate and mucosal blood flow, and reduce acid. Without them the mucosa is exposed, and in addition acidic NSAIDs can irritate directly. The result may be vomiting, erosion, ulcer, bleeding or perforation. Signs to teach owners: vomiting, black tarry stool, poor appetite and lethargy. Misoprostol, a prostaglandin analogue, and acid suppressants may be used in selected cases, but the best protection is correct drug choice, avoiding combinations and not giving long courses without need.

Kidney. When blood pressure or blood volume is low, prostaglandins widen the afferent arterioles and protect glomerular filtration. NSAIDs remove this support. The risk is highest in dehydration, shock, anaesthesia with low blood pressure, heart failure, existing kidney disease and in old animals. Hydration and avoiding NSAIDs in these states is the key.

Other points. Avoid NSAIDs together with corticosteroids, which greatly raises the risk of gastric ulcer. Do not switch directly between NSAIDs, and allow the washout time on the label. NSAIDs can also affect platelet function, and may be undesirable before surgery in some animals. Liver injury is an uncommon, individual reaction with some drugs.

Protein binding is another point. NSAIDs are highly bound to plasma protein, so animals with low albumin, for example from liver or protein-losing disease, may

have more free drug and a higher chance of adverse effects. Using two NSAIDs together is not safer, since both add to the same mechanism-based harm.

Animals should be monitored with a clinical check and, in long-term use, with periodic blood and urine tests of kidney and liver function. Owners should be taught to stop the drug and call the clinic if vomiting, poor appetite or dark stool appear.

Paracetamol and cats

Paracetamol (acetaminophen) is a good antipyretic and mild analgesic with little anti-inflammatory effect. In most species it is cleared mainly by conjugation with glucuronic acid, with a small part oxidised to a toxic intermediate that glutathione normally neutralises.

Cats are deficient in glucuronidation, because they have low activity of the relevant enzyme. Metabolism is pushed towards the toxic oxidation route and sulphation saturates quickly. Glutathione runs out, and the toxic metabolite damages red cells. Haemoglobin is oxidised to **methaemoglobin**, which cannot carry oxygen, and Heinz bodies form. Typical signs are brown or muddy mucous membranes, difficulty breathing, facial and paw oedema, and later liver injury. Even a small amount can be dangerous in a cat, so it should not be given.

Dogs tolerate paracetamol better but can develop liver damage and methaemoglobinaemia at higher exposure. Acetylcysteine, which restores glutathione, is a key antidote in poisoning. The same glucuronidation weakness helps explain why cats are sensitive to some other drugs, and why aspirin is cleared slowly in cats.

Food-animal use

NSAIDs are used in cattle, buffalo, pigs, sheep and goats for fever, mastitis, lameness, calving injuries, respiratory disease and endotoxaemia. Because products are consumed as milk and meat, every drug needs a **withdrawal period** and a **maximum residue limit**. Use only a product and a species that the label allows, and follow the time before milk or slaughter. In India, permitted drugs, residue limits and withdrawal rules are set by notifications and may change, so **check the current notification** and product label.

Some NSAIDs are not suitable for food-producing animals or are restricted. Never use extra-label NSAIDs casually in a dairy herd. Young calves, dehydrated animals and those with mastitis-related toxaemia are at higher kidney and gastric risk, so fluids and supportive care are as important as the NSAID itself.

Vulture-related restrictions in India

In the 1990s and 2000s, populations of Gyps vultures in South Asia fell very sharply. The cause was identified as **diclofenac**, used in cattle and buffalo. When a treated animal died shortly after treatment and the carcass was eaten, vultures developed visceral gout and kidney failure. Residues in a carcass can be enough to poison birds feeding on it.

India took regulatory action against veterinary diclofenac in the mid 2000s, and later steps addressed human diclofenac formulations used in animals and some other NSAIDs. The exact list of banned, restricted or advisory products changes with notifications, so students must **check the current notification** of the drug regulator and state authorities. Meloxicam is widely described as a safer alternative for vultures, but any new drug should be considered against current evidence.

The message for a practitioner is wider than one drug. Know the status of every NSAID you use in livestock, avoid human formulations in animals, and dispose of carcasses responsibly. The vulture story is a classic example of a drug harming a non-target species through the food chain.

Concept cleared

Concept cleared: Why fever drops but normal temperature does not
Think of a thermostat set too high by a chemical (PGE2). The NSAID removes that chemical, and the thermostat returns to normal, so the body cools. If the thermostat is already normal, as in heat stroke, there is nothing to reset, and an NSAID does not help.

Concept cleared: Why cats are unique with paracetamol

Most animals have a wide safe road (glucuronidation) for clearing paracetamol. Cats have only a narrow lane, so traffic piles up and diverts into a dangerous side road that makes a toxic product and uses up glutathione. The result is methaemoglobin.

Concept cleared: Aspirin is irreversible

Most NSAIDs are like a person standing in a doorway who can walk away. Aspirin is like a lock that is welded shut. A platelet has no nucleus to make new COX, so the block lasts until the platelet is replaced.

Concept cleared: The vulture chain

A drug given to a cow does not stay with the cow. If she dies soon after, the carcass carries residue to vultures, whose kidneys cannot cope. One treatment decision in a village affected a whole species across a region.

Memory aid: NSAID cautions

G-R-P-F: Gut, Renal, Platelet, Food chain. Check each before choosing an NSAID. And remember: cats and paracetamol never mix.

Compare and contrast

COX-1 and COX-2

Feature	COX-1	COX-2
Expression	Constant in most tissues	Induced in inflammation, also present normally in some organs such as kidney
Main role	Stomach protection, kidney perfusion, platelets	Pain, inflammation, fever
Result of blocking	Gastric injury, renal effects, bleeding tendency	Pain relief, but some renal and healing effects
Drug idea	Non-selective NSAIDs block both	COX-2 preferring drugs aim for fewer stomach effects

Adverse effect risk and what to do

Problem	Mechanism	Risk group	Practical step
Gastric ulcer	Loss of protective prostaglandins	Combined with corticosteroids, long courses	Avoid combinations, watch for black stools
Renal injury	Loss of afferent dilation	Dehydrated, hypotensive, old, kidney disease	Hydrate, avoid NSAIDs in these states
Paracetamol toxicity	Poor glucuronidation, methaemoglobin	Cats	Never give; acetylcysteine in poisoning
Residue in food	Drug in milk and meat	Food animals	Follow withdrawal period and notification
Vulture poisoning	Diclofenac in carcass	Scavenging birds	Avoid banned products, dispose of carcasses safely

Species notes

Dog

Dogs are commonly given veterinary-licensed NSAIDs for osteoarthritis and post-operative pain. Human NSAIDs and combining with steroids carry a high risk of gastric ulcer.

Cat

Cats clear many NSAIDs slowly and paracetamol is dangerous. Use only products and regimes labelled for cats and be careful with kidney status.

Cattle and buffalo

Used for fever, mastitis and lameness, but milk and meat withdrawal and current Indian notifications must be followed. Avoid banned diclofenac products.

Horse

Flunixin and phenylbutazone-type drugs are used for colic and musculoskeletal pain. Watch the stomach and kidney, and note that the drug may mask pain or signs of progressive disease.

Pigs, sheep and goats
NSAIDs are used for fever and lameness. Check that the product and species are approved and observe the withdrawal period.

Clinical pearls

Self-test: 10 questions

1. NSAIDs mainly act by inhibiting

They block COX and so reduce prostaglandin and thromboxane synthesis.

2. NSAIDs reduce fever by lowering

Lower PGE2 allows the hypothalamic set point to return to normal.

3. Aspirin differs from most NSAIDs because it

Irreversible COX block in platelets lasts for the platelet life span.

4. Which tissue function depends mainly on COX-1 products?

COX-1 generated prostaglandins maintain mucus, bicarbonate and mucosal blood flow.

5. NSAID renal injury is most likely in an animal that is

In low perfusion states, prostaglandins maintain glomerular flow, and NSAIDs remove that support.

6. Which combination is especially risky for gastric ulcer?

Both reduce mucosal defence and the combined risk is high.

7. Why is paracetamol toxic in cats?

Poor glucuronidation shifts metabolism to oxidation, leading to methaemoglobin and Heinz bodies.

8. A key antidote to paracetamol poisoning acts by

Acetylcysteine replenishes glutathione to neutralise the toxic metabolite.

9. Vulture population decline in South Asia was linked to

Vultures feeding on carcasses of treated livestock developed visceral gout and kidney failure.

10. Before using an NSAID in a dairy cow in India, the veterinarian should

Residue limits, approved drugs and restrictions are set by notifications that change.

Key points to revise

1. NSAIDs inhibit COX and reduce prostaglandins and thromboxane.
2. Analgesia, anti-inflammatory and antipyretic effects all derive from lower prostaglandins.
3. COX-1 supports stomach, kidney and platelets, COX-2 is mainly induced in inflammation.
4. COX-2 preference does not remove all risk.
5. Stomach ulcer and renal injury are mechanism-based adverse effects.
6. Aspirin irreversibly acetylates COX.
7. Cats lack glucuronidation, so paracetamol causes methaemoglobinaemia.

8. Diclofenac residues in carcasses poisoned Gyps vultures in South Asia, and Indian rules are set by notification.

Go deeper on this site

- Ch 13. Corticosteroids (in this book)
- Ch 11. Eicosanoids, serotonin and kinins (in this book)
- Meloxicam in cats: safety cautions
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Nonsteroidal Anti-inflammatory Drugs in Animals
- Merck Veterinary Manual: Overview of Anti-inflammatory Agents
- University of Minnesota Libraries: Principles of Pharmacology study guide

CHAPTER 13 OF 33

Corticosteroids

Glucocorticoids act on nuclear receptors to switch off many inflammatory and immune pathways at once. This chapter covers the mechanism, the two main uses, the adverse effects, why long courses suppress the adrenal gland, and why steroids and NSAIDs should not be combined.

After this chapter you can

- Explain how glucocorticoids change gene transcription to reduce inflammation
- Distinguish anti-inflammatory from immunosuppressive use and the reason the latter needs higher exposure
- List the main adverse effects of prolonged glucocorticoid therapy
- Explain how the hypothalamic-pituitary-adrenal axis is suppressed and why withdrawal must be gradual
- Explain why glucocorticoids and NSAIDs together raise the risk of gastrointestinal ulceration

What corticosteroids are

The adrenal cortex makes two groups of steroid hormones. **Glucocorticoids** such as cortisol control metabolism and inflammation. **Mineralocorticoids** such as aldosterone control sodium and potassium balance. Drugs such as prednisolone, dexamethasone, betamethasone and triamcinolone are synthetic glucocorticoids.

These drugs differ in potency, duration and in how much salt-retaining activity they keep. Dexamethasone is far more potent and longer acting than prednisolone, and has almost no mineralocorticoid effect. The practical point is that the choice of drug, and not only the dose, decides how long the effect lasts and how severe the side effects are.

A common confusion is to treat all steroids as one thing. Anabolic steroids and sex steroids are different drugs with different receptors. In this chapter, corticosteroid means glucocorticoid.

Mechanism of action

Glucocorticoids are lipid-soluble, so they cross the cell membrane and bind a receptor in the cytoplasm. The drug-receptor complex moves into the nucleus and changes gene expression. This is the nuclear receptor family described in the chapter on receptors, and it explains why the onset is slow (hours) and the effect outlasts the plasma half-life.

Two main things follow. The complex **increases** the production of some anti-inflammatory proteins. One of these, often called lipocortin, inhibits phospholipase A_2. With less phospholipase A_2, less arachidonic acid is released, so fewer prostaglandins, leukotrienes and platelet-activating factor are made. The complex also **decreases** the production of cytokines and of cyclo-oxygenase-2, and reduces the activity and movement of white cells into tissue.

Compare this with NSAIDs, which block cyclo-oxygenase only. Steroids act higher up the pathway, and on more mediators, which is why they are the stronger anti-inflammatory drugs.

Anti-inflammatory and immunosuppressive use

The same mechanism gives two clinical uses, and students should keep them separate.

- **Anti-inflammatory use**: relief of itching and inflammation in allergic skin disease, inflammatory airway disease, arthritis flares, and spinal or brain swelling. The aim is the lowest effective exposure for the shortest time.
- **Immunosuppressive use**: control of immune-mediated disease such as immune-mediated haemolytic anaemia, immune-mediated thrombocytopenia, pemphigus and some lymphoid conditions. Here the exposure needed is higher and the course is longer, so adverse effects are more likely.

Glucocorticoids reduce lymphocyte numbers and function, lower antibody production and impair the phagocytes. This is useful in autoimmune disease but is also the reason infections become worse or silent during treatment.

Other uses include replacement therapy in hypoadrenocorticism, treatment of shock and some emergencies in specific protocols, and certain drug-induced actions such as induction of parturition in cattle. Because a steroid can mask signs, take a diagnosis first. Giving a steroid before a lymph node biopsy, for example, can change the histology and make lymphoma harder to confirm.

Adverse effects

Most serious problems follow long-term or high exposure. A short course for an allergic flare is usually well tolerated. Adverse effects are best learned as an extension of normal physiology: too much cortisol produces the picture of Cushing syndrome, called **iatrogenic hyperadrenocorticism** when the cause is a drug.

- Increased thirst, urination and appetite, with weight gain and a pot-bellied look.
- Muscle wasting and weakness, thin skin, poor wound healing and hair loss.
- Worsening or new diabetes mellitus, because glucocorticoids oppose insulin.
- Greater risk of infection, including urinary tract and skin infection, and masking of fever.
- Gastrointestinal irritation and ulceration.
- Sodium and water retention with potassium loss, more with drugs that retain some mineralocorticoid action.
- In horses, a risk of laminitis, especially with high exposure.

- Delayed bone and wound healing, and in pregnancy, risk of abortion or premature birth, especially in late gestation in ruminants.

Drugs such as triamcinolone and long-acting depot forms carry the same risks and are harder to stop once injected, because the effect cannot be recalled.

Adrenal suppression and withdrawal

The body controls cortisol by negative feedback. The hypothalamus releases CRH, the pituitary releases ACTH, and ACTH tells the adrenal cortex to make cortisol. When a glucocorticoid drug is given, the brain senses plenty of steroid and switches off CRH and ACTH. The adrenal cortex, no longer stimulated, shrinks. This is **suppression of the hypothalamic-pituitary-adrenal axis**.

If the drug is stopped suddenly after prolonged use, the animal has no steroid from the drug and little from its own adrenal glands. The result can be weakness, vomiting, low blood pressure and collapse, a picture of secondary hypoadrenocorticism. The same risk appears in an animal under stress, such as surgery, while recovering from a long course.

Therefore long courses are **tapered** slowly, not stopped. In some cases alternate-day dosing is used because it allows the axis a partial recovery on the off-day, and an intermediate-acting drug such as prednisolone suits this better than long-acting dexamethasone. Recovery of the axis can take weeks after stopping, so the clinician should keep this risk in mind during that period.

Note that suppression follows a feedback mechanism, so even topical, ophthalmic and injectable depot preparations can contribute when used for long periods.

Why not with NSAIDs

Gastric and intestinal mucosa depends on protective prostaglandins to maintain mucus, bicarbonate and blood flow. NSAIDs reduce these prostaglandins by blocking cyclo-oxygenase. Glucocorticoids also lower prostaglandin production and in addition slow mucosal repair and thin protective tissue. Used together, the two drugs add their harmful effects on the gut, and reports describe a clearly higher risk of gastrointestinal ulceration, bleeding and perforation than either drug alone.

This is a pharmacodynamic interaction, not a kinetic one, so a longer gap between doses does not fully remove the risk. When changing from one class to the other, a

washout interval is needed, and the length should be taken from the product information and current references.

Common confusion: some students think adding a gastroprotectant makes the combination safe. It lowers risk but does not remove it, and it does not prevent the kidney and bleeding effects of NSAIDs. The safe rule is to choose one class at a time. If the patient is also on other ulcerogenic drugs or has liver or kidney disease, the case for avoiding combination is even stronger.

In short, treat the steroid as a strong tool with a price. Use the lowest effective exposure, choose one anti-inflammatory class at a time, and review the animal regularly for the signs listed above.

Concept cleared

Concept cleared: Nuclear receptor delay
Think of a steroid as an instruction sent to the factory office, not a switch on the machine. The office must rewrite its orders and the factory must make new products, so the effect arrives hours later and also takes time to fade after the drug has left the blood.

Concept cleared: Steroids act higher than NSAIDs
Picture a river of inflammation. An NSAID closes one gate in the river (cyclo-oxygenase). A steroid reduces the water at the source by lowering phospholipase A2 activity and many cytokines. Hence a stronger effect but also more side effects.

Concept cleared: Adrenal suppression
A farmer hires a contract worker to do the job of the family worker. After months the family worker retires. If the contract worker leaves suddenly, no one is left to do the work. Slowly tapering gives the family worker time to return.

Concept cleared: Same mechanism, two uses

The dose and time decide whether the steroid is a mild anti-inflammatory or a strong immunosuppressant. The longer and stronger the course, the more the animal looks like a Cushing patient.

Memory aid: Steroid adverse effects

Remember 'CUSHING': Calories and appetite up, Urination and thirst up, Skin thin, Healing slow, Infection risk, Nutrient (muscle) loss, Glucose up.

Compare and contrast

Anti-inflammatory versus immunosuppressive use

Feature	Anti-inflammatory use	Immunosuppressive use
Typical aim	Reduce itch, swelling, pain	Control immune-mediated disease
Exposure	Lowest effective	Higher
Duration	Short or intermittent	Weeks to months, with taper
Adverse effects	Usually mild	More frequent and serious
Example	Allergic dermatitis flare	Immune-mediated haemolytic anaemia

Glucocorticoids versus NSAIDs

Feature	Glucocorticoids	NSAIDs
Receptor or target	Nuclear receptor, gene changes	Cyclo-oxygenase enzyme
Onset	Hours	Often faster
Mediators reduced	Prostaglandins, leukotrienes, cytokines	Mainly prostaglandins
Immune effect	Immunosuppressive	Minimal
Key organ risks	Endocrine, infection, GI	GI, kidney, platelets

Species notes

Dog

Dogs are fairly sensitive to glucocorticoids. Polyuria, polydipsia and polyphagia appear early, and iatrogenic Cushing syndrome is common after long courses.

Cat

Cats tolerate steroids better than dogs in terms of visible adverse effects, and prednisolone rather than prednisone is generally preferred. Diabetes mellitus and heart failure risk deserve attention.

Horse

High exposure is linked to laminitis, so the lowest effective course is used, particularly in animals with endocrine disease.

Cattle

Late in pregnancy, glucocorticoids can induce parturition, which is both a use and a risk. Steroids may also reduce milk yield and hide infection.

Food animals in India

Check the current notification on permitted use, withdrawal periods and residue limits before giving any steroid to a food-producing animal.

Clinical pearls

Self-test: 10 questions

1. Glucocorticoids produce most of their anti-inflammatory effect by:

They act on nuclear-type receptors and alter transcription, including induction of phospholipase A2 inhibitors.

2. Which enzyme is indirectly inhibited by lipocortin?

Less phospholipase A2 activity means less arachidonic acid release and fewer eicosanoids.

3. Why does the effect of prednisolone last longer than its plasma half-life?

Altered protein synthesis persists after the drug has left the plasma.

4. Which is an immunosuppressive indication?

Immune-mediated haemolytic anaemia needs suppression of antibody production and phagocyte activity.

5. Polyuria, polydipsia and muscle wasting after a long course suggest:

Excess exogenous glucocorticoid mimics Cushing syndrome.

6. Prolonged steroid therapy suppresses the adrenal cortex because of:

High steroid levels suppress CRH and ACTH so the cortex atrophies.

7. The safest way to end a long course of glucocorticoids is to:

Tapering gives the adrenal axis time to recover.

8. Why should a steroid not be combined with an NSAID?

Both lower protective prostaglandins and steroids impair mucosal repair; the harmful effects add up.

9. Which statement about steroids and infection is correct?

Reduced lymphocyte and phagocyte function lets infection progress with fewer signs.

10. Why should a biopsy ideally be taken before starting a steroid?

Steroids may shrink lymphoid tissue and alter histology, hiding the disease.

Key points to revise

1. Glucocorticoids bind cytoplasmic receptors and alter gene transcription.
2. Lipocortin-mediated phospholipase A2 inhibition lowers prostaglandins and leukotrienes.
3. Effect begins after hours and outlasts the plasma half-life.
4. Anti-inflammatory use needs less exposure than immunosuppressive use.
5. Prolonged use causes iatrogenic Cushing syndrome, diabetes, infection and GI ulceration.
6. Negative feedback suppresses the HPA axis and the adrenal cortex atrophies.
7. Abrupt withdrawal after long use can cause an adrenal crisis, so taper.
8. Glucocorticoids plus NSAIDs sharply increase the risk of GI ulceration.

Go deeper on this site

- Ch 14. Joint-protective and disease-modifying drugs (in this book)
- Ch 12. NSAIDs and antipyretics (in this book)
- Meloxicam in cats: safety cautions
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Corticosteroids in Animals
- MSD Veterinary Manual: Corticosteroids in Animals
- Merck Veterinary Manual: Nonsteroidal Anti-inflammatory Drugs in Animals

CHAPTER 14 OF 33

Joint-protective and disease-modifying drugs

Chondroprotective agents are used in osteoarthritis in the hope of protecting cartilage and not only relieving pain. This chapter explains cartilage and joint fluid, polysulfated glycosaminoglycan, pentosan, hyaluronate and oral supplements, and why the evidence for many of them is weaker than the marketing.

After this chapter you can

- Describe how osteoarthritis damages cartilage and why pain relief alone does not stop it
- Define chondroprotective and disease-modifying and explain the difference from analgesics
- Explain the proposed actions, routes and cautions of polysulfated glycosaminoglycan and pentosan polysulfate
- Explain the role of hyaluronate in joint lubrication and its main species of use
- Judge the strength of evidence for chondroprotectives and nutraceuticals

Osteoarthritis in brief

Osteoarthritis is a slow, progressive joint disease. Articular cartilage loses proteoglycan and collagen, the joint capsule and synovium become inflamed, and the bone below the cartilage changes. Pain, stiffness and reduced movement follow. It is common in older dogs and in working or sport horses, and also occurs in cats and in farm animals.

Cartilage has no blood supply and few cells, so it repairs poorly. Inflammatory mediators and enzymes such as matrix metalloproteinases break down the matrix faster than the chondrocytes can replace it. A vicious circle follows: breakdown products inflame the joint, and inflammation drives more breakdown.

Most treatment is **symptomatic**: NSAIDs for pain, weight control, exercise management and physiotherapy. The drugs in this chapter aim at something extra, protecting the joint structure.

Chondroprotective and disease-modifying: the terms

A **chondroprotective** agent is one that is claimed to protect cartilage, for example by reducing enzymatic breakdown or stimulating matrix production. A **disease-**

modifying drug is one that has been shown to change the course of the disease, not only the symptoms. These two ideas are often confused.

Many agents have shown effects in test tubes and cell cultures. That is not the same as proven benefit in a living animal with naturally occurring disease. Good evidence needs controlled trials with clear outcome measures such as lameness scores, force-plate data or cartilage structure.

For this reason, students should always ask three questions about a joint product: what is the proposed mechanism, what is the best evidence in the target species, and what are the risks and costs. Another point: products sold as nutritional supplements are not always held to the same standard of proof or quality control as licensed drugs.

Polysulfated glycosaminoglycan and pentosan

Polysulfated glycosaminoglycan (PSGAG) is a semisynthetic compound made from bovine tracheal cartilage, with chondroitin sulfate as the main component. It is used in dogs and horses. In dogs it is given by intramuscular injection. In horses it is given intramuscularly or into the joint. After injection it reaches the blood and is incorporated into cartilage.

The exact mechanism is not known. Laboratory studies show that it inhibits prostaglandin E_2 and some cartilage-degrading enzymes, and that it can raise the production of hyaluronic acid, proteoglycan and collagen. These findings fit the idea of protecting and rebuilding cartilage, but their clinical size is debated.

Pentosan polysulfate sodium is a related heparin-like compound used in dogs and horses, and reports in dogs describe less cartilage damage.

Cautions follow from the heparin-like structure. Both agents can interfere with clotting, especially at high exposure, and aspirin may prolong bleeding further. PSGAG should not be put into a septic joint, because it can worsen infection. Intra-articular injection also requires strict asepsis. Check the label for the exact precautions for each product and species.

Hyaluronate

Hyaluronan (hyaluronic acid, hyaluronate) is a natural component of synovial fluid and cartilage. It gives joint fluid its viscosity and lubricates the surfaces, and it helps to cushion load. In osteoarthritis the molecules in joint fluid are smaller and less concentrated, so lubrication falls.

Injected hyaluronate is used mainly in horses, where purified preparations are put directly into the joint. It may improve lubrication, reduce prostaglandin E_2 production and ease pain. Adverse effects in horses are usually few, and the main risks are those of any joint injection, namely infection and joint flare.

A common confusion is to think the injected molecules stay in the joint for long and rebuild cartilage. They are cleared fairly quickly, so benefit is thought to come from both direct lubrication and from effects on the joint lining that outlast the presence of the drug. Hyaluronate is often combined with a corticosteroid in equine joint therapy, which should be done only by clinicians who understand the risks of repeated intra-articular steroid.

Other agents mentioned in references include orgotein, given into joints in some species, which has a slow onset over weeks.

Oral supplements and evidence

Glucosamine and chondroitin sulfate are the best known oral joint supplements. They are building blocks of cartilage matrix, and the theory is that supplying them helps the cartilage to repair. Omega-3 fatty acids, green-lipped mussel extract and avocado-soybean extracts are also sold. These are widely used by owners, and are often chosen because they seem safe.

The scientific problem is that oral absorption, delivery to cartilage and the real clinical benefit are uncertain. Studies are often small, products vary in content, and the placebo response in pain scoring is strong, because owners and clinicians tend to see improvement in an animal given any treatment. The honest position for a student is that evidence is limited and mixed for most nutraceuticals, and that those with the most support in dogs are generally the dietary omega-3 fatty acids, not glucosamine alone. Check current reviews before claiming a benefit.

In practice these products rarely replace analgesics. They are best seen as supporting measures to an overall plan.

Using these drugs sensibly

The foundation of osteoarthritis care is weight reduction, controlled exercise, physiotherapy and appropriate analgesia. NSAIDs relieve pain and inflammation in dogs and horses. Some NSAIDs, such as aspirin, naproxen and ibuprofen, are considered chondrotoxic in laboratory work because they lower cartilage proteoglycan synthesis. Carprofen and meloxicam are regarded as neutral or possibly beneficial, though the clinical meaning is still being clarified. This is one reason NSAID choice in a long-term joint patient is a considered decision.

Chondroprotectives are then added to this base when the clinician and owner accept that the proof is partial. Judge success by the animal: mobility, comfort and activity, recorded before and after, not by the product claims. If there is no clear benefit after a fair trial, stop the product and save the cost.

Other points for exam answers: do not inject any joint without aseptic technique, avoid PSGAG in infected joints, watch for bleeding tendency with heparin-like compounds, and remember that regulation of veterinary supplements and of compounded products varies, so check the current notification and product licensing in India before recommending a product.

In short, these drugs support the joint but do not replace basic care. Record mobility before and after treatment, review the plan regularly, and be honest with owners about what the evidence can and cannot promise.

Concept cleared

Concept cleared: Cartilage repair is slow

Cartilage is like a road with no workers living nearby. Damage is easy but repair crews must come from far away, so a break-down faster than repair gives a pothole that keeps growing.

Concept cleared: Symptom versus structure

An NSAID lowers the pain alarm. A true disease-modifying drug would fix the damage that sets off the alarm. Most joint products are somewhere between, and the proof is partial.

Concept cleared: Lab effect is not clinical benefit

A drug that lowers an enzyme in a dish has passed only the first test. It still has to show better walking in real animals in a controlled trial.

Concept cleared: Hyaluronate as joint oil

Joint fluid works like engine oil. In osteoarthritis the oil becomes thin. Adding hyaluronate thickens it and lubricates for a time, but it is not a new engine.

Memory aid: Three questions for any joint product

Ask M-E-R: Mechanism, Evidence in the target species, Risk and cost.

Compare and contrast

Main joint-protective agents

Agent	Route	Proposed action	Main caution
Polysulfated glycosaminoglycan	Intramuscular (dog); intramuscular or intra-articular (horse)	Lowers PGE2 and degrading enzymes; supports matrix synthesis	Heparin-like, clotting effects; avoid in septic joint
Pentosan polysulfate sodium	Injection, dogs and horses	Heparin-like; reported less cartilage damage in dogs	Clotting interference
Hyaluronate	Intra-articular, mainly horses	Lubrication, less PGE2, pain relief	Infection risk of joint injection
Oral glucosamine and chondroitin	Oral	Matrix building blocks (proposed)	Uncertain evidence and product quality

Analgesic versus chondroprotective aim

Feature	NSAID	Chondroprotective agent
Main aim	Relieve pain and inflammation	Protect or support cartilage
Evidence of effect	Strong for pain relief	Variable, often limited
Speed	Days	Weeks or longer
Role	Core treatment	Add-on

Species notes

Dog

PSGAG is given by intramuscular injection, and pentosan has been studied in dogs. NSAIDs and weight loss remain the basis of treatment; omega-3 fatty acids have the better supported nutritional role.

Horse

Intra-articular hyaluronate and PSGAG are used in joint disease of performance horses, with strict aseptic technique. Check competition rules on drugs before use.

Cat

Osteoarthritis is common but under-recognised in older cats. Analgesic choice is limited by the cat's drug metabolism, so supportive measures matter. Check product labels and current references.

Cattle and buffalo

Joint products are rarely used for economic reasons. Lameness is managed by treating the cause, and any drug use needs attention to withdrawal times under current Indian rules.

Working animals in India

Draught bullocks, buffaloes and horses show arthritis with heavy work. Rest and load management are cheap and effective, and often more important than injections.

Clinical pearls

Self-test: 10 questions

1. Which statement about cartilage is correct?

Poor blood supply and few chondrocytes limit repair.

2. A disease-modifying osteoarthritis drug is one that:

Disease-modifying implies a proven effect on progression, not only symptoms.

3. PSGAG is derived from:

It is a semisynthetic compound from bovine tracheal cartilage with chondroitin sulfate as the main component.

4. PSGAG should not be injected into:

It is contraindicated in septic joints.

5. Why can PSGAG and pentosan affect bleeding?

Their heparin-like structure can interfere with clotting.

6. Hyaluronate is mainly used by which route and species?

Purified hyaluronan is injected into joints in horses.

7. Which statement on oral glucosamine and chondroitin is most accurate?

Absorption, delivery and clinical benefit are uncertain.

8. Why is a strong placebo effect a problem in supplement trials?

Subjective pain scoring is easily biased without blinding and controls.

9. Which NSAID group is considered chondrotoxic in laboratory work?

These lower cartilage proteoglycan synthesis, while carprofen and meloxicam appear neutral.

10. The core of osteoarthritis management is:

Supplements and injections are add-ons to the basic plan.

Key points to revise

1. Osteoarthritis involves cartilage breakdown, synovial inflammation and bone change.
2. Chondroprotective means claimed to protect cartilage; disease-modifying means proven to change the course.
3. PSGAG is derived from bovine tracheal cartilage and used in dogs and horses.
4. PSGAG proposed actions: reduces PGE2 and degrading enzymes, supports hyaluronan, proteoglycan and collagen.
5. PSGAG and pentosan are heparin-like and may affect clotting.
6. Hyaluronate lubricates the joint and is mainly used intra-articularly in horses.
7. Evidence for oral glucosamine and chondroitin is limited and mixed.
8. NSAIDs, weight loss and exercise management are the base of treatment.

Go deeper on this site

- Ch 15. Drugs for heart failure and inotropes (in this book)
- Ch 13. Corticosteroids (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index

- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Chondroprotective Agents in Animals
- MSD Veterinary Manual: Chondroprotective Agents in Animals
- Merck Veterinary Manual: Nonsteroidal Anti-inflammatory Drugs in Animals

CHAPTER 15 OF 33

Drugs for heart failure and inotropes

Heart failure drugs improve contraction, reduce workload on the heart, or block harmful neurohormonal activation. This chapter covers cardiac glycosides, pimobendan, dobutamine and ACE inhibitors, with the species points that matter in practice.

After this chapter you can

- Explain the main problems of the failing heart and how each drug class addresses them
- Describe the mechanism and narrow safety margin of digoxin
- Explain pimobendan as an inodilator and its contraindication
- Describe dobutamine as a short-term intravenous inotrope
- Explain how ACE inhibitors work and the realistic size of their benefit

The failing heart

In heart failure the heart cannot pump enough blood at normal filling pressure to meet the body's needs. The body responds by activating the sympathetic system and the renin-angiotensin-aldosterone system. These responses help in the short term, because they raise heart rate, constrict vessels and retain salt and water. In the long term they overload the heart and cause congestion, with oedema, ascites or pleural effusion.

Drugs therefore have three jobs. First, improve the strength of contraction (**positive inotropes**). Second, reduce preload and afterload, the volume and the resistance the heart works against. Third, block the harmful neurohormonal activation.

Diuretics such as furosemide relieve congestion and are the most commonly used drugs in heart failure, but this chapter concentrates on the other groups.

A common confusion is to think that a stronger beat is always better. Increasing contraction raises oxygen demand and can provoke arrhythmias, so inotropes are used with care and for the right type of failure.

Cardiac glycosides: digoxin

Digoxin comes from the foxglove plant (*Digitalis*). It inhibits the membrane **sodium-potassium ATPase** pump in heart muscle cells. Sodium builds up inside the cell, and the sodium-calcium exchanger then removes less calcium, so intracellular calcium rises and each contraction is stronger. Digoxin also increases vagal tone, slows conduction through the atrioventricular node, and so slows the ventricular rate in atrial fibrillation.

Its inotropic effect is modest, and its **safety margin is narrow**, so the toxic level is close to the useful one. Toxicity is made more likely by low potassium, kidney disease and interacting drugs. Loop diuretics such as furosemide lower potassium, and amiodarone and some other drugs raise digoxin levels. Early signs are gastrointestinal, including anorexia and vomiting, followed by arrhythmias. Cats are more sensitive than dogs.

Because of this, serum monitoring is advised, and digoxin has largely been replaced by pimobendan for most cases of canine failure. Its remaining value is rate control in supraventricular tachyarrhythmias such as atrial fibrillation, often with other drugs. Remember too that the same plant glycosides cause poisoning from oleander and foxglove in animals.

Pimobendan: an inodilator

Pimobendan has two linked actions, which is why it is called an **inodilator**. It **sensitises** the contractile proteins to calcium, which strengthens contraction without a large rise in intracellular calcium or oxygen use. It also inhibits **phosphodiesterase 3**, raising cAMP in vascular smooth muscle, which gives balanced dilation of arteries and veins. The heart thus contracts better and works against less resistance.

In dogs it is approved for congestive failure caused by atrioventricular valve disease or dilated cardiomyopathy, and it improves quality of life and survival. It is contraindicated where the problem is outflow obstruction, as in subaortic stenosis, because a stronger beat against a fixed obstruction can worsen it. The main adverse effects are gastrointestinal.

In cats it is not approved, and evidence is mixed. It is used in selected cases that no longer respond to standard therapy. Do not apply the dog rule to cats without checking current references. Hypertrophic cardiomyopathy in cats is an example where a stronger beat is not the aim.

Dobutamine

Dobutamine is a synthetic catecholamine acting mainly on **beta-1 receptors**. Binding of beta-1 receptors raises cAMP in cardiac cells and strengthens contraction. It does not release noradrenaline, and compared with dopamine it has a stronger inotropic and weaker heart-rate effect.

It is given only as a **continuous intravenous infusion**, because the half-life is a few minutes and it is destroyed in the gut. It is used for short-term support in acute, severe failure, cardiogenic shock and low cardiac output under anaesthesia. It cannot be used for long-term control.

Monitoring of heart rate, rhythm and blood pressure is needed, because tachycardia and ventricular arrhythmias can occur. In cats, lower infusion rates are advised because of longer half-life and central nervous stimulation, with seizures reported. Tolerance can develop with prolonged use since receptors down-regulate, an example of the receptor regulation described earlier.

ACE inhibitors

Angiotensin-converting enzyme (ACE) converts angiotensin I to angiotensin II. Angiotensin II constricts vessels, triggers aldosterone release and promotes remodelling of heart muscle. ACE inhibitors such as enalapril and benazepril block this step, so they lower afterload, reduce salt and water retention and may limit remodelling.

They are used as part of combination therapy in dogs with heart failure and in some cats. Realistic expectations are important. In dogs with congestive failure, the

benefit is generally mild and, in some reports, short lived, and aldosterone levels can rise again despite treatment, called **aldosterone breakthrough**. They are not a replacement for a diuretic or pimobendan.

Adverse effects include low blood pressure and azotemia, because angiotensin II helps to maintain filtration pressure in the kidney. Kidney values and electrolytes should be checked, especially when used with diuretics or in dehydrated animals. ACE inhibitors should not be used in pregnancy. Their value in other conditions, such as protein-losing kidney disease, is covered in the renal chapters.

Putting the drugs together and species notes

Treatment is chosen by the stage and cause of failure. In a dog with congestive failure from mitral valve disease, a typical plan combines a loop diuretic to clear congestion, pimobendan to improve output, and an ACE inhibitor, with other drugs added by the clinician. Dobutamine is reserved for critical care. Digoxin is kept for rate control in specific arrhythmias.

A few rules help in the exam. A stronger drug is not always better. Match the drug to the problem: congestion needs a diuretic, low output needs an inotrope, high afterload needs a vasodilator. Each has a trade-off, for example the arrhythmia risk of inotropes and the kidney risk of ACE inhibitors and diuretics.

Cattle and horses show heart failure less often, and drug use is limited by cost and, in food animals, by residue concerns, so check the current notification on permitted drugs. Whatever the species, owners need clear teaching about monitoring: breathing rate at rest, appetite and weight, and the need for repeat kidney and electrolyte tests.

In short, match each drug to its job, start with the diagnosis, and review the response. Resting breathing rate, appetite, body weight and repeat laboratory tests guide any change in the plan.

Concept cleared

Concept cleared: Digoxin and calcium

Digoxin jams the sodium pump. Sodium stays inside, so the cell stops pushing calcium out as well. More calcium is left to trigger contraction, like a pump that is switched off so water level in the tank rises.

Concept cleared: Inodilator

A cart-horse with a lighter cart. Pimobendan strengthens the horse (inotrope) and removes some of the load (vasodilation), so the same effort moves more.

Concept cleared: Neurohormonal brake

ACE inhibitors cut off angiotensin II, which is like removing the tightening screw on the vessels and the salt-retaining signal. The gain is steady but small.

Concept cleared: Dobutamine is a rescue

Its half-life is minutes, like a drip that must keep running. It is for a crisis in the ICU, not for home care.

Memory aid: Four heart failure tools

'DPDA': Digoxin (rate), Pimobendan (inodilator), Dobutamine (ICU rescue), ACE inhibitor (afterload and salt). Diuretics clear the congestion alongside.

Compare and contrast

Heart failure drugs at a glance

Drug	Target	Main effect	Main caution
Digoxin	Na+/K+ ATPase	Mild inotropy, slows AV conduction	Narrow margin; low potassium, kidney disease
Pimobendan	Calcium sensitisation and PDE3	Inotropy plus vasodilation	Outflow obstruction; GI signs; cats not approved
Dobutamine	Beta-1 receptor	Short-term inotropy	Arrhythmia; infusion only; cats seizures
ACE inhibitor	Angiotensin-converting enzyme	Less afterload and salt retention	Hypotension, azotemia

Inotropes: dobutamine versus digoxin

Feature	Dobutamine	Digoxin
Route	Intravenous infusion	Oral (or slow intravenous in special cases)
Duration	Minutes after stopping	Days
Use	Acute severe failure	Rate control in atrial fibrillation
Safety margin	Titrated to effect	Narrow

Species notes

Dog
Pimobendan is approved for failure from valve disease or dilated cardiomyopathy and has largely replaced digoxin. ACE inhibitors and a loop diuretic are used alongside it.

Cat
Cats are more sensitive to digoxin and to dobutamine's nervous system effects. Pimobendan is not approved in cats and evidence is mixed, so it is reserved for selected cases.

Horse
Heart failure is uncommon and treatment is mainly a diuretic, with digoxin used for some atrial

Cattle
Failure usually appears as brisket oedema and jugular distension. Treatment is rarely practical, and

fibrillation cases. Check current references and competition rules.

residue rules apply if any drug is used.

Zoo and exotic animals
Species differences in sensitivity to cardiac glycosides are large. Use only with specialist guidance.

Clinical pearls

Self-test: 10 questions

1. Digoxin increases contractility by inhibiting:

Raised intracellular sodium reduces calcium removal, so calcium rises.

2. Digoxin toxicity is more likely with:

Low potassium increases sensitivity to glycoside effect.

3. The earliest signs of digoxin toxicity are often:

Anorexia and vomiting commonly appear before arrhythmias.

4. Pimobendan is called an inodilator because it:

It combines calcium sensitisation with PDE3 inhibition.

5. Pimobendan is contraindicated in:

A stronger beat against a fixed outflow obstruction can worsen it.

6. Dobutamine acts mainly on:

It is a synthetic catecholamine with mainly beta-1 activity.

7. Why is dobutamine given by continuous infusion?

It acts for only minutes, so effect needs constant delivery.

8. An ACE inhibitor lowers afterload by:

Less angiotensin II means less vasoconstriction and sodium retention.

9. A common adverse effect of ACE inhibitors that needs monitoring is:

Reduced angiotensin II lowers glomerular filtration pressure, so kidney values should be checked.

10. In cats, which statement is correct?

Cats are more sensitive to digoxin, and pimobendan is not approved for them.

Key points to revise

1. Heart failure drugs improve contraction, lower workload or block neurohormonal activation.
2. Digoxin inhibits Na+/K+ ATPase, raising intracellular calcium.
3. Digoxin has a narrow safety margin and cats are more sensitive than dogs.
4. Pimobendan sensitises contractile proteins to calcium and inhibits PDE3.
5. Pimobendan is approved for dogs with valve disease or dilated cardiomyopathy failure.
6. Dobutamine is a beta-1 agonist given by short-term intravenous infusion.

7. ACE inhibitors block angiotensin II formation and reduce afterload and salt retention.
8. ACE inhibitor benefit in canine failure is modest and aldosterone breakthrough can occur.

Go deeper on this site

- Ch 16. Antiarrhythmic drugs (in this book)
- Ch 17. Vasodilators and antihypertensive drugs (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Positive Inotropes for Use in Animals
- Merck Veterinary Manual: Heart Failure in Dogs and Cats
- Merck Veterinary Manual: Diuretics for Use in Animals

CHAPTER 16 OF 33

Antiarrhythmic drugs

Antiarrhythmic drugs correct or control abnormal heart rhythm by changing ion movement across heart-cell membranes. This chapter explains the Vaughan-Williams classes, why these drugs can themselves cause arrhythmias, and the common rhythm disturbances of dogs and horses.

After this chapter you can

- Explain how arrhythmias arise from abnormal automaticity, triggered activity and re-entry
- State the Vaughan-Williams classes with a mechanism and an example for each
- Describe why antiarrhythmics can be proarrhythmic and why electrolytes matter
- Recognise the common arrhythmias of dogs and horses and the drug classes used conceptually

- Apply species cautions to antiarrhythmic use

Why hearts go out of rhythm

A normal heartbeat starts in the sinoatrial node, crosses the atrioventricular (AV) node, and spreads through the ventricles in an orderly way. Each cardiac cell fires an **action potential** built from the movement of sodium, calcium and potassium ions. An **arrhythmia** is any disturbance of this sequence in rate, regularity or site of origin.

Three basic mechanisms explain almost every arrhythmia. **Abnormal automaticity** means a cell outside the sinus node starts firing on its own. **Triggered activity** means after-depolarisations during or just after an action potential set off extra beats. **Re-entry** means an impulse travels round a circuit of tissue with slow conduction in one limb, so it keeps re-exciting the heart. Re-entry is the commonest cause of sustained tachycardia and of atrial fibrillation.

Each antiarrhythmic class targets one of these mechanisms by changing a channel or receptor. Knowing the mechanism helps you predict both the benefit and the harm.

The Vaughan-Williams classification

The classification groups drugs by their main effect on the cardiac action potential. It is a teaching framework. Many drugs act on more than one channel, so the classes overlap.

- **Class I: sodium-channel blockers.** They slow the upstroke of the action potential in fast tissue such as ventricle and atrium. Ia (quinidine, procainamide) also prolongs repolarisation. Ib (lidocaine, mexiletine) shortens it and acts mainly on diseased or rapidly firing tissue. Ic (flecainide, propafenone) slows conduction strongly and is little used in animals.
- **Class II: beta-blockers** (propranolol, atenolol, metoprolol, esmolol). They block sympathetic drive, slow the sinus rate and slow AV conduction.
- **Class III: potassium-channel blockers** (amiodarone, sotalol). They prolong repolarisation and the refractory period, which makes re-entry harder. Sotalol also has beta-blocking action.

- **Class IV: calcium-channel blockers** (diltiazem, verapamil). They slow the AV node and are useful for supraventricular tachycardia.
- **Others:** digoxin and adenosine do not fit the four classes. Digoxin slows AV conduction mainly by raising vagal tone.

A simple way to use the scheme is to ask where the rhythm originates. Ventricular rhythms respond to Class I and III drugs. Supraventricular rhythms with fast ventricular rates respond to drugs that slow the AV node, namely classes II, IV and digoxin.

Drugs by site of action

Sodium-channel blockers. Lidocaine is given intravenously for ventricular tachycardia in dogs because it acts quickly and wears off quickly. It has a narrow safety margin, and signs of excess include tremor, seizures and vomiting. Cats are generally more sensitive, so it is used with great caution. Mexiletine is an oral relative. Quinidine is used in horses for atrial fibrillation and is discussed below.

Beta-blockers. They reduce arrhythmias driven by adrenaline and slow the ventricular rate in supraventricular tachycardia. Their negative inotropic effect can precipitate or worsen heart failure in a weak heart, so they are used carefully in animals with decompensated disease. Non-selective drugs may also cause bronchospasm, which matters in cats and in animals with airway disease.

Potassium-channel blockers. Sotalol is widely used for ventricular arrhythmias in dogs. Amiodarone has many effects and a long list of adverse effects, so it is reserved for selected cases.

Calcium-channel blockers and digoxin. Diltiazem and digoxin are commonly combined to control the ventricular rate in atrial fibrillation. Digoxin has a narrow therapeutic index, and hypokalaemia and renal dysfunction increase its toxicity. Verapamil is a stronger negative inotrope and carries more risk in failing hearts.

Arrhythmias in dogs

Dogs most often present with **ventricular premature complexes** and **ventricular tachycardia**, with **atrial fibrillation** and **supraventricular tachycardia** next. Underlying causes include cardiomyopathy, mitral valve disease, myocarditis, gastric dilatation-volvulus, splenic disease, trauma, anaemia and drug effects.

Two breed examples are worth knowing. Boxers and some other breeds develop an arrhythmogenic cardiomyopathy with ventricular arrhythmias and risk of syncope. Giant breeds with dilated cardiomyopathy commonly develop atrial fibrillation, which is treated mainly by slowing the AV node rather than by restoring sinus rhythm.

Treatment is not decided by the ECG alone. Isolated, slow ventricular beats in a stable dog often need no drug. Treatment is considered when the rate is fast, the rhythm is multiform or runs of tachycardia occur, or there are signs such as weakness or collapse. Always look for and treat the cause first.

Arrhythmias in horses

Many equine athletes have physiological bradyarrhythmias, such as sinus arrhythmia and second-degree AV block, which reflect high vagal tone. These disappear with exercise and need no treatment. Do not mistake them for disease.

Atrial fibrillation is the commonest clinically important arrhythmia. It often causes poor performance and exercise intolerance in an otherwise healthy horse. In a horse with no significant heart disease, conversion to sinus rhythm can be achieved by drug therapy, for example quinidine, or by electrical cardioversion. Quinidine has real hazards: hypotension, ventricular tachycardia, gastrointestinal upset and swelling of the nasal mucosa. It also raises plasma digoxin levels, so combined use needs care. Horses are monitored closely during treatment.

Ventricular tachycardia in horses is usually secondary to myocardial disease, electrolyte disturbance or drug effect, and is treated with drugs such as lidocaine under ECG monitoring. Check the current references for protocols.

Proarrhythmia, electrolytes and safe use

Antiarrhythmic drugs can **cause** arrhythmias. This is called proarrhythmia. Drugs that prolong repolarisation can allow dangerous triggered activity, and sodium-channel blockers can slow conduction until re-entry becomes easier. This is why a drug is chosen for a documented, clinically significant rhythm, not for every abnormal beat.

Potassium and magnesium disturbances make arrhythmias worse and reduce the response to drugs. Correct hypokalaemia and hypomagnesaemia first, especially in

animals on loop diuretics. Remember that hyperkalaemia, for example in urethral obstruction or hypoadrenocorticism, can itself produce bradyarrhythmias.

Always record an ECG before, during and after therapy, and treat the underlying disease. Drug interactions matter: diuretic-induced hypokalaemia with digoxin is a classic example.

Concept cleared

Three mechanisms of arrhythmia
Abnormal automaticity, triggered activity and re-entry. Re-entry underlies most sustained tachycardias.

Vaughan-Williams classes
I sodium-channel, II beta-blocker, III potassium-channel, IV calcium-channel. Digoxin and adenosine sit outside.

Proarrhythmia
Antiarrhythmic drugs can create new arrhythmias, particularly with electrolyte disturbance or heart disease.

Treat the rhythm, and its cause
Treat when the rhythm is fast, sustained or causing signs, and always look for the underlying disease and electrolyte problem.

Memory aid: Remembering the classes
Sodium, Beta, Potassium, Calcium gives 1, 2, 3, 4 in the order S-B-P-C. Create your own phrase from these letters. Remember that sodium is first because it opens the action potential.

Compare and contrast

Vaughan-Williams classes

Class	Target	Examples	Main use
I	Sodium channel	Lidocaine, quinidine, mexiletine	Ventricular arrhythmias; quinidine for equine atrial fibrillation
II	Beta receptor	Atenolol, propranolol, esmolol	Catecholamine-driven or supraventricular tachycardia
III	Potassium channel	Sotalol, amiodarone	Ventricular arrhythmias
IV	L-type calcium channel	Diltiazem, verapamil	Slowing AV node in supraventricular rhythms

Dog versus horse arrhythmia picture

Feature	Dog	Horse
Commonest concern	Ventricular premature complexes and tachycardia	Atrial fibrillation
Benign findings	Respiratory sinus arrhythmia	Second-degree AV block, sinus arrhythmia at rest
Typical approach	Treat the cause; drug if fast or signs present	Convert in healthy horses; rate control rarely needed
Key drug caution	Lidocaine toxicity; digoxin narrow margin	Quinidine toxicity and digoxin interaction

Species notes

Dog
Ventricular arrhythmias are common and may follow splenic disease or gastric dilatation-volvulus. Atrial fibrillation in giant breeds is managed with AV node slowing.

Cat
Cats are sensitive to lidocaine, and propranolol may cause bronchospasm. Ventricular arrhythmias are less common than in dogs.

Horse
Atrial fibrillation with poor performance is the key arrhythmia.

Ruminants
Arrhythmias are mostly secondary to electrolyte, toxic or metabolic

Quinidine has marked toxicity and horses must be monitored. High vagal tone causes harmless blocks.

disease, for example hypocalcaemia, and are corrected by treating the cause.

Clinical pearls

Self-test: 10 questions

1. Which Vaughan-Williams class do beta-blockers belong to?

Class II consists of beta-blockers such as atenolol and propranolol.

2. Lidocaine is mainly used for which rhythm in dogs?

Lidocaine is a sodium-channel blocker given intravenously for ventricular arrhythmias.

3. Class III drugs act mainly by

Class III drugs, such as sotalol and amiodarone, prolong the action potential and refractory period.

4. The commonest mechanism of sustained tachyarrhythmias is

A circuit of tissue with slow conduction lets the impulse re-excite the heart repeatedly.

5. Which arrhythmia commonly causes poor performance in an otherwise healthy horse?

Atrial fibrillation is the commonest clinically important equine arrhythmia and often limits athletic work.

6. A known hazard of quinidine in horses is

Quinidine can cause hypotension, ventricular tachycardia, gastrointestinal signs and nasal mucosal swelling.

7. Proarrhythmia means

Antiarrhythmics can induce new rhythm disturbances, especially with electrolyte imbalance or heart disease.

8. Which electrolyte disturbance should be corrected before antiarrhythmic therapy?

Low potassium and magnesium promote arrhythmias and blunt drug response.

9. Digoxin slows the AV node mainly by

Digoxin has a vagomimetic action on the AV node and so slows ventricular rate in atrial fibrillation.

10. Which is true of an isolated, slow, uniform ventricular premature beat in a stable dog?

Treatment depends on rate, complexity and clinical signs, not on the presence of an ectopic beat alone.

Key points to revise

1. Arrhythmias arise from abnormal automaticity, triggered activity or re-entry.
2. Class I blocks sodium channels.
3. Class II drugs are beta-blockers.
4. Class III drugs prolong repolarisation by blocking potassium channels.
5. Class IV drugs are calcium-channel blockers that slow the AV node.
6. Antiarrhythmics can be proarrhythmic.
7. Atrial fibrillation is the key equine arrhythmia.

8. Correct electrolytes and treat the underlying disease.

Go deeper on this site

- Ch 17. Vasodilators and antihypertensive drugs (in this book)
- Ch 15. Drugs for heart failure and inotropes (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Manual: Antiarrhythmic Drugs (Vaughan Williams Classification)
- Merck Veterinary Manual: Heart Failure in Dogs and Cats
- Merck Veterinary Manual: Diuretics for Use in Animals

CHAPTER 17 OF 33

Vasodilators and antihypertensive drugs

How drugs widen blood vessels or slow the heart to lower pressure and workload: arterial, venous and mixed vasodilators, calcium-channel blockers and beta-blockers. The chapter stresses why hypotension is the central risk and how to avoid it.

After this chapter you can

- Distinguish arterial, venous and balanced vasodilators and relate each to preload and afterload
- Explain the mechanism and veterinary use of amlodipine, hydralazine, nitrates, nitroprusside and sildenafil
- Describe how beta-blockers act and why they must not be stopped suddenly or started in decompensated failure
- Contrast dihydropyridine and non-dihydropyridine calcium-channel blockers
- Identify the causes of drug-induced hypotension and how to reduce the risk

Blood pressure, preload and afterload

Blood pressure depends on cardiac output and on resistance in the arterioles. The heart works against **afterload**, which is mainly arteriolar resistance, and is filled by **preload**, which is the volume returning through the veins. Vasodilators lower pressure or cardiac workload by relaxing vascular smooth muscle.

The site of action decides the effect. **Arterial dilators** lower afterload and arterial pressure. **Venous dilators** pool blood in the veins and lower preload, which relieves pulmonary congestion. **Balanced dilators** do both. Knowing which side a drug acts on tells you when to use it and what will go wrong if the dose is too high.

In animals, systemic hypertension is most often secondary to another disease, such as chronic kidney disease or hyperthyroidism in cats, so the underlying cause must also be addressed. Vasodilators are also used in heart failure to reduce the work the failing ventricle must do.

Arterial vasodilators

Hydralazine relaxes arteriolar smooth muscle and has no useful effect on veins. Its exact molecular mechanism is not fully settled. It is potent, so the main danger is systemic hypotension, and the reflex that follows is a rise in heart rate and fluid retention by the kidney. It is therefore used with caution and often with other drugs.

Amlodipine is a calcium-channel blocker that acts mainly on small arteries. It is the calcium-channel blocker most used for hypertension in cats and dogs, especially in cats with kidney disease. It dilates arterioles strongly but has little effect on the force of cardiac contraction or on conduction, which is why it behaves very differently from diltiazem. A recognised adverse effect is gingival overgrowth.

Prazosin is an alpha-1 blocker that gives mixed dilation. Tolerance develops quickly, and it is now rarely used for primary heart disease in small animals.

A common confusion is to think all calcium-channel blockers are alike. They are not, as the next sections show.

Venous, balanced and pulmonary vasodilators

Nitroglycerin and other organic nitrates release nitric oxide, which raises cGMP in smooth muscle and relaxes it. At clinical doses the effect is mostly venous, so preload falls. Use is mainly in acute congestive failure, and evidence is largely

anecdotal. Tolerance develops with sustained use, and accidental skin exposure of handlers is a practical concern with topical forms.

Sodium nitroprusside is a very potent nitric oxide donor that dilates both arteries and veins. It is given only by infusion under close blood pressure monitoring, for hypertensive crisis or severe life-threatening failure. Because it is metabolised to cyanide, it is used only for a short period.

ACE inhibitors block formation of angiotensin II and slow breakdown of bradykinin. They are balanced dilators with a mild effect on afterload. In hypertension they are usually combined with another arterial dilator rather than used alone for severe disease. They can reduce kidney perfusion pressure and cause azotemia, especially with dehydration, diuretics or NSAIDs.

Sildenafil inhibits phosphodiesterase 5, so cGMP is not broken down. It dilates the pulmonary vessels more than the systemic ones and is used as an adjunct in canine pulmonary hypertension.

Beta-blockers

Beta-blockers compete with adrenaline and noradrenaline at beta receptors. Blocking cardiac beta-1 receptors lowers heart rate, slows atrioventricular conduction and reduces the force of contraction. Oxygen demand of the heart falls and diastolic filling time improves. They are used for fast supraventricular and some ventricular rhythms, for hypertrophic cardiomyopathy in cats, and to control the heart rate effects of hyperthyroidism.

- **Propranolol** is non-selective, blocking beta-1 and beta-2.
- **Atenolol** is beta-1 selective and is the beta-blocker used most in veterinary practice.
- **Carvedilol** blocks beta-1, beta-2 and alpha-1 receptors.

Beta-2 blockade narrows airways, so non-selective drugs should be avoided in animals with asthma or other primary airway disease. Selectivity is relative and fades at high doses, so even atenolol needs care.

Two rules matter in practice. First, a beta-blocker should never be started in an animal with active pulmonary oedema, because the heart depends on sympathetic drive at that time. Second, long use up-regulates receptors, so **abrupt withdrawal**

can cause rebound tachycardia and hypertension. Stop by tapering. Adverse effects are bradycardia, hypotension and myocardial depression, especially when systolic function is poor.

Calcium-channel blockers in the heart

Calcium entering through L-type channels triggers contraction of muscle and drives the sinus and AV nodes. Blocking these channels relaxes smooth muscle and slows nodal tissue. The class has two practical groups.

- **Dihydropyridines** such as amlodipine act mainly on vascular smooth muscle. They lower arterial pressure with little direct cardiac depression.
- **Non-dihydropyridines**, mainly **diltiazem** and verapamil, act on the heart. They have negative inotropic effect, slow the rate and slow AV conduction. Diltiazem is used for rate control in atrial fibrillation and other supraventricular tachycardias, and is of no use for ventricular arrhythmias.

Diltiazem can cause hypotension, bradycardia and worsening heart failure, and gastrointestinal upset is common with sustained-release products in cats. It should generally not be combined with a beta-blocker because both depress the node and the muscle, and the effect adds up.

Verapamil is not discussed in the sources used for this chapter, so confirm its use in a veterinary formulary.

Hypotension: why it happens and how to avoid it

Hypotension is the common thread of this chapter. It appears when an animal receives a potent dilator, when two or three drugs that lower pressure are given together, or when the animal is already dehydrated, anaesthetised or in heart failure.

- Combine drugs that lower pressure by different mechanisms, such as an ACE inhibitor with amlodipine, only after starting each low and increasing slowly.
- Diuretics add to the effect of vasodilators by lowering circulating volume.
- General anaesthetics and acepromazine are also vasodilators, so an animal on antihypertensives needs careful monitoring during anaesthesia.

- Measure blood pressure before and after changes, and check kidney values when ACE inhibitors are used.

Signs of overdose include weakness, collapse, pale mucous membranes and fainting. Very high pressure, with a systolic reading above about 160 to 180 mm Hg, can damage the eye, brain, kidney and heart, and is treated more urgently, but the treatment goal is gradual reduction, not a sudden normal value.

In practice, start with one drug at a low starting dose, recheck pressure after a suitable interval, and add a second drug only if needed. Owners should be told to report weakness, fainting or loss of appetite promptly.

Concept cleared

Concept cleared: Preload and afterload
Think of a pump filling a bucket through a narrow pipe. Preload is how full the pump gets before it pushes. Afterload is how hard the pipe resists. Venous dilators reduce the filling, arterial dilators widen the pipe, and balanced dilators do both.

Concept cleared: Two kinds of calcium-channel blocker
Amlodipine is a tap-opener for vessels: it relaxes arterioles and leaves the heart alone. Diltiazem is a brake on the heart: it slows the nodes and weakens each beat. They share a name but do different jobs.

Concept cleared: Beta-blocker withdrawal
If a driver keeps pressing the brake for weeks, the brake system becomes over-sensitive. Releasing it suddenly lets the car lurch forward. Receptors up-regulate under blockade, so sudden stopping lets adrenaline act on too many receptors.

Concept cleared: Additive hypotension

Each blood-pressure-lowering drug takes a little pressure away. Several together can take away more than the animal can spare, especially when volume is low from dehydration or diuretics.

Memory aid: Venous for volume, arterial for afterload

V for Venous and Volume (preload, relieve congestion); A for Arterial and Afterload (lower pressure). Beta-blocker rule: Brake slowly, never Brake-release suddenly. Calcium: Amlodipine Acts on Arteries; Diltiazem Decelerates the heart.

Compare and contrast

Vasodilators by site and use

Drug	Main site	Mechanism	Main concern
Hydralazine	Arterioles	Relaxes arteriolar smooth muscle	Hypotension, reflex tachycardia
Amlodipine	Arterioles	L-type calcium channel block	Gingival overgrowth, hypotension
Nitroglycerin	Veins	Nitric oxide donor, cGMP rise	Tolerance, handler exposure
Nitroprusside	Arteries and veins	Nitric oxide donor	Profound hypotension, cyanide
ACE inhibitor	Balanced	Less angiotensin II, bradykinin kept	Azotemia, hypotension
Sildenafil	Pulmonary vessels	PDE5 inhibition, cGMP kept	Systemic hypotension possible

Beta-blockers and calcium-channel blockers

Feature	Beta-blocker	Dihydropyridine CCB	Diltiazem
Example	Atenolol, propranolol	Amlodipine	Diltiazem
Main target	Cardiac beta receptors	Vascular calcium channels	Cardiac and nodal calcium channels
Heart rate	Falls	Little change	Falls
Force of contraction	Falls	Little change	Falls
Main use	Tachyarrhythmia, feline HCM	Hypertension	Supraventricular tachycardia
Key caution	Do not stop abruptly	Gingival overgrowth	Do not pair with beta-blocker

Species notes

Cat

Amlodipine is the usual first choice for hypertension, which is often secondary to kidney disease or hyperthyroidism. Atenolol is the common beta-blocker, for example in hypertrophic cardiomyopathy. Diltiazem sustained-release often causes gastrointestinal signs.

Dog

Hypertension is usually secondary to kidney disease, endocrine disease or protein-losing disease. Amlodipine and ACE inhibitors are used, and sildenafil is an adjunct for pulmonary hypertension.

Horse

Antihypertensive therapy is uncommon in routine equine practice. Acepromazine, a phenothiazine with alpha-1 blocking vasodilator effect, can cause hypotension, so it should be used

Cattle

Cardiovascular vasodilator therapy is rarely used in cattle, and no drug of this chapter is a routine food-animal treatment. Check the current notification before using any such drug in a food-producing animal.

with care in dehydrated or shocked animals.

Dog (anaesthesia)
Dogs on vasodilators or beta-blockers need blood pressure monitoring under anaesthesia, because anaesthetic drugs add to the pressure-lowering effect.

Clinical pearls

Self-test: 10 questions

1. Which drug acts mainly on veins and lowers preload at clinical doses?

Nitroglycerin releases nitric oxide and relaxes mainly venous smooth muscle.

2. Which calcium-channel blocker is mainly a vascular arteriolar dilator with little cardiac depression?

Amlodipine, a dihydropyridine, acts mainly on arterioles.

3. A recognised adverse effect of amlodipine in dogs and cats is:

Gingival overgrowth is reported with amlodipine.

4. Why should a beta-blocker not be stopped suddenly?

Long blockade up-regulates receptors, so withdrawal can cause rebound tachycardia and hypertension.

5. Which beta-blocker is beta-1 selective and most used in veterinary practice?

Atenolol is beta-1 selective and the most used.

6. Sildenafil is useful in canine pulmonary hypertension because it:

PDE5 inhibition keeps cGMP high and dilates pulmonary vessels.

7. Which combination carries the highest additive risk for conduction block and failure?

Both depress nodal conduction and contractility, so effects add up.

8. Why is nitroprusside used only for short periods?

Nitroprusside is metabolised to cyanide, so use is limited and monitored.

9. Propranolol should be avoided in animals with asthma because of:

Non-selective beta blockade narrows the airways.

10. Which situation most raises the risk of drug-induced hypotension?

Low circulating volume and additive pressure-lowering drugs together produce hypotension.

Key points to revise

1. Arterial dilators reduce afterload; venous dilators reduce preload; balanced dilators do both.
2. Hydralazine is a potent arteriolar dilator and can cause hypotension.

3. Amlodipine is a dihydropyridine calcium-channel blocker used for hypertension, with gingival overgrowth as an adverse effect.
4. Nitrates act mostly on veins through nitric oxide and cGMP, and tolerance develops.
5. Sildenafil inhibits PDE5 and is used for canine pulmonary hypertension.
6. Atenolol is beta-1 selective; propranolol is non-selective.
7. Beta-blockers must be tapered, not stopped suddenly.
8. Diltiazem slows the heart and should not be combined with a beta-blocker.

Go deeper on this site

- Ch 18. Diuretics and drugs acting on the kidney (in this book)
- Ch 16. Antiarrhythmic drugs (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Vasoactive Drugs for Use in Animals
- Merck Veterinary Manual: Antiarrhythmics for Use in Animals
- Merck Veterinary Manual: Angiotensin-Converting Enzyme Inhibitors for Use in Animals

CHAPTER 18 OF 33

Diuretics and drugs acting on the kidney

How loop, thiazide, potassium-sparing and osmotic diuretics act on different parts of the nephron, what each does to electrolytes, how the kidney handles drugs, and which drugs damage the kidney.

After this chapter you can

- Trace the nephron and state where each diuretic class acts
- Explain the electrolyte and acid-base effects of loop, thiazide and potassium-sparing diuretics

- Describe the actions, uses and cautions of mannitol and carbonic anhydrase inhibitors
- Explain filtration, secretion, reabsorption and the effect of urine pH on drug excretion
- List common nephrotoxic drugs and the factors that increase the risk

The nephron and the logic of diuretics

Each kidney nephron filters plasma at the glomerulus, and the tubule then takes back most of the filtered sodium and water. A **diuretic** blocks sodium reabsorption at some site, so more sodium stays in the tubule and water follows it. The site decides how strong the drug is, because the proximal tubule and the loop take back far more sodium than the distal parts.

- **Proximal tubule**: carbonic anhydrase inhibitors and osmotic diuretics.
- **Thick ascending loop of Henle**: loop diuretics, the strongest class.
- **Early distal tubule**: thiazides.
- **Late distal tubule and collecting duct**: potassium-sparing diuretics.

A drug acting upstream is partly compensated by downstream segments, which take back some of the sodium. This is why diuretics from different classes are sometimes combined, and why the combination raises the risk of electrolyte loss and dehydration.

Loop diuretics

Furosemide and **torsemide** block the Na-K-2Cl co-transporter in the thick ascending limb. This segment normally builds the concentration gradient in the medulla, so blocking it gives a large volume of dilute urine. The ceiling of effect is high, so the dose can be scaled from mild to life-threatening congestion.

Furosemide is the most widely used diuretic in veterinary medicine. It acts quickly and briefly, and a constant-rate infusion produces more diuresis than the same total given as boluses. Torsemide is more potent, lasts longer, and is better absorbed by mouth in dogs. It does not lose effect with repeated use as readily as furosemide.

Main uses are pulmonary oedema and ascites from congestive heart failure, and oedema or fluid overload in other conditions. Common adverse effects follow from

the mechanism:

- Loss of potassium, sodium and magnesium, and a metabolic alkalosis.
- Dehydration and a fall in blood volume, which can lower cardiac output, reduce kidney perfusion and cause azotemia.
- Hypokalaemia can increase digoxin toxicity.
- Ototoxicity at high intravenous exposure, and increased aminoglycoside toxicity.

NSAIDs blunt the diuretic effect because prostaglandins help maintain kidney blood flow. In kidney disease, higher doses of furosemide may be needed because less drug reaches the tubular site, but cautious monitoring is essential.

Thiazides and potassium-sparing diuretics

Thiazides such as hydrochlorothiazide block the Na-Cl co-transporter in the early distal tubule. They have mild to moderate potency and need adequate renal blood flow, so they work poorly when kidney perfusion is low and are not used in azotemic patients. In dogs and cats they are rarely first choice and are mostly added to a loop diuretic in refractory heart failure. Unlike loop diuretics, they reduce urinary calcium loss, and may cause hypercalcaemia. They also waste potassium. Paradoxically, thiazides reduce urine volume in diabetes insipidus, a use that is explained in the endocrine chapters.

Potassium-sparing diuretics act in the late distal tubule and collecting duct. **Spironolactone** blocks the aldosterone receptor, so fewer sodium channels and potassium pumps are made and sodium is excreted while potassium is kept. **Triamterene and amiloride** block the sodium channel directly, but are less used in animals.

These drugs are weak diuretics by themselves. Spironolactone is added in chronic heart failure for its protective effect against aldosterone-driven fibrosis, and it is never used alone for congestion. The main risk is **hyperkalaemia**, particularly together with an ACE inhibitor, in kidney disease, or without a loop diuretic. The peak effect of spironolactone takes some days.

Osmotic diuretics and carbonic anhydrase inhibitors

Mannitol is filtered at the glomerulus but is not reabsorbed. It holds water in the tubule by osmotic force, which keeps urine flowing and may protect tubular cells in

acute kidney injury. It also draws water out of tissues into the vascular space, which is why it is used to lower raised intracranial pressure. The expansion of blood volume can overload an animal that already has heart failure or pulmonary oedema, and mannitol should not be repeated if no response appears. In large adult animals, a solvent such as DMSO is sometimes substituted because mannitol is costly.

Carbonic anhydrase inhibitors such as acetazolamide act in the proximal tubule. Without carbonic anhydrase, bicarbonate is not reclaimed, so sodium bicarbonate and water are lost and the plasma becomes acidotic. The diuretic effect is weak and fades because acidosis limits it. Their modern uses are mainly outside the kidney, such as reducing aqueous humour production in glaucoma.

Common confusion: mannitol is an *osmotic* drug that needs a functioning, perfused kidney to give urine, and it should not be given to an anuric animal expecting a response.

How the kidney handles drugs

Drug elimination by the kidney is the sum of three processes. **Glomerular filtration** removes free, unbound drug, so highly protein-bound drugs are filtered poorly. **Tubular secretion** actively moves many drugs, especially organic acids such as penicillins and furosemide, into the tubule through transporters. Competition at these transporters is the basis of drug interactions, and it explains why furosemide reaches its site of action by secretion. **Tubular reabsorption** returns lipid-soluble drug to blood by passive diffusion.

Urine pH changes reabsorption because only the unionised form crosses membranes. Alkalinising the urine ionises weak acids, which are then trapped in the urine and excreted faster. Acidifying the urine does the same for weak bases. This principle is used in some poisonings.

When kidney function falls, drugs that depend on renal excretion accumulate, and the dose or interval may need adjustment. Examples are aminoglycosides and some ACE inhibitors. Always check the product information for the species and consult the current formulary.

Nephrotoxicity

The kidney is exposed to a high blood flow and concentrates drugs in the tubules, so it is a frequent target of toxicity. Important causes in animals:

- **NSAIDs** block prostaglandins that keep afferent arterioles dilated. In dehydration or low blood volume, this can cause ischaemic injury. The risk rises with ACE inhibitors and diuretics.
- **Aminoglycosides** accumulate in proximal tubular cells and cause tubular necrosis. Risk is increased by dehydration, kidney disease and prolonged use.
- **Amphotericin B** is nephrotoxic, and some tetracyclines at high exposure may harm an already damaged kidney.
- **Ethylene glycol** and lilies in cats are non-drug examples examined in toxicology.
- **Contrast agents and some chemotherapy drugs** can also injure the tubule.

Risk factors are dehydration, existing renal disease, old age, hypotension, and combinations of nephrotoxic drugs. Prevention is to correct fluid deficits first, use the lowest effective dose for the shortest time, avoid drug combinations that lower renal perfusion, and monitor urea, creatinine and urine output.

Concept cleared

Concept cleared: Why loop diuretics are strongest
Picture a motorway with three toll gates. The first gates collect most of the traffic, the last only a little. Loop diuretics shut a gate where a large share of sodium would otherwise be collected, so far more sodium and water leave. Distal drugs shut a gate where little traffic passes, so their effect is mild.

Concept cleared: Potassium loss and sparing
Sodium reabsorption in the late tubule is traded for potassium. When more sodium arrives there, as after loop or thiazide drugs, the exchange takes more potassium into the urine. Potassium-sparing drugs shut that exchange, so potassium stays in the body.

Concept cleared: Osmotic diuresis

Mannitol is like a sponge that cannot be squeezed out in the tubule. It stays inside and holds water with it, so urine flows even though sodium handling is unchanged.

Concept cleared: Ion trapping

A weak acid in alkaline urine loses its charge-free form and becomes ionised. The ionised form cannot cross back, so it is trapped in the urine and leaves the body.

Memory aid: Down the nephron

Order of sites, top to bottom: Carbonic anhydrase and Mannitol (proximal), Loop, Thiazide, Spironolactone. Think: 'Can My Little Tiny Sprout grow'. Loop wastes potassium and calcium; thiazide wastes potassium but saves calcium; spironolactone saves potassium.

Compare and contrast

Diuretic classes

Class	Site	Mechanism	Key adverse effect
Loop (furosemide, torsemide)	Thick ascending limb	Blocks Na-K-2Cl co-transporter	Low K, Na, Mg; dehydration; ototoxicity
Thiazide	Early distal tubule	Blocks Na-Cl co-transporter	Low K, high Ca, azotemia risk
Potassium-sparing (spironolactone)	Late distal and collecting duct	Aldosterone receptor block	Hyperkalaemia
Osmotic (mannitol)	Proximal tubule and loop	Non-reabsorbed osmotic load	Volume overload, dehydration if repeated
Carbonic anhydrase inhibitor	Proximal tubule	Bicarbonate not reclaimed	Metabolic acidosis

Common nephrotoxic drugs

Drug	How it harms	Main risk factor
NSAIDs	Reduced prostaglandin-dependent renal blood flow	Dehydration, hypotension
Aminoglycosides	Tubular cell uptake and necrosis	Prolonged use, kidney disease
Amphotericin B	Direct tubular injury and vasoconstriction	High cumulative exposure
Loop diuretic with aminoglycoside	Volume loss plus added toxicity	Concurrent use

Species notes

Dog
Furosemide is the standard diuretic for pulmonary oedema in heart failure, and torsemide and spironolactone are added in chronic cases. Monitor kidney values and electrolytes.

Cat
Cats are more sensitive to loop diuretics than dogs and can become dehydrated or azotaemic quickly. Facial skin lesions have been reported with spironolactone.

Horse
Furosemide is used in some conditions such as pulmonary haemorrhage and oedema. Its use in racing is regulated, so check the current rules of the governing body.

Cattle
Furosemide has been used for udder oedema. Check the current regulatory notification for permitted use and withdrawal in food-producing animals before treating.

All species
Treat dehydration before using NSAIDs or aminoglycosides, and avoid combining them with other agents that lower renal blood flow.

Clinical pearls

Self-test: 10 questions

1. Which diuretic acts on the thick ascending limb of the loop of Henle?

Furosemide blocks the Na-K-2Cl co-transporter in this segment.

2. The main risk of spironolactone is:

It spares potassium, so potassium can rise, especially with ACE inhibitors.

3. Which statement about thiazides is correct?

Thiazides reduce calcium loss and may cause hypercalcaemia.

4. Mannitol produces diuresis because it:

It acts as a non-reabsorbed osmotic load.

5. Carbonic anhydrase inhibitors cause:

Bicarbonate is lost in urine, so plasma becomes acidotic.

6. Which drug combination raises the risk of ototoxicity and nephrotoxicity?

Furosemide can potentiate aminoglycoside toxicity.

7. Why do NSAIDs risk kidney injury in a dehydrated animal?

Prostaglandin-dependent dilation of afferent arterioles is lost, causing ischaemia.

8. Alkalinising urine speeds excretion of:

Weak acids become ionised and are trapped in alkaline urine.

9. Which statement about loop diuretics is correct?

Loop diuretics waste potassium and chloride, producing alkalosis.

10. Which is a key way to reduce aminoglycoside nephrotoxicity?

Dehydration and prolonged exposure increase tubular accumulation and injury.

Key points to revise

1. Diuretics block sodium reabsorption at specific nephron sites, and water follows sodium.
2. Loop diuretics block the Na-K-2Cl co-transporter in the thick ascending limb.
3. Loop diuretics cause hypokalaemia, hyponatraemia, hypomagnesaemia and metabolic alkalosis.
4. Thiazides act in the early distal tubule and reduce calcium excretion.
5. Spironolactone blocks aldosterone receptors and can cause hyperkalaemia.
6. Mannitol is an osmotic diuretic that is filtered and not reabsorbed.
7. Acetazolamide inhibits carbonic anhydrase and produces metabolic acidosis.
8. NSAIDs and aminoglycosides are leading nephrotoxic drugs, and dehydration raises the risk.

Go deeper on this site

- Ch 19. Drugs of the urinary tract (in this book)
- Ch 17. Vasodilators and antihypertensive drugs (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Diuretics for Use in Animals
- Merck Veterinary Manual: Diuretics Used to Treat Urinary Disease in Animals
- Merck Veterinary Manual: Angiotensin-Converting Enzyme Inhibitors for Use in Animals

CHAPTER 19 OF 33

Drugs of the urinary tract

How drugs change urine chemistry and lower urinary tract function: acidifiers and alkalinisers, drugs used for stones, drugs for urinary incontinence and urethral spasm, and urinary antiseptics. The emphasis is on mechanism and on matching the drug to the stone or the sphincter problem.

After this chapter you can

- Explain how urine pH is altered and why the target pH differs with stone type
- Name the main urinary acidifiers and alkalinisers and state their cautions
- Describe medical dissolution and prevention of struvite, urate, cystine and calcium oxalate uroliths
- Match drugs for urinary incontinence and urethral spasm to the receptor or muscle they act on
- Explain how methenamine and nitrofurantoin work as urinary antiseptics and where they fail

Why urine chemistry is a drug target

The urinary tract can be treated from two directions. One is the **chemistry of the urine**: its pH, volume and the concentration of dissolved minerals. The other is the **nerve and muscle control** of the bladder and urethra. Drugs in this chapter act on one or the other.

Urine pH matters because crystals form only when a mineral is present above its solubility, and solubility depends strongly on pH. Struvite dissolves in acid urine and precipitates in alkaline urine. Urate and calcium oxalate behave differently, so one pH target cannot suit every stone. Before giving any drug that changes urine pH, the stone type or the problem being treated must be known.

A common confusion is to treat a urine pH number as a disease. It is only a tool. Diet, urine volume, infection and the frequency of urination often matter as much as the drug.

Urinary acidifiers

Acidifiers lower urine pH by giving the body an acid load that the kidney then excretes. The usual agents are **ammonium chloride** and **dl-methionine**. They are preferred when struvite (magnesium ammonium phosphate) stones or crystals are the concern. Dietary acidification is often used alongside or instead of drugs.

Acidification also helps when a urinary antiseptic such as methenamine needs acid urine to work, and it can increase the renal excretion of weak bases through ion trapping. This links back to the earlier chapter on drug excretion.

The main caution is that **chronic acidification produces systemic metabolic acidosis**. In animals with kidney disease, or in young growing animals, this can be harmful. Acidifiers should not be started without a full clinical evaluation and should be monitored. Ammonium compounds are also unsuitable where hepatic function is poor, because the ammonium load must be handled by the liver.

In cats, struvite plugs causing urethral obstruction have also been flushed through a catheter with an acidic solution (Walpole's solution). This is a local, not systemic, use of acid.

Urinary alkalinisers

Alkalinisers raise urine pH. **Potassium citrate** is the most useful. Citrate is metabolised to bicarbonate, which makes the urine more alkaline. It is given with food.

Potassium citrate has a second action that is easy to miss: citrate binds calcium to form more soluble salts, so it also **inhibits calcium oxalate crystal formation**. This is why it is used both for urate stones and as part of calcium oxalate prevention. Sodium bicarbonate is another alkaliniser, but the sodium load is a problem in animals with heart or kidney disease or hypertension.

Alkalinisation is used for urate stones, for example in Dalmatians and in dogs with portosystemic shunts, where excess ammonium urate is excreted. It also improves

the activity of some drugs (aminoglycosides work better in alkaline urine) and speeds excretion of weak acids.

Allopurinol is often mentioned alongside these drugs but is not an alkaliniser. It inhibits xanthine oxidase and reduces uric acid production. Its use needs a low-purine diet, otherwise xanthine stones can form.

Drugs and diet for uroliths

Stones are named by their main mineral: struvite, calcium oxalate, urate, cystine, silica and others. Identifying the mineral guides treatment. Struvite, urate and cystine stones can be **dissolved medically** by changing urine composition, which works best for bladder stones with a compliant owner. Calcium oxalate stones cannot be dissolved and must be removed, then prevention is attempted.

Struvite. In dogs these stones are usually linked to urease-producing bacteria such as *Staphylococcus*. The bacteria split urea into ammonia, raising pH and favouring struvite. Treatment is therefore an effective antibiotic chosen by culture plus a dissolution diet. In cats, sterile struvite stones are common and diet alone is often enough.

Urate. Allopurinol and urine alkalinisation, with diet.

Cystine. These form in animals with an inherited tubular defect and are managed with diet, alkalinisation and thiol-containing binding drugs.

Calcium oxalate. Prevention rests on increasing water intake and dilute urine, avoiding acidifying diets, and potassium citrate where indicated.

Dissolution fails when infection is uncontrolled, when the owner feeds other food, or when the stone is not constantly bathed in urine, as in urethral or kidney stones. Radiography and ultrasound, urinalysis and culture are repeated during treatment. Specific protocols follow consensus guidelines.

Incontinence and urethral spasm

Storage and voiding depend on the detrusor muscle (bladder wall) and the urethral sphincters. Parasympathetic muscarinic receptors contract the detrusor. Sympathetic alpha-1 receptors tighten the internal urethral sphincter and beta

receptors relax the detrusor. The external sphincter is skeletal muscle under somatic control.

Urethral sphincter mechanism incompetence is the commonest cause of urinary leakage in spayed bitches. The aim is to raise urethral tone. **Phenylpropanolamine**, an indirect alpha-agonist, does this. Its side effects include restlessness, hypertension and tachycardia. **Oestrogens** (for example estriol) are thought to increase alpha-receptor sensitivity of the urethral smooth muscle. High oestrogen exposure risks bone marrow toxicity in dogs, so the choice of agent matters.

Detrusor instability (urge incontinence) is treated with antimuscarinic drugs such as oxybutynin or propantheline, which relax the detrusor. **Detrusor atony**, with a weak, overfilled bladder, needs a parasympathomimetic such as bethanechol, but only after any obstruction is excluded, because bethanechol against a blocked urethra is dangerous.

Urethral spasm or functional obstruction, particularly in male cats and dogs, is treated by relaxing the sphincter. Alpha-1 blockers (prazosin, phenoxybenzamine) relax the internal sphincter. Skeletal muscle relaxants such as diazepam or dantrolene act on the external sphincter. Hypotension is the main side effect of alpha blockers.

Urinary antiseptics

Urinary antiseptics are drugs that act mainly within the urine and lower tract and achieve little effect elsewhere in the body. They are used for lower urinary tract infection, not for kidney or systemic infection.

Methenamine (as hippurate or mandelate) is inactive until it breaks down in acid urine into **formaldehyde**, which kills bacteria non-specifically. So it needs a urine pH low enough, and it should not be combined with sulfonamides, which can precipitate with formaldehyde. Resistance is unlikely because the action is non-specific. Its role is chiefly long-term prevention of recurrent infection, not treatment of an active infection.

Nitrofurantoin is excreted in the urine in active form and reaches high concentrations there while blood levels stay low. It is less effective in alkaline urine and in renal failure, where it fails to concentrate and may accumulate.

Gastrointestinal upset is the common side effect, and long-term use can damage the lung and nerves in humans.

Indian availability and legal status of these products vary, so check the current notification and product listings before prescribing. In all cases urine culture and sensitivity should guide therapy, and antimicrobial stewardship applies equally to urinary infections.

Concept cleared

pH follows the stone
Struvite dissolves in acid urine; urate and cystine dissolve better in alkaline urine. Always name the stone before choosing the pH direction.

Citrate does two jobs
Potassium citrate raises urine pH and also binds calcium into soluble salts, so it helps against urate and calcium oxalate stones.

Sphincter versus detrusor
Leakage from a weak sphincter needs more urethral tone (alpha-agonist). Retention from a spastic sphincter needs relaxation (alpha-blocker). Detrusor drugs go the other way.

Antiseptic means local
Methenamine and nitrofurantoin work in urine, not in tissues. They suit cystitis prevention, not pyelonephritis or septicaemia.

Memory aid: STRUVITE loves ACID
Struvite dissolves in acid, forms in alkaline, infected urine. Urate and cystine are the opposite: alkalinise.

Compare and contrast

Acidifiers versus alkalinisers

Feature	Acidifiers	Alkalinisers
Examples	Ammonium chloride, dl-methionine	Potassium citrate, sodium bicarbonate
Main stone target	Struvite	Urate, cystine, calcium oxalate prevention
Main risk	Metabolic acidosis	Sodium or potassium load, struvite if infection present
Drug effect on antimicrobials	Helps methenamine, nitrofurantoin	Helps aminoglycosides

Drugs for bladder and urethral dysfunction

Problem	Drug type	Example
Weak urethral sphincter	Alpha-agonist, oestrogen	Phenylpropanolamine, estriol
Unstable detrusor	Antimuscarinic	Oxybutynin, propantheline
Atonic bladder	Parasympathomimetic	Bethanechol
Urethral spasm	Alpha-1 blocker, skeletal relaxant	Prazosin, diazepam

Species notes

Dogs

Struvite stones are usually infection-related; treat the infection as well as the diet. Dalmatians form urate stones. Spayed bitches commonly respond to sphincter-tightening drugs.

Cats

Sterile struvite stones and plugs are common and often dissolve on diet. Calcium oxalate is increasingly common, and over-acidifying diets may favour it.

Ruminants

Horses

Urolithiasis in male goats, sheep and steers causes obstruction at the urethral process or sigmoid flexure. Ammonium chloride is used in feed in some herds for prevention; check the current guidance.

Urolithiasis is less common; stones are usually calcium carbonate in alkaline urine. Herbivore urine is naturally alkaline, so acidifying is hard.

Birds

Birds excrete uric acid, not urea, so urate handling is normal; use of small animal urinary drugs is not routine.

Clinical pearls

Self-test: 10 questions

1. Which stone type is best dissolved in acid urine?

Struvite is more soluble at lower pH, and acid diets dissolve it. Calcium oxalate cannot be dissolved medically.

2. A main risk of chronic urinary acidification is:

Acid load leads to systemic acidosis, especially in animals with kidney disease.

3. Potassium citrate helps prevent calcium oxalate stones because it:

Citrate complexes calcium, and it also raises urine pH.

4. Allopurinol acts by:

Blocking xanthine oxidase reduces uric acid production.

5. Phenylpropanolamine is used for:

It is an alpha-agonist that increases urethral smooth muscle tone.

6. Which drug is an antimuscarinic for detrusor instability?

Oxybutynin relaxes the detrusor; bethanechol does the opposite.

7. Bethanechol must not be used when:

It contracts the detrusor and can rupture the bladder against an obstruction.

8. Methenamine is active because it:

In acid urine methenamine breaks down to formaldehyde, a non-specific antibacterial.

9. Which is an alpha-1 blocker used for functional urethral obstruction?

Prazosin relaxes the internal urethral sphincter.

10. Nitrofurantoin is a poor choice in:

Reduced renal function means the drug does not concentrate in urine and may accumulate.

Key points to revise

1. Struvite dissolves in acid urine.
2. Ammonium chloride and dl-methionine acidify urine.
3. Chronic acidification can cause metabolic acidosis.
4. Potassium citrate alkalinises and binds calcium.
5. Allopurinol inhibits xanthine oxidase and is used for urate stones.

6. Phenylpropanolamine increases urethral tone.
7. Oxybutynin relaxes the detrusor.
8. Methenamine releases formaldehyde in acid urine.

Go deeper on this site

- Ch 20. Haematinics, anticoagulants, coagulants and blood substitutes (in this book)
- Ch 18. Diuretics and drugs acting on the kidney (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Controlling Urine pH in Animals
- Merck Veterinary Manual: Overview of Urolithiasis in Small Animals
- Merck Veterinary Manual: Urolithiasis in Dogs

CHAPTER 20 OF 33

Haematinics, anticoagulants, coagulants and blood substitutes

Drugs that build red cells (iron, vitamin B12), prevent clotting (heparin, warfarin), promote clotting (vitamin K, tranexamic acid) and restore blood volume or clotting factors (plasma and plasma expanders), with the mechanism and clinical logic behind each.

After this chapter you can

- Explain why iron deficiency and vitamin B12 deficiency give different types of anaemia
- Describe how heparin and warfarin prevent clotting and why their monitoring differs
- Explain the role of vitamin K in clotting factor synthesis and its use in rodenticide poisoning
- Describe how tranexamic acid works as an antifibrinolytic

- Distinguish crystalloids, colloids and plasma products and the situations for each

Haematinics and the idea of building blood

A **haematinic** supplies a nutrient needed to make red blood cells. The nutrient must be the one that is actually missing, so the first step is to find the cause of the anaemia. Giving iron to an animal whose anaemia comes from another cause is useless, and iron overload is harmful.

The red cell appearance shows the problem. **Iron deficiency** gives small, pale cells (microcytic, hypochromic) because haemoglobin cannot be made. **Vitamin B12 or folate deficiency** gives large immature cells (macrocytic, megaloblastic) because DNA synthesis and cell division fail. Erythropoietin, made by the kidney, drives red cell production, and a failing kidney is a cause of non-regenerative anaemia.

Always ask why the deficiency exists. In animals, iron deficiency usually means chronic blood loss, for example from heavy parasite burdens such as hookworms, ticks or haemonchosis, or from a bleeding gastrointestinal lesion. Treating the loss is as important as supplying the iron.

Iron

Iron is the central atom of haem, and it is also needed for myoglobin and many enzymes. Oral iron, usually ferrous salts, is absorbed in the duodenum. Absorption is better in the fasting state, but giving iron with food reduces gastric upset. The body has no efficient way to excrete iron, so absorption is regulated and storage is as ferritin.

Oral iron suits dietary deficiency and mild chronic loss. Treatment is slow, and takes weeks to months to rebuild red cell mass and stores. **Parenteral iron**, such as iron dextran, is used for initial treatment when oral drug is not tolerated or not practical, and in young animals.

Newborn piglets are the classic example. Sow's milk has little iron and piglets grow rapidly, so without supplementation they develop anaemia in the first weeks.

Adverse effects are dose-related. Oral iron causes gastrointestinal upset, and large overdoses cause serious injury to the gut, heart and liver. Injection can be painful

and can stain tissue. Iron should not be given to an animal with a normal iron status. Erythropoietic drugs used in chronic kidney disease work only if iron is available, so iron is usually given with them.

Vitamin B12 and erythropoietic drugs

Vitamin B12 (cobalamin) is needed for DNA synthesis and for red cell maturation. Animals depend on gut microbes or diet for it. In ruminants, rumen bacteria make B12 from **cobalt**, so cobalt-deficient pasture produces B12 deficiency, poor appetite and ill-thrift, and the treatment is cobalt or B12 supply. Cobalt deficiency is a regional problem, so local advice should be sought.

In dogs and cats, deficiency is mostly due to poor absorption, for example in inflammatory bowel disease or exocrine pancreatic insufficiency, since B12 uptake in the ileum needs intrinsic factor and healthy mucosa. The answer is injection, because oral supplementation will not overcome a malabsorption defect fully. Toxicity of B12 is very low.

Erythropoiesis-stimulating agents such as epoetin and darbepoetin are used for anaemia of chronic kidney disease. A serious problem is that animals may make antibodies against the product that also neutralise their own erythropoietin, causing pure red cell aplasia. This is why the drug is used selectively and with monitoring.

Anticoagulants: heparin and warfarin

Clotting is a cascade in which each factor activates the next, ending in thrombin converting fibrinogen to fibrin. Anticoagulants prevent new clots or extension of existing ones. They do not dissolve a clot that is already formed.

Heparin works at once and only by injection. It binds **antithrombin** and speeds up its inhibition of thrombin (factor IIa) and factor Xa. Unfractionated heparin acts on both, while **low-molecular-weight heparins** such as enoxaparin and dalteparin act mainly on Xa and have a more predictable effect. Heparin is used for thromboembolic disease and in disseminated intravascular coagulation, and to keep catheters and circuits patent. The therapeutic window is narrow, and monitoring uses clotting time (ACT, aPTT) or anti-Xa activity. The main complication is bleeding. **Protamine** neutralises heparin.

Warfarin blocks vitamin K epoxide reductase, so the liver cannot recycle vitamin K and makes inactive factors II, VII, IX and X. Effect is delayed by days because existing factors must first be used up. Warfarin has great variation between individuals and a narrow therapeutic index, and it is no longer recommended for routine veterinary use because safer alternatives exist. The same mechanism, however, explains **anticoagulant rodenticide poisoning**, which is common in dogs.

Coagulants: vitamin K and tranexamic acid

Vitamin K (phytonadione) is the cofactor for the liver enzyme that adds carboxyl groups to factors II, VII, IX and X, which they need in order to bind calcium and work. It is the specific antidote to warfarin-type rodenticides, to dicoumarol poisoning from spoiled sweet clover in cattle, and it is used in liver failure or deficiency. It does not act at once, because new factors take hours to be made, so plasma products may be needed in a bleeding animal. After second-generation rodenticide poisoning, treatment is continued for weeks, since these compounds persist. Intravenous injection has been linked to anaphylactoid reactions with some products, and intramuscular injection can bleed into muscle.

Tranexamic acid is an antifibrinolytic. It blocks the lysine-binding sites of plasminogen, so plasmin cannot form and bind to fibrin, and clots persist. It is used where excess clot breakdown contributes to bleeding, including surgery and some haemorrhage. Adverse effects include vomiting and a risk of thrombosis, and the dose must be reduced in kidney failure.

A frequent confusion: vitamin K helps the clotting factors to be made, while tranexamic acid protects the clot from breakdown. They act at different stages and are not interchangeable.

Blood substitutes and plasma expanders

In haemorrhage or shock, the first need is to restore circulating volume and then oxygen-carrying capacity or clotting factors if they are lacking.

- **Crystalloids** such as balanced electrolyte solutions and normal saline spread rapidly into the whole extracellular space, so only a fraction stays in the vessels. They are first-line for most dehydration and shock.

- **Colloids** such as hydroxyethyl starch and gelatin contain large molecules that hold water in the vessels by oncotic pressure, and so expand plasma volume longer. Starch products can impair clotting and have been linked to kidney injury in some patients, so use is selective and the current product guidance should be checked.
- **Plasma products** such as fresh frozen plasma supply clotting factors, albumin and antithrombin. They are used for coagulopathies, including rodenticide poisoning with active bleeding.
- **Whole blood or red cell concentrate** replaces oxygen-carrying capacity, and needs blood typing or cross-matching, especially in cats and in dogs that have been transfused before.

All transfusions risk allergic, febrile and lung injury reactions, and infusion must be slowed in animals that cannot tolerate fluid overload, such as those with heart disease.

Concept cleared

Concept cleared: Microcytic versus macrocytic anaemia
Haemoglobin is like paint, and cell division is like cutting fabric. Without iron the cells are made on time but are small and pale because there is little paint. Without B12 the cutting stalls, so cells grow big and immature before dividing.

Concept cleared: Heparin versus warfarin
Heparin is a hand on the brake of already-circulating factors, so it works at once. Warfarin stops the factory from making new factors, so it works only after the old stock runs out, which takes days.

Concept cleared: Vitamin K as a charger
Factors II, VII, IX and X are made as flat batteries and need vitamin K to charge them. Warfarin and rodenticides block recharging, and vitamin K restores it, though new batteries still take hours to make.

Concept cleared: Crystalloid versus colloid

Crystalloids are like water poured onto a garden, which soaks into everything. Colloids are like water in a sponge, which stays in the vessel for longer because large molecules hold it there.

Memory aid: Vitamin K factors

Factors 1972 depend on vitamin K: II, VII, IX, X (ten, nine, seven, two). For anaemia size: Iron gives Itty-bitty cells, B12 gives Big cells. Heparin is Hurried (fast, injection); Warfarin is Waiting (slow, days).

Compare and contrast

Haematinics and clotting drugs

Drug	Action	Main use	Key caution
Iron	Supplies haem iron	Iron-deficiency anaemia, piglets	GI upset, overload toxicity
Vitamin B12	DNA synthesis, red cell maturation	Malabsorption, cobalt deficiency	Very low toxicity
Heparin	Enhances antithrombin; inhibits IIa and Xa	Thromboembolism, DIC	Bleeding; monitor clotting
Warfarin	Blocks vitamin K recycling	Historic anticoagulant; rodenticide mechanism	Narrow index; no longer recommended
Vitamin K	Allows synthesis of II, VII, IX, X	Rodenticide, dicoumarol, liver failure	Delay of hours; IV reactions
Tranexamic acid	Blocks plasminogen binding to fibrin	Hyperfibrinolytic bleeding	Thrombosis risk, vomiting

Fluids for volume replacement

Product	Stays in vessels	Provides	Main concern
Crystalloid	Short time	Water and electrolytes	Oedema if excessive
Colloid (starch, gelatin)	Longer	Oncotic volume support	Clotting effects, kidney injury risk
Plasma product	Longer	Clotting factors, albumin	Allergic and transfusion reactions
Whole blood or red cells	Yes	Oxygen-carrying capacity	Blood typing, reactions

Species notes

Pig

Piglets raised without access to soil are given iron early, as sow milk is low in iron, and untreated piglets develop anaemia.

Cattle and sheep

Rumen bacteria need cobalt to produce vitamin B12, so cobalt-poor pasture causes deficiency. Spoiled sweet clover contains dicoumarol and causes bleeding, treated with vitamin K.

Dog

Anticoagulant rodenticide poisoning is a common emergency, treated with vitamin K and plasma if bleeding. Cobalamin deficiency is seen with malabsorptive bowel disease.

Cat

Cats have distinct blood types and may carry naturally occurring antibodies, so type or cross-match before transfusion. Heparin is given by subcutaneous route in sources reviewed.

Horse

Anaemia is investigated for blood loss or chronic disease before iron is given, since iron therapy is rarely needed and excess can be harmful.

Clinical pearls

Self-test: 10 questions

1. Iron deficiency anaemia produces:

Without iron, haemoglobin cannot be made, so cells are small and pale.

2. Which clotting factors depend on vitamin K?

Factors II, VII, IX and X need vitamin K for carboxylation.

3. Heparin works by:

Heparin binds antithrombin, increasing inhibition of thrombin and factor Xa.

4. Why does warfarin take days to act?

It stops new factor synthesis, and the circulating factors decay over days.

5. The antidote for heparin overdose is:

Protamine binds and neutralises heparin.

6. Tranexamic acid acts by:

This prevents plasmin formation and fibrin breakdown.

7. Why do piglets need iron supplementation?

Low milk iron and fast growth lead to anaemia without supplementation.

8. Cobalt deficiency in cattle causes disease because:

Cobalt is a component of vitamin B12 made by rumen bacteria.

9. In active bleeding from rodenticide poisoning, vitamin K alone may be insufficient because:

Plasma products give factors immediately while vitamin K takes effect.

10. Which fluid stays in the vessels longest?

Large molecules hold water in the vessels by oncotic pressure.

Key points to revise

1. Iron deficiency causes microcytic hypochromic anaemia; B12 deficiency causes macrocytic anaemia.
2. Piglets need supplementary iron because sow milk contains little.
3. Ruminants need cobalt to make vitamin B12.
4. Heparin enhances antithrombin and inhibits thrombin and factor Xa; protamine reverses it.
5. Warfarin inhibits vitamin K recycling and is no longer recommended for routine use.
6. Vitamin K is needed for factors II, VII, IX and X and is the antidote for anticoagulant rodenticides.
7. Tranexamic acid is an antifibrinolytic that blocks plasminogen binding.
8. Crystalloids leave the vessels quickly; colloids and plasma products stay longer.

Go deeper on this site

- Ch 21. Respiratory drugs (in this book)
- Ch 19. Drugs of the urinary tract (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index

- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Drugs Acting on the Blood or Blood-Forming Organs in Animals
- Merck Veterinary Manual: Systemic Pharmacotherapeutics of the Cardiovascular System
- Merck Veterinary Manual: Pharmacology

CHAPTER 21 OF 33

Respiratory drugs

How drugs act on the airways: bronchodilators, mucolytics, expectorants, antitussives, decongestants and respiratory stimulants. The chapter stresses why a cough or wheeze should be treated at its cause, and where each class helps or harms.

After this chapter you can

- Explain how beta-2 agonists, anticholinergics and methylxanthines relax airway smooth muscle
- Distinguish mucolytics from expectorants and state the evidence behind each
- Describe when a cough should and should not be suppressed
- Explain why decongestants are rarely used in animals and why some are dangerous
- Describe the action and limits of doxapram as a respiratory stimulant

Principles of respiratory drug therapy

Respiratory signs such as cough, wheeze, nasal discharge and laboured breathing are **symptoms**, not diagnoses. Drugs that act on the airway are mostly supportive. The main treatment is usually the removal of the cause: an antimicrobial for bacterial pneumonia, a glucocorticoid and environmental change for equine asthma, a diuretic for cardiogenic pulmonary oedema.

The drug classes in this chapter are grouped by the goal: open the airway (bronchodilators), thin or move secretions (mucolytics and expectorants), quieten the cough reflex (antitussives), clear the nose (decongestants) and drive breathing (respiratory stimulants). Anti-inflammatory and antimicrobial drugs are covered in other chapters.

A useful habit is to ask before prescribing: is the airway narrowed by muscle spasm, by mucus, by oedema, or by inflammation? A bronchodilator helps only the first. This single question prevents most prescribing errors.

Bronchodilators

Airway smooth muscle is controlled by two opposing signals. Parasympathetic fibres release acetylcholine, which acts on muscarinic M_3 receptors and causes contraction. Beta-2 adrenergic receptors, linked to Gs and a rise in cAMP, cause relaxation. Bronchodilators either stimulate the relaxing pathway or block the constricting one.

- **Beta-2 agonists** such as salbutamol (albuterol), terbutaline and clenbuterol raise cAMP in smooth muscle and relax it. Inhaled salbutamol is a rescue drug for acute bronchoconstriction. Long-acting agents such as salmeterol are slow in onset and are not for acute rescue.
- **Anticholinergics** block muscarinic receptors. Atropine does this but also causes tachycardia, dry mucus and gut stasis. Ipratropium is a quaternary derivative that is poorly absorbed after inhalation, so systemic effects are less likely.
- **Methylxanthines** such as theophylline and aminophylline inhibit phosphodiesterase, so cAMP is not broken down, and they block adenosine receptors. They have a narrow safety margin.

Common confusion: a bronchodilator does *not* treat inflammation. Beta-2 agonists used alone in chronic asthma can leave the inflammation uncontrolled, so they are combined with a glucocorticoid. Also, airflow may stay poor despite a bronchodilator when the real problem is mucus plugging or wall oedema.

Mucolytics and expectorants

These two terms are often mixed up. **Mucolytics** change the mucus itself, making it less viscous. **Expectorants** are meant to increase the volume or the clearance of

secretions so that the cough becomes more productive.

Acetylcysteine is the classic mucolytic. It breaks disulphide bonds in mucoprotein, so mucus thins. Given as a nebulised solution, it can cause reflex bronchoconstriction, so a bronchodilator is given first. Bromhexine and its metabolite ambroxol, and dembrexine in some countries for horses, alter mucus structure and improve mucociliary clearance. Check the products licensed locally.

Traditional expectorants include ammonium salts, iodides such as potassium iodide, and volatile oils such as eucalyptus. They are believed to stimulate secretion through a reflex from the stomach, but well-designed studies in animals are lacking. Iodide products should not be given to pregnant, hyperthyroid or lactating animals because iodine crosses the placenta and enters milk.

Guaifenesin is a centrally acting muscle relaxant. It may be listed as an expectorant, but its benefit on secretion is uncertain.

Note that the most reliable aid to mucus clearance is simple: good hydration, humidified air, and, where possible, controlling dust and ammonia in the housing. Systemic dehydration makes mucus thicker.

Antitussives

Cough is a protective reflex. It clears secretions and foreign material, so a **productive** cough should not be suppressed. Suppressing it can let mucus pool in the lung and allow infection to persist.

Antitussives are suitable for a dry, unproductive, exhausting cough, such as one caused by tracheal collapse or chronic bronchitis where it disturbs rest, or when the cough itself keeps irritating the airway. Most act on the cough centre in the medulla.

- **Opioids** such as codeine, hydrocodone and butorphanol are the commonest. Butorphanol is a potent antitussive in dogs but causes sedation. Codeine slows gut motility and should be avoided after intestinal surgery.
- **Maropitant**, an NK1 antagonist, has reduced coughing in dogs with chronic bronchitis in a study, which fits the role of substance P in the cough pathway.
- **Dextromethorphan** is widely used in people but is poorly effective in dogs because of its short half-life and poor oral bioavailability.

Remember that opioid antitussives are controlled substances in India. Check the current regulations on storage and prescription before use.

Cough in animals usually points to disease such as kennel cough, bronchitis, feline or equine asthma, or heart disease. In a cardiac patient, a cough caused by left atrial enlargement pressing on the bronchus is treated by managing the heart, not by suppressing the cough alone.

Decongestants

Nasal decongestants are alpha-adrenergic agonists such as phenylephrine, oxymetazoline and pseudoephedrine. They constrict the blood vessels of the nasal mucosa, reduce swelling and open the nasal passage. They are used rarely in animals.

There are three reasons for caution. First, most nasal obstruction in animals is caused by infection or a foreign body, and these need their own treatment. Second, topical decongestants can cause **rebound congestion** if used for more than a few days, because the vessels dilate again when the drug wears off. Third, oral pseudoephedrine and similar sympathomimetics are toxic to dogs and cats. Accidental ingestion of human cold tablets causes agitation, tachycardia and hypertension, and is a recognised poisoning in small animals. Many human cold products also contain paracetamol, which is dangerous in cats.

Antihistamines are sometimes used for allergic rhinitis, but their benefit in animals is modest.

The practical message for students: never hand an owner a human cold remedy for a pet, and treat the cause of nasal discharge rather than the discharge.

Respiratory stimulants and oxygen

Doxapram is the main respiratory stimulant in veterinary practice. At low doses it stimulates the peripheral chemoreceptors in the carotid and aortic bodies, and at higher doses it stimulates the respiratory centre in the medulla. It is used to hasten recovery of breathing after anaesthesia and, in some practices, to stimulate newborn animals that are slow to breathe.

Its limits matter more than its uses. The effect is short, so respiratory depression can return when it wears off, particularly when the depressant drug is long-acting. Stimulating breathing increases oxygen demand, and it can cause excitement, hypertension and arrhythmia. It does not replace ventilation, airway clearance or oxygen. In a hypoxic animal, the first steps are a clear airway, oxygen and, where needed, assisted ventilation.

When the cause is an opioid, a specific antagonist such as naloxone is more logical. When the cause is an alpha-2 agonist, atipamezole is the specific reversal. A non-specific stimulant is the second choice.

Methylxanthines such as caffeine are used in human neonates for apnoea. Do not extend this to animals without a veterinary source.

Concept cleared

Concept cleared: Bronchodilator is not an anti-inflammatory
A bronchodilator loosens the tight muscle ring round a pipe. It does not clean the rust or the sludge inside it. If the airway is narrowed by swelling and mucus, relaxing the muscle gives only partial relief, so an anti-inflammatory is also needed.

Concept cleared: Mucolytic versus expectorant
A mucolytic is like adding water to thick paste so it flows. An expectorant is meant to make the body produce more fluid mucus or move it out. The first changes the mucus, the second targets the secretion process.

Concept cleared: Why not to suppress a productive cough
A cough is the airway's broom. Taking away the broom from a dirty floor does not clean the floor. Suppress only a dry, useless cough that harms the animal.

Concept cleared: Rebound congestion

A topical decongestant squeezes nasal vessels shut. When its effect ends, the vessels spring open wider than before, like a spring held down. Long use makes the nose worse.

Memory aid: Open, thin, quiet, clear, drive

Five goals in order: Open the airway (bronchodilators), Thin the mucus (mucolytics and expectorants), Quiet the cough (antitussives), Clear the nose (decongestants), Drive the breathing (stimulants). Remember: B, M, A, D, R.

Compare and contrast

Bronchodilator classes

Class	Examples	Mechanism	Main caution
Beta-2 agonist	Salbutamol, terbutaline, clenbuterol	Gs, raises cAMP, relaxes smooth muscle	Tachycardia, tremor, tolerance; does not control inflammation
Anticholinergic	Ipratropium, atropine	Blocks M3 muscarinic receptors	Atropine dries mucus and slows gut; ipratropium has fewer systemic effects
Methylxanthine	Theophylline, aminophylline	Inhibits phosphodiesterase, blocks adenosine receptors	Narrow safety margin

Mucolytic versus expectorant versus antitussive

Class	Goal	Example	Use when
Mucolytic	Thin mucus	Acetylcysteine, bromhexine	Thick, hard-to-clear secretions
Expectorant	Aid clearance of secretions	Ammonium salts, iodides, volatile oils	Evidence in animals is weak
Antitussive	Suppress cough reflex	Butorphanol, codeine, hydrocodone	Dry, unproductive, distressing cough only

Species notes

Dog

Dry coughs of tracheal collapse and chronic bronchitis may be given an opioid antitussive. Accidental ingestion of human decongestants or a chewed salbutamol inhaler can cause severe tachycardia and low potassium.

Cat

Feline asthma is treated with inhaled glucocorticoid and a bronchodilator by spacer and mask. Codeine is poorly suited to cats, and human cold medicines containing paracetamol are dangerous.

Horse

Equine asthma is managed first by reducing dust in hay and stable. Inhaled bronchodilators and glucocorticoids are used, and clenbuterol is a bronchodilator whose use in competition horses is subject to medication rules.

Cattle

Respiratory disease in calves is mostly infectious, so antimicrobials and supportive care matter more than bronchodilators or antitussives. Check withdrawal periods before using any drug in food animals.

Neonates

A newborn that does not breathe needs airway clearing, stimulation, warmth and oxygen first. Doxapram is only an adjunct.

Clinical pearls

Self-test: 10 questions

1. Which receptor mediates airway smooth muscle relaxation when stimulated by salbutamol?

Beta-2 receptors act through Gs and raise cAMP, relaxing smooth muscle.

2. Why is ipratropium preferred to atropine for inhalation?

Ipratropium is a quaternary derivative with poor absorption after inhalation.

3. A mucolytic acts by:

Mucolytics such as acetylcysteine break bonds in mucus and thin it.

4. Acetylcysteine nebulisation may cause which problem?

Aerosolised acetylcysteine can trigger bronchospasm, so a bronchodilator is given first.

5. Which cough is most suited to an antitussive?

Productive coughs clear secretions and should not be suppressed.

6. A problem with long use of topical nasal decongestants is:

Vessels dilate again beyond baseline when the vasoconstrictor wears off.

7. Which statement about human decongestants is correct?

Oral sympathomimetics such as pseudoephedrine cause serious toxicity in small animals.

8. Doxapram stimulates breathing mainly by acting on:

Low doses act on carotid and aortic body chemoreceptors, higher doses on the medulla.

9. In an animal with opioid-induced respiratory depression, the most logical drug is:

A specific antagonist reverses the cause; a non-specific stimulant is second choice.

10. Why can a bronchodilator fail to relieve airflow obstruction?

Obstruction from wall oedema and mucus is not relieved by muscle relaxation alone.

Key points to revise

1. Respiratory drugs are mostly symptomatic and supportive.
2. Beta-2 agonists relax airway smooth muscle by raising cAMP.
3. Anticholinergics block muscarinic constriction; ipratropium is poorly absorbed.
4. Methylxanthines inhibit phosphodiesterase and have a narrow safety margin.
5. Mucolytics change the mucus; expectorant evidence in animals is weak.
6. Antitussives are for dry, unproductive coughs only.
7. Topical decongestants cause rebound congestion; oral ones are toxic to small animals.
8. Doxapram stimulates chemoreceptors and the medulla but is short-acting.

Go deeper on this site

- Ch 22. Gastric acid suppressants, antiemetics and prokinetics (in this book)
- Ch 23. Laxatives, purgatives, antidiarrhoeals and probiotics (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Inhalation Treatment of Airway Disease in Animals
- Merck Veterinary Manual: Expectorants and Mucolytic Drugs in Animals
- Merck Veterinary Manual: Antitussive Drugs in Animals

CHAPTER 22 OF 33

Gastric acid suppressants, antiemetics and prokinetics

How drugs reduce gastric acid, protect ulcerated mucosa, stop vomiting and speed up gut emptying. The chapter links each drug to its receptor or pump target so that the choice in a vomiting or ulcer case makes sense.

After this chapter you can

- Explain how H2 blockers and proton pump inhibitors reduce acid secretion and why PPIs are stronger
- Describe how sucralfate protects ulcers and why its timing and interactions matter
- Compare the receptor targets of maropitant, ondansetron and metoclopramide
- Explain what a prokinetic does and when it must not be used
- Outline the logic of appetite stimulants and their limits

Why control acid and vomiting

Gastric acid is made by the parietal cells of the stomach. It helps digestion and kills many ingested microbes, but it also damages the mucosa when protective mechanisms fail. Ulcers are seen with NSAID or corticosteroid use, stress, mast cell tumours, liver or kidney disease and severe systemic illness. Vomiting is a separate problem: it is a reflex with several inputs, and one drug rarely blocks all of them.

This chapter groups the drugs by purpose: reduce acid, coat the ulcer, stop the vomit, and move the gut contents forward. Always treat the cause as well. A drug that hides a foreign body or an obstruction can be harmful.

Reducing acid: H2 blockers and proton pump inhibitors

The parietal cell is driven by three signals: histamine (H2 receptor), gastrin and acetylcholine. All three end at the same final step, the **H+/K+-ATPase**, or proton pump, which pushes acid into the lumen.

H2 receptor antagonists (famotidine, ranitidine, cimetidine) compete with histamine at the H2 receptor. They block only one of the three signals, so suppression is

partial. Famotidine is the most potent of the group, while cimetidine inhibits liver enzymes and can interfere with the metabolism of other drugs. With repeated use, tolerance develops, and stopping suddenly may cause rebound acid secretion, so withdrawal is usually gradual. Ranitidine has been withdrawn from many markets; check the current availability.

Proton pump inhibitors (omeprazole, pantoprazole, esomeprazole) act at the final common step. They are prodrugs that are activated in the acid space of the parietal cell and bind the pump irreversibly. Acid returns only when new pumps are made, so one dose can act for days, and suppression is deeper than with H2 blockers. Because they need active pumps and an acid environment, oral PPIs are given in protected (enteric) forms and usually before feeding. Pantoprazole and esomeprazole are options when injection is needed.

Common confusion: higher gastric pH is not always better. Long-term suppression may alter the gut microbiota and reduce absorption of some drugs, so prolonged use needs a clear reason.

Protecting the ulcer: sucralfate and related agents

Sucralfate is a complex of aluminium and sulphated sucrose. In an acid stomach it turns into a sticky paste that binds preferentially to the ulcer crater and forms a physical barrier against acid and pepsin. It is hardly absorbed, so it is safe systemically, and its action is local.

Three practical points follow from this mechanism. First, it needs acid to activate, so it is best given on an empty stomach and is somewhat contradictory with heavy acid suppression. Second, it can bind other drugs in the gut (for example some fluoroquinolones, tetracyclines and levothyroxine), so give it apart from other oral drugs. Third, it can be constipating. The Merck Veterinary Manual notes that evidence for its effect in animals is limited and that it is considered inferior to PPIs for gastroduodenal ulcers, so it is an adjunct rather than a stand-alone treatment in severe cases.

Misoprostol, a prostaglandin E analogue, is a different approach: it replaces the protective prostaglandins lost with NSAID use. It must not be given to pregnant animals, as it may cause abortion.

Antiemetics: matching the drug to the pathway

Vomiting is coordinated by the vomiting centre in the brainstem. It receives input from the **chemoreceptor trigger zone** (CRTZ), which sits outside the blood-brain barrier and detects toxins and drugs; from the vestibular apparatus (motion sickness); from higher centres; and from the gut via the vagus. The main transmitters are dopamine (D2), serotonin (5-HT3), histamine (H1), acetylcholine (muscarinic) and **substance P** (NK1 receptor).

- **Maropitant** blocks NK1 receptors. Because substance P is the final common transmitter in the vomiting centre, it works against many triggers, central and peripheral, and also reduces visceral pain input. It is licensed in dogs and cats, and it is also useful for motion sickness. Check product labels for species and age limits.
- **Ondansetron** blocks 5-HT3 receptors on vagal afferents in the gut and in the CRTZ. It is especially useful when serotonin release is high, as with chemotherapy and severe enteritis.
- **Metoclopramide** blocks D2 receptors in the CRTZ and has prokinetic action (below). It is a weaker antiemetic in cats and dogs than maropitant for many causes.
- **Phenothiazines** (chlorpromazine, prochlorperazine) block dopamine and histamine and also sedate and lower blood pressure.

Remember that antiemetics are not a substitute for fluids and diagnosis. Animals that are vomiting because of a gastrointestinal obstruction need the obstruction removed.

Prokinetics

Prokinetics increase coordinated propulsive motility. They help in delayed gastric emptying, reflux oesophagitis, ileus and some cases of constipation.

Metoclopramide blocks D2 receptors, which removes a dopamine brake on the gut, and it also stimulates 5-HT4 receptors to promote acetylcholine release. It acts mainly on the stomach and proximal small bowel. It is not effective in the colon. It crosses the blood-brain barrier and can cause restlessness or behaviour changes.

Cisapride acts through 5-HT4 receptors and is effective across the stomach and colon, which is why it is used in feline megacolon. Availability is limited in many

places, so check what is available. **Ranitidine** and related cholinesterase inhibiting effects have also been described in some references, but the evidence is variable.

The key safety rule: **never give a prokinetic when there is a mechanical obstruction**. Increasing contractions against a blockage risks pain and perforation.

Appetite stimulants

Anorexia delays recovery, and in cats prolonged anorexia can lead to hepatic lipidosis. Appetite stimulants work only after the underlying disease, pain and nausea are addressed.

- **Mirtazapine** blocks alpha-2 and 5-HT2/5-HT3 receptors. It raises appetite and has an antiemetic effect. Kidney or liver disease prolongs its action, so interval matters. A transdermal cat product exists in some countries.
- **Capromorelin** mimics ghrelin, the hunger hormone, and is licensed for dogs in some countries.
- **Cyproheptadine**, a serotonin and histamine antagonist, has been used in cats.
- **Benzodiazepines** can stimulate eating briefly but are unreliable.

Stimulants are an aid, not a replacement for nutrition. If an animal does not eat, a feeding tube is often the better option.

Concept cleared

Final common pathway
PPIs block the last step of acid secretion, the proton pump, so they outperform drugs that block one of several input signals.

Prodrug activation by acid
PPIs need an acidic space to become active, which is why oral forms are protected from stomach acid and the timing before feeding matters.

Substance P as the common vomiting transmitter

NK1 blockade by maropitant covers many vomiting triggers, while ondansetron and metoclopramide cover narrower pathways.

Prokinetic against obstruction

Stimulating motility against a physical blockage can cause pain and rupture, so rule out obstruction first.

Memory aid: Acid drugs by step

H2 = one lane closed (histamine), PPI = the gate shut (pump), sucralfate = a bandage on the wound. Three drugs, three levels.

Compare and contrast

Acid-reducing and protecting drugs

Drug	Target	Strength / onset	Key caution
Famotidine	H2 receptor (competitive)	Moderate; partial block	Tolerance, rebound on abrupt stop
Cimetidine	H2 receptor	Weaker	Inhibits liver enzymes, drug interactions
Omeprazole	H+/K+-ATPase (irreversible)	Strong; lasts days	Long-term use needs justification
Sucralfate	Local ulcer coating	Local, not systemic	Binds other oral drugs; give separately
Misoprostol	Prostaglandin E analogue	Mucosal protection	Contraindicated in pregnancy

Antiemetics and prokinetics

Drug	Receptor action	Best used for	Note
Maropitant	NK1 antagonist	Broad: central and peripheral vomiting, motion sickness	Check species and age on label
Ondansetron	5-HT3 antagonist	Chemotherapy and enteritis vomiting	Narrower pathway
Metoclopramide	D2 antagonist, 5-HT4 agonist	Nausea plus gastric emptying	Not for obstruction; CNS effects
Cisapride	5-HT4 agonist	Gastric and colonic motility	Limited availability
Mirtazapine	Alpha-2 and 5-HT antagonist	Appetite and nausea	Slower clearance in organ disease

Species notes

Dog

Vomiting is common; maropitant is widely used. Check for foreign body before any prokinetic. PPIs have longer action in dogs than many expect.

Cat

Cats are sensitive to some drugs (for example salicylates and some opioid or dopamine effects). Prolonged anorexia risks hepatic lipidosis, so early feeding support matters.

Horse

Equine gastric ulcer syndrome is treated mainly with PPIs such as omeprazole; the product label and current regulations decide use, particularly for competition horses.

Ruminants

Forestomach fermentation differs, so monogastric acid drugs are not routinely applied; abomasal ulcers are treated on the basis of cause and local guidance.

Pig

Gastric ulceration near the oesophageal region is linked to fine-ground feed and stress;

management is generally more important than acid drugs.

Clinical pearls

Self-test: 10 questions

1. Which drug irreversibly blocks the gastric H+/K+-ATPase?

Omeprazole is a proton pump inhibitor that binds the pump irreversibly, so acid suppression lasts until new pumps are made.

2. Maropitant works by blocking which receptor?

Maropitant blocks NK1 receptors for substance P, the final common transmitter in the vomiting centre.

3. Why should sucralfate be given apart from other oral drugs?

Sucralfate forms a sticky paste that can bind co-administered drugs and reduce their absorption.

4. A prokinetic is contraindicated in:

Stimulating contractions against an obstruction risks pain and perforation.

5. Which statement about H2 blockers is correct?

H2 blockers block only the histamine signal, so suppression is partial compared with PPIs.

6. Which drug is mainly a 5-HT3 antagonist?

Ondansetron blocks 5-HT3 receptors on vagal afferents and in the chemoreceptor trigger zone.

7. Metoclopramide is NOT effective as a prokinetic in the:

Metoclopramide acts mainly on the upper gut and has little colonic effect, unlike cisapride.

8. Which agent replaces protective prostaglandins lost with NSAID use?

Misoprostol is a prostaglandin E analogue; it is contraindicated in pregnancy.

9. Capromorelin stimulates appetite by acting as a mimic of:

Capromorelin is a ghrelin receptor agonist and so signals hunger.

10. Abrupt withdrawal of long-term H2 blocker may cause:

Chronic suppression can up-regulate acid secretion, so stopping suddenly may produce a rebound.

Key points to revise

1. Parietal cells are stimulated by histamine, gastrin and acetylcholine, all converging on the proton pump.
2. H2 blockers block one input; PPIs block the pump irreversibly and are stronger.
3. Sucralfate is a local, acid-activated ulcer barrier with limited systemic effect.
4. Sucralfate can bind other drugs, so separate dosing.
5. Maropitant acts on NK1 receptors; ondansetron on 5-HT3; metoclopramide on D2.
6. Prokinetics must not be used in mechanical obstruction.
7. Cisapride acts on the colon through 5-HT4, unlike metoclopramide.
8. Appetite stimulants help only after nausea, pain and the underlying disease are addressed.

Go deeper on this site

- Ch 23. Laxatives, purgatives, antidiarrhoeals and probiotics (in this book)
- Ch 21. Respiratory drugs (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Drugs Used to Treat Gastrointestinal Ulcers in Monogastric Animals
- Merck Veterinary Manual: Drugs Used to Treat Diarrhea in Monogastric Animals
- Merck Veterinary Manual: Vomiting in Dogs

CHAPTER 23 OF 33

Laxatives, purgatives, antidiarrhoeals and probiotics

How the main laxative groups work, what adsorbents and opioid antidiarrhoeals really do, why oral rehydration is the life-saving step in diarrhoea, and what the evidence says about probiotics and prebiotics.

After this chapter you can

- Classify laxatives by mechanism and give an example and a caution for each
- Explain why adsorbents have limited proven benefit in diarrhoea
- Explain how oral rehydration solutions work through sodium-glucose co-transport
- Define probiotic, prebiotic and synbiotic
- Judge the quality of evidence and product quality problems in probiotics

Constipation, diarrhoea and the purpose of treatment

The gut moves about as much fluid across its wall each day as the animal drinks. A small shift in absorption or secretion therefore changes the stool quickly. **Diarrhoea** is increased stool water, usually with increased frequency, caused by excess

secretion, reduced absorption, increased osmotic load or faster transit. **Constipation** is the opposite: hard, dry, infrequent stool.

Drugs in this chapter change stool consistency, but the first questions are always about the cause. Diarrhoea may be infectious, dietary, parasitic or toxic. Constipation may be due to low fibre, dehydration, pain, pelvic narrowing, or obstruction. A laxative given to an animal with an obstruction can be dangerous, and an antidiarrhoeal given to an animal with an invasive infection can hold bacteria and toxins in the gut.

The most important treatment in acute diarrhoea is replacing fluid and electrolytes. Most other drugs are secondary.

Types of laxative and purgative

A laxative softens stool and eases passage. A **purgative** or cathartic acts strongly and produces fluid stool. The difference is mainly one of degree and dose.

- **Bulk-forming laxatives** (psyllium, methylcellulose, bran, fibre sources) absorb water and add indigestible mass. The stretched bowel wall stimulates peristalsis. They need adequate water, otherwise they can worsen the problem.
- **Hyperosmotic laxatives** (magnesium sulphate or hydroxide, sodium sulphate, lactulose, polyethylene glycol, sugar alcohols) are poorly absorbed and hold water in the lumen. This distends the bowel and promotes movement. Excess dose causes dehydration.
- **Lubricants** (liquid paraffin, mineral oil, white petroleum) coat the faeces and the mucosa so that passage is easier. Prolonged use can reduce absorption of fat-soluble vitamins, and aspiration of the oil is a risk if dosed carelessly.
- **Emollients or surfactants** (docusate salts) lower the surface tension of the stool so that water enters it. Docusate should not be combined with mineral oil, since it may increase oil absorption.
- **Stimulant laxatives** (senna, castor oil, bisacodyl) irritate the mucosa or stimulate the enteric nerves, increasing motility and secretion. They can cause heavy fluid and electrolyte loss and colic.

Lactulose is also used in liver failure. Gut bacteria break it down to acids, which acidify the colon, and ammonia is trapped as ammonium ion that cannot be absorbed. This lowers the ammonia load on the failing liver.

Magnesium salts are partly absorbed and cleared by the kidney. In renal disease, magnesium can accumulate to toxic levels.

Species notes on laxatives

The choice of laxative follows anatomy. In the horse, the large colon has narrow points and large volumes of fluid, so impaction colic is common. Mineral oil by stomach tube and osmotic salts are used for impaction, along with fluids. The belief that bran mash is laxative is not supported by the standard reference. Repeated doses of a stimulant such as senna should be avoided in horses because of the risk of severe purging. Boiled linseed oil is dangerous because of metallic driers.

In the cat, megacolon is managed with diet, osmotic agents such as lactulose and sometimes prokinetics. Sodium phosphate enemas must not be given to cats because they can cause fatal electrolyte disorders.

In ruminants, the large rumen volume dilutes purgatives. Mineral oil and magnesium sulphate are used in some conditions, but these are covered in the ruminant chapter.

In all species, dehydration is both a cause and a consequence. A laxative works best when the animal is well hydrated.

Antidiarrhoeals and adsorbents

Antidiarrhoeal drugs fall into a few groups.

- **Adsorbents and protectants** such as kaolin-pectin, bismuth subsalicylate and activated charcoal. Kaolin-pectin is claimed to bind toxins and coat the mucosa, but clinical studies have not shown that it shortens illness or reduces fluid loss. It can also bind other oral drugs and reduce their absorption. Activated charcoal binds many toxins and drugs and is not absorbed, but it does not treat the diarrhoea itself.
- **Opioid antimotility drugs** such as loperamide and diphenoxylate increase segmental contractions, slow transit and increase absorption. They can be harmful in infectious diarrhoea because they slow the clearance of the pathogen. Loperamide can cause severe central nervous system effects in dogs with the MDR1 mutation.

- **Antisecretory drugs** such as bismuth subsalicylate reduce fluid secretion. Salicylate is absorbed, so it should be avoided in cats and used cautiously in others.
- **Antimicrobials** are indicated only when there is evidence of invasive bacterial infection or systemic illness. Most acute diarrhoeas do not need them.

A common confusion: stopping the diarrhoea is not the same as treating the patient. A calf with watery diarrhoea can die from dehydration and acidosis even while stool looks firmer on an opioid.

Oral rehydration

In the small intestine, glucose is absorbed together with sodium by a co-transporter on the villus cell. Water follows by osmosis. This coupled uptake continues to work even when toxins such as those of *E. coli* have switched on secretion in the crypts. Oral rehydration solution (ORS) uses this principle to replace fluid and sodium by mouth.

A good ORS contains sodium, glucose or another substrate, and often a base such as acetate or bicarbonate to correct acidosis. Calf electrolyte products also provide glycine and other aids. Because the solution should be iso-osmotic or slightly hypo-osmotic, mixing it with too much powder or adding extra sugar can worsen diarrhoea.

Oral rehydration is used for mild to moderate dehydration in animals that can still swallow. Severe dehydration, shock, inability to stand or suck, or ileus needs intravenous fluids. ORS also should not replace the calf's milk feeding for long, as the animal still needs energy.

This is the point where students often misjudge: the drug that saves most lives in diarrhoea is not an antidiarrhoeal, it is salt, sugar and water.

Probiotics, prebiotics and the evidence

A **probiotic** is a live microorganism which, in adequate amounts, gives a benefit to the host. Common examples are *Lactobacillus*, *Bifidobacterium*, *Enterococcus* and the yeast *Saccharomyces*. A **prebiotic** is a non-living food component, such as fructo-oligosaccharide or inulin, that feeds beneficial bacteria. A **synbiotic** combines both. In livestock they are often called direct-fed microbials.

Proposed mechanisms are production of organic acids that lower gut pH, production of antimicrobial substances, competition with pathogens for nutrients and sites, and support of the gut barrier and immune system.

The evidence is mixed. In calves, a review of direct-fed microbials reported benefit in some trials and no effect in others, with the most plausible value in stressed animals. Most products are mixtures of strains, so it is hard to know which organism does what, and strains of the same species can behave differently.

Product quality is a major concern. Organisms die with heat, moisture, oxygen and storage. In calves, adding a product to hot milk replacer can kill it, and antimicrobials in feed can interfere. Labels may not match the actual content. Probiotics should not replace fluids, nutrition and treatment of the cause. Regulation of such products varies. Check the current guidance of the relevant Indian authority.

Probiotics are generally safe in healthy animals, but live organisms in severely ill or immunosuppressed animals need caution.

Concept cleared

Concept cleared: Osmotic laxative
Think of a salt shaker on a cut tomato. Salt that cannot be absorbed sits in the gut and pulls water into the lumen, just as salt draws water from tomato. The extra water softens and moves the stool.

Concept cleared: Bulk laxative needs water
A bulk laxative is like a dry sponge. Wet, it swells and fills the bowel. Dry, in a dehydrated animal, it just becomes a hard lump. Always ensure water intake.

Concept cleared: Why ORS works in diarrhoea
Secretion is a leaking tap, but the sodium-glucose pump is a separate door that still works. ORS opens that door, so water and salt enter the body even while the tap leaks.

Concept cleared: Probiotic versus prebiotic

A probiotic is the seed, a living microbe. A prebiotic is the fertiliser that helps the useful seeds grow. A synbiotic gives both.

Memory aid: Laxatives: B-H-L-E-S

Bulk, Hyperosmotic, Lubricant, Emollient, Stimulant, from the gentlest, slow ones to the harshest. Antidiarrhoeal order of priority: Fluids first, then protect, then slow, and antimicrobials last.

Compare and contrast

Laxative groups

Group	Example	Mechanism	Caution
Bulk	Psyllium, bran	Absorbs water, adds mass, stretches wall	Needs adequate water
Hyperosmotic	Magnesium sulphate, lactulose, PEG	Holds water in lumen	Dehydration; magnesium in renal disease
Lubricant	Mineral oil	Coats stool, eases passage	Vitamin A, D, E, K malabsorption; aspiration
Emollient	Docusate	Lowers stool surface tension	Do not combine with mineral oil
Stimulant	Senna, castor oil, bisacodyl	Irritates mucosa, raises motility and secretion	Fluid and electrolyte loss, colic

Antidiarrhoeal groups

Group	Example	Action	Limitation
Adsorbent	Kaolin-pectin, charcoal	Binds toxins and drugs	No proven shortening of illness; binds other drugs
Opioid	Loperamide	Slows transit, raises absorption	Avoid in infectious diarrhoea; MDR1 dogs at risk
Antisecretory	Bismuth subsalicylate	Reduces secretion	Salicylate absorption; avoid in cats
Rehydration	ORS	Replaces fluid and sodium by co-transport	Not enough in shock or ileus

Species notes

Dog

Loperamide can cause serious neurological signs in dogs carrying the MDR1 mutation, which is seen in some herding breeds. Avoid antimotility drugs in infectious diarrhoea such as parvovirus.

Cat

Do not use sodium phosphate enemas. Salicylate products such as bismuth subsalicylate are best avoided. Lactulose and diet are used for megacolon.

Horse

Mineral oil and osmotic salts are used for impaction, with fluids. Do not repeat stimulant doses. Foal diarrhoea needs fluid and electrolyte care first.

Calf

Calf scours kills mainly by dehydration, acidosis and electrolyte loss. Oral electrolyte solutions are the base of treatment, and milk feeding should continue. Probiotic evidence is mixed.

Cattle and small ruminants

Check withdrawal times and local rules before using any drug in food animals. Ruminant-specific

purgatives are discussed in the next chapter.

Clinical pearls

Self-test: 10 questions

1. Which laxative group works by holding water in the intestinal lumen?

Poorly absorbed salts and sugars retain water by osmosis.

2. What must be ensured when giving a bulk laxative?

Without water the bulk can harden the stool.

3. A risk of prolonged mineral oil use is:

Oil dissolves fat-soluble vitamins and carries them out.

4. Which enema is dangerous in cats?

Sodium phosphate enemas can cause fatal hyperphosphataemia and hypocalcaemia in cats.

5. Lactulose helps in hepatic encephalopathy because it:

Bacterial breakdown to acids lowers colonic pH and ammonium is not absorbed.

6. What is the evidence for kaolin-pectin in diarrhoea?

Studies have not shown benefit, and adsorption of other drugs is possible.

7. Why is loperamide avoided in infectious diarrhoea?

Slowing transit can retain organisms and toxins.

8. Oral rehydration solutions work because:

Coupled sodium-glucose uptake remains functional in secretory diarrhoea.

9. A prebiotic is:

Prebiotics such as inulin are food for beneficial microbes.

10. Which statement about probiotic products in calves is correct?

Trials show mixed outcomes, and heat, oxygen and moisture kill organisms.

Key points to revise

1. Laxative groups are bulk, hyperosmotic, lubricant, emollient and stimulant.
2. Bulk laxatives need adequate water.
3. Magnesium salts can accumulate in renal disease.
4. Lactulose acidifies the colon and traps ammonia in hepatic encephalopathy.
5. Adsorbents have little proven clinical benefit.
6. Opioid antimotility drugs are unsuitable in infectious diarrhoea.
7. ORS works because glucose-coupled sodium uptake persists during secretory diarrhoea.
8. Probiotics are live microbes, prebiotics are their food; evidence is mixed and strain-specific.

Go deeper on this site

- Ch 24. Ruminant digestive drugs (in this book)
- Ch 22. Gastric acid suppressants, antiemetics and prokinetics (in this book)

- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Cathartic and Laxative Drugs Used in Monogastric Animals
- Merck Veterinary Manual: Drugs Used to Treat Diarrhea in Monogastric Animals
- USDA APHIS: Direct-fed microbials (probiotics) in calf diets

CHAPTER 24 OF 33

Ruminant digestive drugs

Drugs and procedures that act on the rumen: rumenotorics, antibloat agents, antizymotics, buffers and acidifiers, bypass nutrients and cud or rumen-fluid inoculation. The chapter explains why restoring the rumen environment matters more than any single drug.

After this chapter you can

- Explain what the rumen microbial population does and why drugs can upset it
- Describe rumenotorics and the cautions on parasympathomimetics
- Distinguish frothy bloat from free-gas bloat and match antibloat agents to each
- Explain when buffers and acidifiers are and are not appropriate
- Describe rumen inoculation (transfaunation) and bypass nutrients

The rumen as a fermentation vat

The rumen, reticulum and omasum are a fermentation chamber. Bacteria, protozoa and fungi break down fibre and starch into volatile fatty acids (VFAs), which supply most of the ruminant's energy, and into microbial protein. Saliva, rich in bicarbonate, buffers the acids. Regular contractions mix the contents, and eructation removes the gas.

This system works only within a narrow range of pH, substrate and motility. When any of these fails, the animal shows **indigestion**: reduced appetite, reduced rumen contractions, abnormal rumen contents, and falling milk yield.

Two points guide all drug use here. First, drugs given by mouth enter a large volume of fluid, so they are diluted and may be altered by microbes. The rumen environment can inactivate some drugs, and some oral antimicrobials upset the microbial balance. Second, the best treatment is usually to correct the cause, such as diet, and to restore the microbial population. Drugs are only one tool.

Rumenotorics

Rumenotorics (ruminotorics) are agents meant to stimulate forestomach motility and fermentation. Traditional preparations contain bitters such as nux vomica, minerals, cofactors and sugars. Their current evidence is limited, and restoring the normal rumen environment is considered more satisfactory.

Parasympathomimetics such as neostigmine and bethanechol increase smooth muscle contraction, but they are seldom suitable. They can cause cholinergic effects such as salivation, abdominal pain and bradycardia, and neostigmine may increase the frequency of contractions without improving their strength. Metoclopramide may cause restlessness in cattle. Several of these drugs are not approved for cattle in some countries, and their value has not been confirmed in controlled trials.

Where hypomotility is due to impaction, mineral oil or a surfactant such as docusate given by tube with massage may help move the contents. Docusate can sharply reduce rumen protozoa, so rumen fluid transfer should follow if motility remains poor.

The practical view: a rumenotoric will not rescue an animal whose problem is hypocalcaemia, a displaced abomasum, pain or a toxic rumen. Look for the primary cause, which is the commonest cause of rumen stasis.

Bloat and antibloat agents

Bloat is excess gas in the rumen. There are two types, and the drug depends on the type.

- **Frothy bloat** (primary) occurs on lush legumes or high-grain diets. Gas is trapped in stable foam, so it cannot be belched. The treatment is to break down foam.
- **Free-gas bloat** (secondary) occurs when eructation is blocked, for example by oesophageal obstruction or vagal damage. Gas is free on top of the contents, and it is relieved by a stomach tube or, in an emergency, a trocar.

Antifoaming agents reduce the stability of the foam so gas can escape. Poloxalene is a surfactant used for treatment and prevention. Silicone products are used in a similar way. Docusate can relieve frothy bloat. Vegetable oils such as groundnut, sunflower and soybean oil are also used. Mineral oil is less suited because it does not mix well with the froth. Monensin, an ionophore, may lower the incidence of frothy bloat in feedlot cattle by changing the rumen flora.

Common confusion: a stomach tube relieves free-gas bloat dramatically but does little for frothy bloat, as froth blocks the tube. An animal that does not respond to the tube should be suspected of frothy bloat. Severe bloat compressing the diaphragm and the vena cava is an emergency, and decompression should not be delayed.

Prevention is by management: avoid sudden access to lush legumes, give dry roughage first, and use anti-foaming agents in the feed or water where this is the practice.

Antizymotics

An **antizymotic** is an agent that inhibits excessive fermentation by microbes. Zymotic means related to fermentation. Such agents were once given for tympany and for conditions of abnormal fermentation.

The idea has limits. The rumen needs fermentation, and a broad inhibitor harms the useful flora as well as the harmful. Many older antizymotic preparations have little supporting evidence. Modern thinking uses specific measures instead: correct the diet, use ionophores such as monensin for managing acidosis and bloat in feedlot systems where permitted, and avoid broad antimicrobials by mouth.

Indian use of ionophores and other feed additives is subject to regulation and may change. Check the current notification before use in dairy or meat animals, and observe withdrawal periods.

When an exam asks for antizymotics, the key points are the definition, the examples listed in your textbook, and the caution that suppressing fermentation also suppresses digestion.

Buffers, alkalinisers and acidifiers

The main condition needing a buffer is **acute ruminal lactic acidosis** after grain engorgement or sudden carbohydrate overload. Lactic acid accumulates, pH falls below about 5.5, the flora change and the animal can become dehydrated and acidotic.

Antacids used in such cases include magnesium hydroxide, magnesium oxide, magnesium carbonate and sodium bicarbonate. They are given as a large volume of warm water. Magnesium oxide and hydroxide strongly alkalinise the rumen and reduce protozoa, so they should be given only when grain overload is confirmed. Sodium bicarbonate raises rumen pH quickly but releases large amounts of carbon dioxide, and in an animal with weak motility this increases the risk of free-gas bloat. Systemic dehydration and acidosis also need correcting, and in severe cases the rumen contents are replaced with fresh fluid.

Acidifiers are used where the rumen pH is too high. In simple indigestion and stasis the pH may be above 7.5. In ammonia (urea) poisoning, high pH favours free ammonia absorption, so a weak acid such as dilute acetic acid or vinegar in cold water helps by lowering pH and slowing urease action.

Do not give alkalinisers or acidifiers routinely in indigestion. Correct the cause first, and match the agent to the measured rumen pH where you can.

Bypass nutrients and rumen inoculation

Microbes degrade most protein and fat that enter the rumen, so a nutrient given by mouth may never reach the intestine in useful form. **Bypass (rumen-protected) nutrients** are treated so that they escape rumen degradation and are digested in the abomasum and small intestine. Examples are protected protein, protected fat and protected amino acids. They are used in high-yielding dairy cows in early lactation to supply what the rumen cannot. Protected drugs and vitamins follow the same logic.

The idea also applies to calves. Before the rumen is developed, the oesophageal groove reflex directs milk straight to the abomasum, so it bypasses the rumen. The reflex weakens with age.

Rumen inoculation or transfaunation gives fresh rumen fluid from a healthy donor. It supplies bacteria, protozoa, VFAs, buffers and nutrients, and is described as the best available rumenotoric. It is used for stasis, after prolonged anorexia and after antimicrobials or docusate have disturbed the flora. The fluid is strained and given by stomach tube. The best dose is not known. If the existing contents are putrefied or very acidic, they may need to be removed first. Donors on a similar ration are preferred. Cud from a healthy animal is a traditional farm version of the same idea.

The success of inoculation depends on the underlying disease responding.

Concept cleared

Concept cleared: The rumen is a living vat
Think of curd-making: the right bacteria in the right conditions give a good result. Add too much acid or kill the starter and the batch is spoiled. Rumen drugs aim to protect the vat, not to override it.

Concept cleared: Frothy versus free-gas bloat
Frothy bloat is a bottle of soda that has foamed over: you cannot pour it out. Free-gas bloat is a bottle with a blocked mouth. The first needs a foam breaker, the second needs a tube or trocar.

Concept cleared: Why bicarbonate can cause bloat
Sodium bicarbonate meeting acid releases carbon dioxide, like a fizzy tablet in water. In a rumen that cannot belch, that gas builds up.

Concept cleared: Bypass nutrient
A courier parcel with a hard wrapper survives the first sorting station (rumen) and is opened only at the final one (abomasum). Protected protein or fat is wrapped so rumen microbes do not consume it.

Memory aid: Ruminant digestive drugs: R-A-A-B-B-I

Rumenotorics, Antibloat, Antizymotics, Buffers, Bypass nutrients, Inoculation.

For bloat remember: Froth needs a Foam breaker; Free gas needs a Flow tube.

Compare and contrast

Frothy and free-gas bloat

Feature	Frothy bloat	Free-gas bloat
Cause	Stable foam from lush legumes or grain	Failure of eructation (obstruction, vagal damage)
Stomach tube	Little relief, froth blocks tube	Rapid relief
Main treatment	Antifoaming agent (poloxalene, silicone, oil, docusate)	Tube or trocar, remove cause
Prevention	Diet management, antifoam, monensin where permitted	Treat primary obstruction

Alkalinisers and acidifiers

Group	Example	Used for	Caution
Alkaliniser	Magnesium hydroxide or oxide	Confirmed grain overload, low rumen pH	Reduces fermentation and protozoa; not routine
Alkaliniser	Sodium bicarbonate	Fast pH rise	Carbon dioxide release, bloat risk
Acidifier	Dilute acetic acid, vinegar	High pH, ammonia poisoning	Treat the cause, not only the pH

Species notes

Cattle

Frothy bloat on lush legume pasture and acidosis after grain overload are the main problems. Check

Buffalo

Buffalo are also prone to bloat and grain overload with wheat or rice-based feeds. The principles are the

withdrawal periods and current Indian rules before using any additive or drug in milk or meat animals.

same as in cattle; do not assume cattle product doses apply, and consult a veterinarian or label.

Sheep and goat

Small ruminants develop acidosis and bloat on sudden grain or lush feed. Volumes of antacids and oils are smaller, so use a species-specific source.

Calf

The oesophageal groove carries milk directly to the abomasum. Oral drugs given to a preruminant calf may bypass the rumen, whereas in an older animal they are diluted in the rumen.

Camel

Camels have a different forestomach, so extrapolating ruminant digestive drug use from cattle should be done with care.

Clinical pearls

Self-test: 10 questions

1. Which type of bloat is relieved dramatically by a stomach tube?

In free-gas bloat the gas is free above the contents and escapes through the tube.

2. An antifoaming agent acts by:

It breaks the stable foam trapping the gas.

3. Which drug may lower frothy bloat incidence in feedlot cattle?

Ionophores alter the rumen flora and may reduce frothy bloat.

4. Why is sodium bicarbonate a risk in acute acidosis with poor motility?

Reaction with acid releases CO2 that the stasis rumen cannot eructate.

5. An acidifier is helpful in which situation?

Lower pH reduces free ammonia absorption and slows urease.

6. Which drug can markedly reduce rumen protozoa?

Docusate lowers protozoa, so transfaunation may be needed afterwards.

7. Why are parasympathomimetics seldom suitable as rumenotorics?

Effects such as salivation, colic and bradycardia limit their use.

8. What is transfaunation?

It restores bacteria, protozoa, VFAs and buffers.

9. A bypass nutrient is designed to:

Protection allows protein or fat to reach the abomasum and intestine intact.

10. The main reason a broad antizymotic is a poor idea is that it:

The rumen depends on fermentation for energy, so broad inhibition harms digestion.

Key points to revise

1. The rumen is a microbial fermentation vat buffered by saliva.
2. Rumenotorics have limited evidence; parasympathomimetics have hazardous cholinergic effects.
3. Frothy bloat needs antifoam; free-gas bloat needs decompression.
4. Poloxalene, silicones, oils and docusate act as antifoams.
5. Antizymotics inhibit fermentation but also harm useful flora.
6. Alkalinisers are for confirmed acidosis, acidifiers for high pH and ammonia poisoning.
7. Bypass nutrients escape rumen degradation to be digested lower down.
8. Transfaunation restores flora with fresh strained rumen fluid.

Go deeper on this site

- Ch 25. Hepatic, pancreatic and biliary drugs (in this book)
- Ch 23. Laxatives, purgatives, antidiarrhoeals and probiotics (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Drugs for Specific Purposes in the Ruminant Digestive System
- Merck Veterinary Manual: Drug Disposition in the Ruminoreticulum
- USDA APHIS: Direct-fed microbials (probiotics) in calf diets

CHAPTER 25 OF 33

Hepatic, pancreatic and biliary drugs

How drugs support the liver, pancreas and bile system: hepatoprotectants, lactulose for hepatic encephalopathy, pancreatic enzyme replacement and choleretics, plus why liver disease changes the way every other drug is handled.

> **After this chapter you can**

- Explain why the liver is central to drug metabolism and what changes in liver disease
- Describe the rationale and the limits of evidence for hepatoprotectants such as silymarin, SAMe and ursodeoxycholic acid
- Explain how lactulose lowers blood ammonia in hepatic encephalopathy
- Describe how pancreatic enzyme replacement works and why it is given with food
- Apply general principles for choosing and adjusting drugs in animals with liver disease

The liver as the body's drug-processing plant

The liver takes up drugs from portal blood, converts them to more water-soluble forms and excretes them in bile or returns them to blood for the kidney. Phase I reactions (mainly cytochrome P450 enzymes) oxidise the drug. Phase II reactions (such as glucuronidation) attach a polar group. Many drugs lose activity in this way, but some are **prodrugs** that must be activated by the liver.

Drugs absorbed from the gut pass through the liver first. This *first-pass effect* can remove a large part of an oral dose before it reaches the general circulation. Liver disease, and especially a portosystemic shunt, lets blood bypass this filter, so oral drugs can reach much higher blood levels than expected.

This chapter covers three linked organs. The liver makes bile and detoxifies; the biliary tract carries bile to the intestine; the exocrine pancreas supplies digestive enzymes. Drugs here either support the organ, replace what it no longer makes, or manage the complications of its failure.

Hepatoprotectants: what they try to do

A **hepatoprotectant** is a drug or supplement given to limit liver injury or help repair. The common ideas behind them are antioxidant action, support of the cell's own protective chemistry and reduction of toxic bile acid damage.

- **Silymarin** (milk thistle extract) is described as an antioxidant and membrane stabiliser. It is widely used, but the clinical evidence in animals is limited.

- **S-adenosylmethionine (SAMe)** supports the production of glutathione, the liver's main antioxidant. It is usually given with the aim of supporting hepatocytes in chronic disease or after toxic injury.
- **N-acetylcysteine** supplies cysteine for glutathione. It is the best-known antidote for paracetamol (acetaminophen) toxicity, which is a real danger in cats.
- **Vitamin E** is a lipid-soluble antioxidant sometimes added in chronic hepatopathies.

A common confusion is to treat these as proven curative drugs. They are supportive. They never replace treating the underlying cause, such as infection, copper accumulation, toxins or obstruction. Also remember that supplements are not tightly regulated, so product quality varies.

Ursodeoxycholic acid and choleretics

A **choleretic** increases bile flow. Bile contains bile acids, which are needed to absorb dietary fat and fat-soluble vitamins (A, D, E, K) and which carry waste out of the body.

Ursodeoxycholic acid (ursodiol) is the most important drug in this group. It is a hydrophilic bile acid. It replaces part of the pool of toxic hydrophobic bile acids, stimulates bile flow and has some anti-inflammatory and immune-modulating effects. It is used in cholestatic and chronic inflammatory liver disease.

The key safety rule is that choleretics are unsuitable when the bile duct is completely blocked. Pushing more bile into an obstructed system can do harm, so obstruction must be excluded (usually by imaging) before use.

Do not confuse a choleretic with a *cholagogue* (stimulates gallbladder emptying) or with drugs that merely relieve dyspepsia. In animals, many traditional herbal 'liver tonics' sold in the field are marketed as choleretics or appetite stimulants. Their evidence is generally weak, so judge them cautiously.

Lactulose and hepatic encephalopathy

Hepatic encephalopathy (HE) is a neurological syndrome in which the failing liver, or a shunt, cannot clear gut-derived toxins. The best-known toxin is **ammonia**, formed when colonic bacteria break down dietary protein and urea. Signs include

depression, circling, head pressing, blindness and seizures, often worse after a protein-rich meal.

Lactulose is a synthetic disaccharide that animals cannot digest or absorb. It reaches the colon intact, where bacteria ferment it to organic acids. This produces three useful effects:

1. The colonic pH falls. Ammonia (NH_3) is converted to ammonium (NH_4^+), which is charged and poorly absorbed, so it is 'trapped' in the lumen.
2. The acid environment discourages ammonia-producing bacteria.
3. The osmotic laxative effect speeds transit and removes toxins in faeces.

The Merck Veterinary Manual describes lactulose as the standard against which other HE treatments are compared. Dose is adjusted to produce a few soft stools per day; too much causes cramping and severe diarrhoea, which dehydrates the animal and can worsen HE. Lactulose can also be given as a retention enema when an animal cannot take oral drugs.

Adjuncts include a protein diet of high quality and appropriate amount (protein is not simply withdrawn), and selected antibiotics given orally to reduce urease-producing gut bacteria. Always treat the trigger as well, such as gastrointestinal bleeding, infection or electrolyte disturbance.

Pancreatic enzyme replacement

In **exocrine pancreatic insufficiency (EPI)** the pancreas does not make enough lipase, amylase and protease. Food passes undigested. The animal eats well but loses weight and passes large, pale, greasy, foul stools. It is seen especially in dogs, often in German Shepherds, and less commonly in cats.

Treatment is **enzyme replacement**, taken by mouth with every meal for life. Key concepts:

- **Acid inactivates lipase.** Much of the enzyme is destroyed in the stomach before it reaches the duodenum, where it must act.
- **Form matters.** The Merck Veterinary Manual states that powdered products are more effective than tablets, capsules and, especially, enteric-coated products. Enteric-coated forms were designed to resist acid, but in dogs they may release their enzyme too late or poorly.

- **Mix with food.** Enzyme must meet the food in the intestine. Giving it away from meals defeats the purpose.
- **Acid suppression.** Antacids are usually unnecessary, but an acid-reducing drug may be tried if response is poor.

Cobalamin (vitamin B_{12}) deficiency is common in EPI, particularly in cats, and is often corrected separately. Do not use enzyme replacement in acute pancreatitis; it is a different disease and does not treat inflammation.

Liver disease and drug dosing

There is no simple blood test that predicts how well a diseased liver will metabolise a drug. Liver enzyme tests (ALT, ALP) show injury, not capacity. Use judgement, and apply a few general principles.

- **Prefer drugs that are not heavily metabolised** or are eliminated mainly by the kidney.
- **Drugs with high first-pass extraction** reach higher levels when blood bypasses the liver, as in a shunt.
- **Low albumin** increases the free fraction of highly protein-bound drugs.
- **Prodrugs** that need hepatic activation may work poorly.
- **Sedatives and anaesthetics**, especially benzodiazepines and other CNS depressants, can push an animal with HE into coma. Choose carefully.
- **Known hepatotoxic drugs**, such as paracetamol in cats, certain azole antifungals and some anticonvulsants, call for caution or monitoring.
- **Cats** are limited in glucuronidation, so some drugs accumulate in them even with a healthy liver.

Reduce the dose or lengthen the interval when in doubt, use the lowest effective amount, monitor clinical response and liver values, and consult the product literature.

Concept cleared

First-pass effect

Oral drugs pass through the liver before reaching the body. Liver disease or a shunt removes this filter and raises systemic exposure.

Ammonia trapping

Lactulose acidifies the colon, converting diffusible NH3 into charged NH4+ that is not absorbed.

Acid-labile lipase

Pancreatic lipase is destroyed by gastric acid, so form of enzyme product and giving with meals matter.

Support, not cure

Hepatoprotectants support liver cells but never replace removing the underlying cause.

Memory aid: Lactulose three actions

ACID: Acidifies colon, Cuts ammonia-producing bacteria, Increases transit, Drains toxins with faeces.

Compare and contrast

Hepatoprotectants compared

Agent	Proposed action	Note
Silymarin	Antioxidant, membrane stabiliser	Limited clinical evidence
SAMe	Raises glutathione	Supportive in chronic disease
N-acetylcysteine	Supplies cysteine for glutathione	Antidote for paracetamol toxicity
Ursodeoxycholic acid	Hydrophilic bile acid, choleretic	Avoid in complete bile duct obstruction

Lactulose versus pancreatic enzymes

Feature	Lactulose	Pancreatic enzymes
Problem treated	Hepatic encephalopathy	Exocrine pancreatic insufficiency
Site of action	Colon	Duodenum, with food
Mechanism	Acidifies and traps ammonia, osmotic laxative	Replaces missing lipase, amylase, protease
Overdose sign	Diarrhoea, dehydration	Rarely serious; oral irritation possible

Species notes

Dogs

Portosystemic shunts and chronic hepatitis are common reasons for lactulose and hepatoprotectants. EPI is usually due to pancreatic acinar atrophy and needs lifelong enzyme replacement.

Cats

Slow glucuronidation makes cats sensitive to paracetamol and some other drugs. Hepatic lipidosis and cholangitis are important liver diseases. EPI often coexists with low cobalamin.

Cattle

Liver disease is often linked to fatty liver in early lactation, liver fluke and plant toxins. Management of the cause is usually more important than hepatoprotectants.

Horses

Hepatic encephalopathy can occur with liver failure. Horses have no gallbladder, so bile flows continuously into the duodenum.

Pigs and poultry

Dietary liver injury is mainly managed by correcting toxins such as mycotoxins in feed rather than by drugs.

Clinical pearls

Self-test: 10 questions

1. Which statement best describes how lactulose reduces ammonia absorption?

Colonic bacteria ferment lactulose to acids, lowering pH and trapping ammonia as ammonium.

2. A common sign of excess lactulose dosing is:

Overdose causes osmotic diarrhoea and dehydration, which can worsen encephalopathy.

3. Ursodeoxycholic acid should be avoided in:

Stimulating bile flow against a blocked duct is hazardous.

4. N-acetylcysteine is best known as an antidote for:

It replenishes cysteine and glutathione, which neutralise the toxic paracetamol metabolite.

5. Why are enteric-coated pancreatic enzymes often less effective in dogs?

Powder is considered more effective than tablets or enteric-coated products.

6. Pancreatic enzyme replacement should be given:

The enzyme must mix with food to digest it.

7. Which change in liver disease most increases the free fraction of highly protein-bound drugs?

Albumin is made by the liver; low levels leave more drug unbound.

8. A portosystemic shunt increases exposure to oral drugs mainly because:

Portal blood skips the liver, so high-extraction drugs reach the circulation unchanged.

9. Which species is notably limited in glucuronidation?

Cats have poor glucuronide conjugation, so some drugs accumulate.

10. Which statement about hepatoprotectants is most accurate?

They support hepatocytes but do not replace cause-directed therapy.

Key points to revise

1. The liver metabolises most drugs; first-pass loss is reduced in shunts and severe disease.
2. Hepatoprotectants are supportive and their clinical evidence is limited.
3. SAMe and N-acetylcysteine support glutathione; N-acetylcysteine is an antidote for paracetamol.
4. Ursodeoxycholic acid is a hydrophilic bile acid and choleretic; avoid it in complete obstruction.
5. Lactulose is fermented in the colon, acidifies it and traps ammonia as ammonium.
6. EPI needs lifelong oral enzyme with every meal, in an acid-stable, effective form.
7. In liver disease prefer renally cleared drugs and avoid unnecessary CNS depressants.
8. Cats are deficient in glucuronidation and are vulnerable to hepatotoxic drugs.

Go deeper on this site

- Ch 26. Hypothalamic and pituitary hormones (in this book)
- Ch 24. Ruminant digestive drugs (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Hepatic encephalopathy in small animals
- Merck Veterinary Manual: Exocrine pancreatic insufficiency in dogs and cats

CHAPTER 26 OF 33

Hypothalamic and pituitary hormones

How the hypothalamus and pituitary control reproduction, water balance, lactation and growth, and how oxytocin, vasopressin, GnRH, gonadotropins, prolactin inhibitors and somatotropin are used in animals. The chapter also notes the regulatory issues around oxytocin and somatotropin in India.

After this chapter you can

- Describe the hypothalamic-pituitary axis and which hormones come from the anterior and posterior pituitary
- Explain the actions, uses and cautions of oxytocin and why its misuse in dairy animals is a concern in India
- Explain the V1 and V2 actions of vasopressin and the use of desmopressin in diabetes insipidus
- Explain why GnRH works as a stimulant when pulsatile but as a suppressant when continuous, and compare FSH, LH, hCG and eCG
- Describe how dopamine agonists lower prolactin and how somatotropin is regulated and used

The hypothalamic-pituitary axis

The hypothalamus is the control room that links the nervous system to the endocrine system. It makes releasing and inhibiting hormones that travel through a small portal blood system to the **anterior pituitary** (adenohypophysis). The anterior pituitary then releases trophic hormones such as FSH, LH, prolactin, growth hormone, TSH and ACTH, which act on target glands.

The **posterior pituitary** (neurohypophysis) is different. It does not make hormones. It stores and releases **oxytocin** and **antidiuretic hormone** (vasopressin), both made in hypothalamic nerve cell bodies and carried down the axons.

Most hormone-based drugs in this chapter work in one of three ways: they replace a missing hormone, they mimic a hormone to push a target organ, or they exploit feedback so that a target gland is switched off. Keep this logic in mind and the long list of drug names becomes easier.

Oxytocin

Oxytocin is a nonapeptide that acts on oxytocin receptors, which are G-protein-coupled and raise intracellular calcium. It has two main targets: the **myometrium** (uterine contraction) and the **myoepithelial cells** of the mammary gland (milk let-down or ejection).

Uterine sensitivity depends on the stage of the cycle. Oestrogen increases oxytocin receptors, so the uterus responds well at term and in the early postpartum period but poorly under progesterone. Low blood calcium also weakens uterine contractions, which is why a cow with hypocalcaemia and retained fetal membranes may need calcium as well as oxytocin.

Uses include assisting uterine contractions in selected cases of uterine inertia once obstruction is excluded, promoting involution and expulsion of fluids after parturition, helping with retained placenta, and supporting milk let-down in true let-down failure.

Cautions. The cervix must be open and the fetus correctly positioned. Giving oxytocin against an obstruction risks uterine rupture and fetal death. Oxytocin has weak antidiuretic-like activity, so very large or prolonged infusions can cause water retention.

Regulation in India. Oxytocin is widely misused to force milk let-down in dairy animals, and misuse has been linked to animal welfare problems and reduced fertility. The Indian government has placed restrictions on its manufacture and sale. Students should check the current notification for exactly who may manufacture, import and sell it, and on what prescription terms.

Vasopressin and desmopressin

Vasopressin (ADH) has two receptor actions. **V2 receptors** in the renal collecting duct raise cAMP and insert aquaporin-2 water channels into the membrane, so water is reabsorbed and urine becomes concentrated. **V1 receptors** on vascular smooth muscle act through calcium and cause vasoconstriction, which is why vasopressin is sometimes used in vasodilatory shock.

Desmopressin (DDAVP) is a synthetic analogue that is mostly V2-selective with a longer duration and little pressor effect. It is the drug of choice for **central diabetes insipidus**, where the pituitary fails to release ADH. It can be given as eye drops or by injection in animals, depending on the product available.

A common confusion is **nephrogenic diabetes insipidus**, where the kidney does not respond to ADH. Desmopressin will not fix this, and the response to a desmopressin trial is in fact one way to tell the two forms apart. Giving too much desmopressin to an animal that is drinking freely can cause water retention and low blood sodium.

GnRH and its analogues

Gonadotropin-releasing hormone (GnRH) is a decapeptide released from the hypothalamus in pulses. Each pulse causes the pituitary to release LH and FSH. The key concept is **pulsatility**. Pulsatile exposure stimulates the gonadotroph cells, while continuous exposure causes receptor desensitisation and down-regulation, so LH and FSH output falls.

This gives two opposite uses of the same drug class:

- **Stimulation**: short-acting analogues such as gonadorelin and buserelin cause an LH surge, used to induce ovulation, to treat follicular cysts, and in timed breeding programmes where GnRH is combined with prostaglandin F2-alpha to synchronise the oestrous cycle in cattle.

- **Suppression**: long-acting agonists such as deslorelin, given as slow-release implants, produce sustained exposure and reversible suppression of the reproductive axis. The labelled species and uses differ between countries, so check the product in your market.

Note that an agonist may cause a short initial flare of gonadal activity before suppression begins.

Gonadotropins: FSH, LH, hCG and eCG

Gonadotropins are glycoprotein hormones that act directly on the ovary or testis.

- **FSH** (from pituitary extracts) stimulates follicle growth and is used for superovulation in embryo transfer programmes.
- **LH** triggers ovulation and luteinisation.
- **hCG** (human chorionic gonadotropin, from the urine of pregnant women) has mainly LH-like action. It is used to induce ovulation or luteinisation of follicles.
- **eCG** (equine chorionic gonadotropin, formerly PMSG, from pregnant mare serum) has both FSH-like and LH-like activity and a long half-life. It is used to stimulate follicle growth in anoestrus animals and for superovulation.

Because hCG and eCG are foreign proteins, repeated use can lead to antibody formation and a falling response. A single long-acting dose of eCG can also keep stimulating follicles after they are no longer wanted, which is one cause of overstimulation.

The common exam confusion is between hCG and eCG. Remember: *hCG is LH-like, eCG is FSH-like with some LH*.

Prolactin inhibitors and somatotropin

Prolactin is controlled mainly by inhibition. Dopamine from the hypothalamus acts on D2 receptors of the lactotroph cells and keeps prolactin low. **Dopamine agonists** such as cabergoline and bromocriptine therefore suppress prolactin. They are used in bitches and queens to stop lactation and to treat pseudopregnancy. Cabergoline is longer acting and usually causes less vomiting than bromocriptine. The reverse also holds: dopamine antagonists such as metoclopramide and domperidone raise prolactin and are sometimes used to stimulate milk production. Cabergoline is also

used with other drugs in some pregnancy termination protocols, subject to local guidance.

Somatotropin (growth hormone) is released under the push of GHRH and the brake of **somatostatin**. It acts partly directly and partly by liver production of IGF-1. Recombinant bovine somatotropin (rbST) increases milk yield in dairy cows by redirecting nutrients to the udder, and carries risks to cow welfare such as mastitis and lameness. Rules on its use differ between countries, and students should check the current Indian notification before treating it as legal or available. Growth hormone is also diabetogenic, so excess causes insulin resistance, as in acromegaly in cats or progestin-induced excess in dogs.

Concept cleared

Concept cleared: Pulsatile versus continuous GnRH
Think of knocking on a door. Short knocks with gaps bring someone out, but a continuous bell press that never stops makes them ignore it. Pulsatile GnRH keeps the pituitary responsive, while continuous GnRH makes its receptors desensitise, so LH and FSH fall.

Concept cleared: Why oxytocin needs oestrogen priming
Oxytocin receptors are like locks that the uterus builds only when oestrogen is high. Near term the locks are many and the oxytocin key works well. Under progesterone dominance there are few locks and the same dose does little.

Concept cleared: Central versus nephrogenic diabetes insipidus
In central DI the message (ADH) is missing, so sending a synthetic message (desmopressin) works. In nephrogenic DI the message arrives but the kidney cannot read it, so more messages do nothing.

Concept cleared: Dopamine as a brake

Prolactin is the only anterior pituitary hormone mainly held down by hypothalamic dopamine. Giving a dopamine agonist presses the brake harder, and giving a dopamine blocker releases the brake.

Memory aid: Posterior pituitary pair

Posterior stores, not makes: OA, as in Oxytocin and ADH. For eCG versus hCG think: e for equine gives FSH plus LH, h for human gives LH-like. For prolactin remember: Dopamine Drops prolactin.

Compare and contrast

Gonadotropin preparations

Preparation	Source	Main activity	Typical use
FSH	Pituitary extract	FSH	Superovulation
hCG	Urine of pregnant women	LH-like	Induce ovulation or luteinisation
eCG (PMSG)	Pregnant mare serum	FSH-like with LH activity, long-lasting	Anoestrus, superovulation
GnRH analogues	Synthetic	Release endogenous LH and FSH	Ovulation induction, follicular cysts, synchronisation

Oxytocin versus vasopressin

Feature	Oxytocin	Vasopressin (ADH)	Desmopressin
Release site	Posterior pituitary	Posterior pituitary	Synthetic
Main receptor	Oxytocin receptor	V1 and V2	Mostly V2
Key action	Uterine contraction, milk let-down	Water reabsorption, vasoconstriction	Water reabsorption
Clinical use	Uterine inertia, retained placenta	Shock (V1), DI	Central diabetes insipidus

Species notes

Cattle

Oxytocin is used in retained placenta and milk let-down problems, and GnRH combined with prostaglandin is the basis of many timed breeding programmes. Oxytocin misuse in dairy animals is a regulatory concern in India.

Dog

Bitches with pseudopregnancy or unwanted lactation respond to dopamine agonists such as cabergoline. Central diabetes insipidus is treated with desmopressin. Dogs with progestin-induced excess growth hormone may show insulin resistance.

Cat

Cats with acromegaly, usually from a pituitary tumour, develop insulin-resistant diabetes. Queens can be treated with dopamine agonists to stop lactation, with attention to vomiting.

Horse

eCG originates in pregnant mares, and oxytocin is used in mares for retained placenta and uterine clearing after foaling, as well as to help milk let-down. Check product labelling for use in lactating mares.

Buffalo

Buffalo are particularly dependent on milk let-down, and the oxytocin misuse problem in Indian dairying

involves both cattle and buffalo. Follow the current Indian notification for legal use.

Clinical pearls

Self-test: 10 questions

1. Which hormones are stored and released by the posterior pituitary?

Oxytocin and ADH are made in hypothalamic neurons and released from the posterior pituitary. The others come from the anterior pituitary.

2. Why is oxytocin dangerous in a case of uterine obstruction?

Strong contractions against an obstructed or unprepared passage can rupture the uterus and kill the fetus.

3. Which receptor mediates the antidiuretic action of vasopressin?

V2 receptors in the collecting duct raise cAMP and insert aquaporin-2 channels.

4. Desmopressin will fail to correct polyuria in which condition?

In nephrogenic DI the kidney does not respond to ADH or its analogues.

5. Continuous exposure to a GnRH agonist results in:

Continuous stimulation desensitises and down-regulates pituitary GnRH receptors.

6. Which preparation is mainly LH-like?

hCG binds the LH receptor and acts like LH. eCG has both FSH and LH-like activity.

7. Which drug is a dopamine agonist used to suppress lactation in bitches?

Cabergoline stimulates D2 receptors on lactotrophs and lowers prolactin. Metoclopramide and domperidone raise prolactin.

8. Which statement about eCG is correct?

eCG comes from pregnant mares, has a long half-life and can cause antibody formation on repeated use.

9. What is the effect of excess growth hormone on glucose metabolism?

Growth hormone is diabetogenic and antagonises insulin action.

10. Which statement is the most appropriate about oxytocin regulation in India?

Controls have been placed on oxytocin because of misuse in dairy animals, and rules can change, so the current notification should be consulted.

Key points to revise

1. The posterior pituitary stores and releases oxytocin and ADH, which are made in the hypothalamus.
2. Oxytocin contracts the uterus and the mammary myoepithelium, and the uterus responds best under oestrogen.
3. Oxytocin carries a risk of uterine rupture if given against obstruction.
4. Oxytocin has regulatory controls in India, so check the current notification.
5. ADH acts through V2 (water retention) and V1 (vasoconstriction).
6. GnRH is stimulatory when pulsatile and suppressive when continuous.
7. hCG is LH-like and eCG is FSH-like with LH activity; repeated use can cause antibodies.

8. Somatotropin raises milk yield and is diabetogenic; its legal status in India should be checked.

Go deeper on this site

- Ch 27. Thyroid and antithyroid drugs (in this book)
- Ch 28. Pancreatic hormones and antidiabetic drugs (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Overview of the pituitary gland
- Merck Veterinary Manual: Diabetes insipidus
- University of Minnesota Libraries: Principles of Pharmacology

CHAPTER 27 OF 33

Thyroid and antithyroid drugs

How thyroid hormones are made and controlled, and how levothyroxine and methimazole are used for hypothyroidism in dogs and hyperthyroidism in cats. The chapter also covers monitoring, adverse effects and the common traps in diagnosis.

After this chapter you can

- Outline thyroid hormone synthesis and feedback control
- Explain levothyroxine therapy for canine hypothyroidism and the principles of monitoring
- Explain how methimazole works and list its adverse effects in cats
- Compare the treatment options for feline hyperthyroidism
- Recognise drugs and illnesses that confuse thyroid testing

Thyroid hormone synthesis and control

The thyroid gland makes **thyroxine (T4)** and a smaller amount of **triiodothyronine (T3)**. T4 is the main secreted product, and tissues convert it into the more active T3

by removing one iodine atom. T3 binds nuclear receptors and changes gene expression, which is why thyroid hormone effects on metabolism, heart rate and growth appear slowly and last for days.

Synthesis has clear steps, and each is a possible drug target:

1. **Iodide trapping**: the follicular cell actively takes up iodide from blood.
2. **Oxidation and organification**: the enzyme thyroid peroxidase (TPO) oxidises iodide and attaches it to tyrosine residues on thyroglobulin.
3. **Coupling**: iodinated tyrosines join to form T4 and T3 on thyroglobulin, which is stored as colloid.
4. **Release**: thyroglobulin is taken back into the cell, broken down, and T4 and T3 are secreted.

Control is by negative feedback. The hypothalamus releases TRH, the pituitary releases TSH, and the thyroid responds. High T4 switches off TRH and TSH. Most circulating thyroid hormone is bound to plasma proteins, and only the free fraction is active.

Why the signs follow the hormone

Thyroid hormone sets the pace of metabolism in almost every tissue. It raises oxygen use, heat production, heart rate and the sensitivity of the heart to catecholamines. It also drives normal skin turnover, hair growth and nerve function. That one idea explains most clinical signs.

When hormone is low, everything slows: the dog is dull and gains weight on little food, feels the cold, grows a poor coat and heals skin infections slowly. When hormone is high, everything speeds up: the cat loses weight despite eating well, has a fast heart and is restless and warm.

This also explains therapy. Levothyroxine in a hypothyroid dog should bring the pace back to normal over weeks, so a dog that becomes agitated and thin on treatment is being overdosed. Methimazole in a cat should slow the pace gradually, so a cat that becomes dull and gains weight may now be over-suppressed and needs a dose review. Always match the signs to the direction of the drug effect.

Hypothyroidism in dogs

Hypothyroidism is common in dogs. It is usually caused by immune-mediated lymphocytic thyroiditis or by idiopathic atrophy of the gland, so the gland slowly fails. Typical signs are lethargy, weight gain, cold intolerance, a dull coat with hair loss and recurrent skin infections. Because many other diseases mimic these signs, laboratory confirmation matters.

Levothyroxine (synthetic L-T4) is the treatment of choice. It replaces the missing hormone, and the dog converts it to T3 as needed. Therapy is lifelong, and the aim is to control the clinical signs and bring blood hormone levels into a suitable range, not to produce a rapid change.

Key practical points:

- The drug has a fairly long half-life in dogs, but absorption varies between products and with food, so a consistent routine is important.
- Clinical response is gradual. Activity may improve within a few weeks, while skin and coat changes take longer.
- Monitoring uses a blood T4 measured at a defined time after the tablet, together with clinical assessment. The sampling time and the target range should follow the guidance for the product used.
- Overdosing causes signs of thyrotoxicosis: restlessness, panting, weight loss, tachycardia and polyphagia.

Diagnosis comes before treatment. Giving thyroid hormone to a euthyroid dog does not help and can suppress the normal gland.

Hyperthyroidism in cats

Hyperthyroidism is the commonest endocrine disease of older cats. It is usually caused by benign adenomatous change in one or both thyroid lobes, and the overactive tissue makes too much hormone. Signs include weight loss despite a good appetite, restlessness, vomiting, polyuria, a fast heart rate and sometimes a palpable thyroid nodule. Untreated disease can cause cardiac changes and high blood pressure.

Treatment options include:

- **Antithyroid drugs** (methimazole, carbimazole), which suppress synthesis and are reversible.

- **Radioactive iodine**, which is taken up by overactive tissue and destroys it, and is often curative but requires a licensed facility.
- **Surgical thyroidectomy**, which can cure the disease but requires anaesthesia of a cat that may have heart disease and risks damage to the parathyroid glands.
- **Iodine-restricted diet**, which works only if the cat eats nothing else.

In India, radioiodine services are limited, so drug treatment or surgery is often the realistic choice. Check what facilities are available locally.

Methimazole and other antithyroid drugs

Methimazole (thiamazole) inhibits thyroid peroxidase, so iodine cannot be attached to thyroglobulin and new T4 and T3 are not made. It does not block release of hormone already stored, so improvement takes a few weeks. It does not cure the underlying tumour, and the gland may continue to enlarge.

Carbimazole is a prodrug that is converted to methimazole in the body. **Propylthiouracil** also blocks TPO and peripheral T4 to T3 conversion, but it is toxic in cats, causing haemolytic anaemia, so it is avoided.

Adverse effects in cats are mostly in the first weeks and include:

- Vomiting and loss of appetite.
- Intense facial itching with skin excoriation.
- Blood disorders such as neutropenia, thrombocytopenia and, less commonly, haemolytic anaemia.
- Liver injury with raised enzymes and jaundice.
- Positive antinuclear antibody tests.

Serious reactions usually mean stopping the drug. Many cats are also given a transdermal gel preparation applied to the ear, which can reduce gastrointestinal upset but may cause local skin irritation.

An important trap is **masked kidney disease**. Hyperthyroidism increases renal blood flow and glomerular filtration. When the thyroid is controlled, blood flow falls and a pre-existing chronic kidney disease may become obvious. Renal values should be checked before and after starting treatment.

Adjuncts and thyroid-related traps

Beta-blockers such as propranolol or atenolol can control the fast heart rate and tremor of hyperthyroidism while the main treatment takes effect. They do not lower thyroid hormone levels. Stable iodide solutions block hormone release for a short time and are sometimes used before surgery.

Interpreting thyroid tests needs care. **Non-thyroidal illness** (sick euthyroid) can lower T4 in a dog that has no thyroid disease. Drugs that can lower measured T4 include glucocorticoids, phenobarbital and potentiated sulfonamides. Long-term sulfonamides can also cause true, reversible hypothyroidism in dogs. Testing during illness or while on these drugs can lead to a wrong diagnosis and unnecessary lifelong therapy.

Other thyroid problems in animals include **goitre** in newborn lambs, kids and calves from iodine deficiency in the diet or from goitrogens such as certain brassica feeds. Here the gland enlarges because low iodine reduces feedback inhibition and TSH rises. The fix is correcting the diet, not an antithyroid drug.

Thyroid hormone is also a banned or controlled substance in some performance contexts, and growth promoters containing antithyroid substances are not acceptable in food animals. Check current regulations in India.

Concept cleared

Concept cleared: Why methimazole is slow
Imagine a factory with a full warehouse. Methimazole shuts down the production line, but the warehouse (stored colloid) still ships products for a while. Hormone levels fall only when the stock runs low, so improvement takes weeks.

Concept cleared: Why the kidney problem appears later
Hyperthyroidism is like a pump running too fast, which pushes extra blood through the kidneys and hides kidney weakness. When the pump is slowed to normal, the weakness shows.

Concept cleared: Sick euthyroid

In serious illness the body lowers thyroid hormone to save energy. The low reading is a response, not a diagnosis, so treating it with levothyroxine does not help.

Concept cleared: Goitre from low iodine

Without iodine the gland cannot make hormone, so T4 falls, TSH rises, and TSH pushes the gland to grow. The gland is enlarged because it is working harder, not because hormone is excessive.

Memory aid: Thyroid synthesis steps

Trap, Oxidise, Organify, Couple, Release: think 'Tom Often Orders Cold Rice'. Methimazole blocks the O steps through TPO. For signs remember: hypothyroid dogs are Slow and Heavy, hyperthyroid cats are Fast and Thin.

Compare and contrast

Hypothyroidism in dogs versus hyperthyroidism in cats

Feature	Canine hypothyroidism	Feline hyperthyroidism
Usual cause	Lymphocytic thyroiditis or atrophy	Benign adenomatous hyperplasia
Typical signs	Lethargy, weight gain, skin disease	Weight loss, ravenous appetite, restlessness
Main drug	Levothyroxine, lifelong	Methimazole or carbimazole
Key risk of therapy	Overdose giving thyrotoxicosis	Blood, liver and skin reactions; masked kidney disease

Options for feline hyperthyroidism

Option	Mechanism	Advantage	Limitation
Methimazole or carbimazole	Inhibit TPO	Reversible, widely available	Lifelong dosing and adverse effects
Radioactive iodine	Destroys overactive tissue	Often curative	Needs a licensed facility
Thyroidectomy	Removes tissue	Can cure	Anaesthetic risk, parathyroid damage
Iodine-restricted diet	Limits substrate	No drugs	Only works if the diet is exclusive

Species notes

Dog

Hypothyroidism is the common disorder and levothyroxine is lifelong. Hyperthyroidism is rare and usually due to a thyroid carcinoma, so surgery or other cancer treatment is the focus rather than antithyroid drugs alone.

Cat

Hyperthyroidism is common in old cats. Methimazole is widely used and requires monitoring of blood counts, liver and kidney values. Propylthiouracil should be avoided. Hypothyroidism is rare and mostly follows treatment.

Cattle

Goitre in newborn calves reflects iodine deficiency in the dam's diet. Correct the diet and check local iodine status, which varies between regions.

Sheep and goat

Newborn lambs and kids born to iodine-deficient dams may show goitre, weakness or high mortality, and the same dietary correction applies.

Horse

Foals from mares with iodine imbalance can develop goitre. Both deficiency and excess of iodine are possible, so supplement based on

dietary assessment rather than guesswork.

Clinical pearls

Self-test: 10 questions

1. Which enzyme is inhibited by methimazole?

Methimazole blocks thyroid peroxidase, preventing iodination of thyroglobulin and hormone synthesis.

2. The drug of choice for canine hypothyroidism is:

Levothyroxine replaces the missing hormone and is given lifelong.

3. Why does methimazole take weeks to act?

Stored hormone in colloid keeps being released until it is used up.

4. Which drug is avoided in cats due to haemolytic anaemia?

Propylthiouracil is toxic in cats.

5. What is carbimazole?

Carbimazole is converted to methimazole in the body.

6. Why should renal values be checked when treating a hyperthyroid cat?

Hyperthyroidism raises glomerular filtration, and falling flow after control may reveal pre-existing kidney disease.

7. Which of these can falsely lower T4 in a dog?

Glucocorticoids, phenobarbital, potentiated sulfonamides and non-thyroidal illness can lower measured T4.

8. A newborn lamb with a goitre most likely reflects:

Low iodine reduces hormone synthesis, raising TSH, which enlarges the gland.

9. Which sign suggests levothyroxine overdose in a dog?

Excess hormone causes thyrotoxic signs such as restlessness, tachycardia and weight loss.

10. Beta-blockers in feline hyperthyroidism are used to:

They relieve adrenergic signs while the main therapy takes effect, but do not reduce hormone production.

Key points to revise

1. T4 is the main secreted hormone and T3 is the more active form made by peripheral conversion.
2. Thyroid peroxidase is the enzyme needed for iodination and coupling.
3. Canine hypothyroidism is mostly lymphocytic thyroiditis or atrophy and needs lifelong levothyroxine.
4. Levothyroxine is monitored by timed T4 and clinical response, not by quick dose changes.
5. Feline hyperthyroidism is treated with drugs, radioiodine, surgery or diet.
6. Methimazole inhibits TPO and is slow in effect.
7. Adverse effects of methimazole include gastrointestinal upset, facial itching, blood and liver problems.
8. Non-thyroidal illness and some drugs lower T4 and can mimic hypothyroidism.

Go deeper on this site

- Ch 28. Pancreatic hormones and antidiabetic drugs (in this book)
- Ch 26. Hypothalamic and pituitary hormones (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Hyperthyroidism
- Merck Veterinary Manual: Hypothyroidism
- Merck Veterinary Manual: Overview of the thyroid gland

CHAPTER 28 OF 33

Pancreatic hormones and antidiabetic drugs

How insulin and glucagon control blood glucose, which insulin types are used in dogs and cats, what oral agents and SGLT2 inhibitors can and cannot do, and the logic of treating diabetic ketoacidosis. The emphasis is on mechanism and on why mistakes happen.

After this chapter you can

- Explain how insulin and glucagon regulate glucose and why insulin lowers potassium
- Group insulin preparations by onset and duration and match them to the usual species choice
- Describe the role and limits of oral hypoglycaemic agents in cats and dogs
- Explain how SGLT2 inhibitors work in cats, who they suit, and the euglycaemic ketoacidosis risk
- Outline the stepwise logic of diabetic ketoacidosis treatment: fluids, potassium, then insulin

Insulin and glucagon: the basic physiology

The pancreatic islets release two opposing hormones. **Insulin** from the beta cells is the hormone of the fed state. **Glucagon** from the alpha cells is the hormone of fasting. Together they hold blood glucose in a narrow range.

Insulin binds a receptor with intrinsic tyrosine kinase activity on the cell surface. The signal moves glucose transporters (GLUT4) to the membrane of muscle and fat cells, so glucose enters. In the liver insulin switches off glucose production and promotes glycogen and fat storage. It also drives potassium into cells. This last action matters in practice: giving insulin lowers serum potassium.

Glucagon does the reverse in the liver, raising glucose through glycogen breakdown and new glucose synthesis. Diabetes mellitus is a failure of insulin action, either because beta cells are lost or damaged, or because tissues respond poorly, or both. Without insulin, glucose stays in the blood and the body burns fat instead, producing ketones.

A common confusion: hyperglycaemia causes the clinical signs of polyuria and polydipsia only after glucose passes the renal threshold. Glucose then spills into urine and drags water with it (osmotic diuresis).

Insulin preparations and how they are chosen

Insulins differ in how fast they start and how long they last. This is the single most important idea for choosing one.

- **Short-acting (regular, soluble) insulin**. Rapid onset and short duration. It is the one used in emergencies such as ketoacidosis because it can be given by infusion or intramuscularly and adjusted quickly.
- **Intermediate-acting (NPH, lente)**. NPH has protamine added to slow absorption. Lente (porcine insulin zinc suspension) is a mixture of crystalline and amorphous zinc insulin. These are the usual starting insulins in dogs, given twice daily. Product availability differs between countries, so check what is marketed locally.
- **Long-acting (protamine zinc insulin, glargine, detemir)**. Slower and flatter action. Protamine zinc insulin and glargine are commonly chosen for newly diagnosed cats, since cats often need a longer duration than dogs. Detemir may be considered when control in dogs is poor.

Insulin is a protein, so it is destroyed by gut enzymes and must be injected, normally subcutaneously. Store it as the label directs and avoid vigorous shaking of

suspensions, which makes dose delivery uneven.

The same insulin does not behave identically in every animal. Absorption, peak and duration vary, so the right insulin is judged by a glucose curve and clinical response, not by label duration alone.

Complications of insulin therapy

The main danger is **hypoglycaemia**: weakness, tremor, collapse, seizures. Causes include too high a dose, a missed meal, or a sudden change in insulin need (for example after remission in a cat or after treating an interfering disease). Owners must be taught the signs and an emergency plan.

Two confusing states follow poor control. In the **Somogyi effect**, an overdose causes hypoglycaemia followed by a counter-regulatory surge of glucagon, adrenaline, cortisol and growth hormone, giving high glucose later. In **insulin resistance**, glucose stays high despite adequate doses. Distinguishing them needs serial glucose measurement, because the treatment for one (reduce dose) is opposite to the other (look for the cause).

Common causes of resistance are concurrent disease (infection, pancreatitis, hyperadrenocorticism, acromegaly), drugs such as glucocorticoids and progestins, obesity, and technique or storage errors. Remember this when prescribing other hormones in a diabetic animal.

Oral agents: what they can and cannot do

Oral drugs only help if some functioning beta-cell mass remains. This is why they have a place in a few cats and almost none in dogs, whose diabetes usually involves severe insulin deficiency.

- **Sulfonylureas** (for example glipizide) close ATP-sensitive potassium channels on beta cells, causing depolarisation, calcium entry and insulin release. They are used only in cats that are well, not thin and not ketotic, and the response is limited and often not sustained. Long-term stimulation may exhaust beta cells.
- **Alpha-glucosidase inhibitors** (acarbose) slow carbohydrate digestion in the gut and blunt the post-meal rise. They are an adjunct to diet and insulin, with gut side effects such as flatulence and diarrhoea.

- **Biguanides and thiazolidinediones** are important in human type 2 diabetes but have little established role in small animals.

The take-home point is that oral agents are not a substitute for insulin in an animal that is sick, ketotic or thin.

SGLT2 inhibitors in cats

Sodium-glucose cotransporter 2 (SGLT2) in the proximal renal tubule reabsorbs most filtered glucose. SGLT2 inhibitors block it, so glucose is lost in urine and blood glucose falls without needing insulin. Two agents (velagliflozin and bexagliflozin) have been licensed for cats in some countries. Availability in India is uncertain, so check the current notification and market status before relying on them.

They suit only selected cats: newly diagnosed, otherwise well, eating normally, and not previously on insulin, so that some beta-cell function remains. They are not for cats with significant liver or kidney disease, pancreatitis, or those who are anorexic, dehydrated or lethargic at diagnosis.

The key hazard is **ketoacidosis, including euglycaemic ketoacidosis**. Because the drug removes glucose through urine, the blood glucose may look normal or only mildly raised even while ketones accumulate. A cat that becomes dull, anorexic or dehydrated must be assessed for ketosis whatever the glucose reading. Treatment is to stop the drug, give insulin, and provide carbohydrate and nutritional support, which also helps prevent hepatic lipidosis. Other effects include glucosuria-related urinary and gut signs.

Diabetic ketoacidosis: a stepwise approach

Diabetic ketoacidosis (DKA) arises when insulin lack lets fat breakdown run unchecked. Ketoacids accumulate, causing metabolic acidosis, dehydration and electrolyte loss. It is an emergency, often triggered by pancreatitis, infection or another concurrent illness.

1. **Rehydrate first.** Intravenous isotonic fluids restore perfusion and also lower glucose by dilution and improved renal clearance.
2. **Replace electrolytes.** Total body potassium and phosphate are depleted, though the serum level may look normal because acidosis shifts potassium out of cells.

Insulin then pushes potassium back in and can cause dangerous hypokalaemia, so supplement potassium and monitor.

3. **Give insulin.** Short-acting insulin is used, by infusion or intermittent injection, usually after fluids have started. The aim is a gradual fall in glucose, not rapid normalisation, because a fast drop can contribute to cerebral oedema.
4. **Treat the trigger** and support nutrition. Add dextrose to fluids when glucose falls while ketosis persists, so insulin can continue to suppress ketone production.
5. **Transition** to longer-acting insulin once the animal is hydrated, eating and stable.

A frequent exam error is to start insulin before fluids and potassium. Remember the order: fluids, potassium, then insulin.

Concept cleared

Insulin lowers potassium
Insulin moves potassium into cells. In DKA, serum potassium may be deceptively normal, and falls once insulin starts, so potassium is replaced alongside insulin.

Duration decides the choice
Regular insulin is for emergencies, intermediate insulins for typical dogs, and long-acting insulins for typical cats. Always confirm by glucose curve.

Oral drugs need beta cells
Sulfonylureas and SGLT2 inhibitors depend on some remaining insulin secretion. They fail or are unsafe when insulin lack is severe.

Normal glucose does not exclude ketoacidosis
SGLT2 inhibitors can cause euglycaemic ketoacidosis. Check ketones in any unwell cat on these drugs.

Memory aid: DKA order: F-P-I

Fluids, Potassium, Insulin. Treat the dehydration and electrolytes before pushing insulin, then treat the trigger.

Compare and contrast

Main insulin groups

Group	Examples	Speed and duration	Typical use
Short-acting	Regular (soluble)	Fast, short	DKA and emergencies
Intermediate	NPH, lente	Moderate, medium	Starting insulin in dogs
Long-acting	Protamine zinc, glargine, detemir	Slow, flatter	Newly diagnosed cats; poorly controlled dogs

Oral and non-insulin agents

Drug	Mechanism	Main limit
Sulfonylurea (glipizide)	Stimulates beta-cell insulin release	Needs functioning beta cells; not for thin or ketotic cats
Acarbose	Slows carbohydrate digestion	Gut side effects; adjunct only
SGLT2 inhibitor	Blocks renal glucose reabsorption	Ketoacidosis risk; only selected cats; check availability

Species notes

Dogs
Diabetes is usually insulin-deficient and permanent. Twice-daily intermediate insulin with consistent diet is the base. Oral agents are not effective.

Cats
Often resembles human type 2 diabetes with insulin resistance, and remission is possible with early good control. Long-acting insulin is common. Avoid glucocorticoids and progestins.

Cattle and small ruminants

Classical diabetes is rare. Ketosis in cows is an energy deficit problem, not insulin failure, and is treated with glucose precursors rather than long-term insulin.

Horses

Insulin dysregulation is linked with equine metabolic syndrome and pituitary disease rather than insulin-dependent diabetes. Management is by diet, exercise and treating the cause.

Clinical pearls

Self-test: 10 questions

1. Which action of insulin explains hypokalaemia during DKA treatment?

Insulin drives potassium into cells, lowering serum levels, so supplementation is needed.

2. Which insulin is preferred for acute DKA management?

Regular insulin acts quickly and can be given by infusion or intermittent injection and adjusted.

3. A sulfonylurea lowers glucose by:

Sulfonylureas close K-ATP channels on beta cells, triggering insulin secretion.

4. Which statement about SGLT2 inhibitors in cats is correct?

They act on the proximal tubule so glucose is lost in urine; they can cause ketoacidosis and suit only selected cats.

5. A cat on an SGLT2 inhibitor becomes anorexic and dull with only mildly raised glucose. The best step is to:

Euglycaemic ketoacidosis can occur with near-normal glucose.

6. In DKA, the correct treatment order is:

Rehydration and electrolyte replacement come before or with the start of insulin to avoid hypokalaemia and shock.

7. Why avoid very rapid glucose reduction in DKA?

Rapid osmolar shifts can contribute to cerebral oedema.

8. Which drugs commonly cause insulin resistance in diabetic animals?

Both antagonise insulin action and worsen control.

9. Which describes the Somogyi effect?

Counter-regulatory hormones are released after hypoglycaemia, raising glucose later.

10. Oral hypoglycaemics are generally ineffective in dogs because:

These agents need remaining beta-cell function, which is typically lost in canine diabetes.

Key points to revise

1. Insulin promotes glucose uptake via GLUT4 and drives potassium into cells.
2. Glucagon raises blood glucose by liver glycogen breakdown and glucose production.

3. Insulin types differ in onset and duration; choice is species and case dependent.
4. Hypoglycaemia is the main complication of insulin therapy.
5. Somogyi effect and insulin resistance look alike but need opposite responses.
6. Oral agents depend on remaining beta-cell function and have limited roles.
7. SGLT2 inhibitors block renal glucose reabsorption and can cause euglycaemic ketoacidosis.
8. DKA treatment is fluids, potassium and phosphate, then insulin, with a gradual glucose fall.

Go deeper on this site

- Ch 29. Adrenal hormones and the glucocorticoid axis (in this book)
- Ch 27. Thyroid and antithyroid drugs (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

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- FDA CVM: Dear Veterinarian letter on Bexacat safety
- Merck Veterinary Manual: Hormonal treatment for integumentary disease in animals

CHAPTER 29 OF 33

Adrenal hormones and the glucocorticoid axis

The hypothalamic-pituitary-adrenal axis, the actions of glucocorticoids and mineralocorticoids, and the drugs used for hypercortisolism (Cushing) and hypocortisolism (Addison). Includes why steroid withdrawal is dangerous and what stress dosing means.

After this chapter you can

- Describe the CRH-ACTH-cortisol axis and its negative feedback
- Distinguish glucocorticoid and mineralocorticoid actions and give examples of each drug

- Explain how trilostane and mitotane treat canine hyperadrenocorticism and their key risks
- Outline maintenance and emergency treatment of Addison disease
- Explain iatrogenic adrenal suppression and the concept of stress dosing

The adrenal axis

The adrenal cortex makes three families of steroid. The outer zone makes **mineralocorticoids** (mainly aldosterone), the middle zone makes **glucocorticoids** (cortisol in most species, corticosterone in rodents) and the inner zone makes sex steroids.

Cortisol release is controlled by a chain: the hypothalamus releases corticotropin-releasing hormone (CRH), the pituitary releases ACTH, and ACTH drives the adrenal cortex. Cortisol then feeds back negatively on both hypothalamus and pituitary. Aldosterone is controlled mainly by the renin-angiotensin system and by serum potassium, not by ACTH, although ACTH has a minor effect.

This difference explains much of the clinical pattern. If ACTH is lost (secondary hypoadrenocorticism, or after long steroid therapy), the cortisol zone shrinks but aldosterone remains. If the cortex is destroyed (primary Addison disease), both are lost.

Actions of glucocorticoids and mineralocorticoids

Glucocorticoids act on intracellular receptors that change gene transcription, so their effects begin over hours. They raise blood glucose, break down protein and redistribute fat, suppress inflammation and immunity, and are needed to maintain blood pressure and respond to stress. Their use as drugs is covered in the earlier chapter on corticosteroids, but the same actions explain the signs of excess: polyuria, polydipsia, polyphagia, muscle wasting, a pot belly, thin skin, and infection risk.

Mineralocorticoids act in the distal nephron, retaining sodium and water and excreting potassium and hydrogen ions. Loss produces hyponatraemia, hyperkalaemia, hypovolaemia and bradycardia.

Drugs overlap. Hydrocortisone has both actions. Prednisolone and dexamethasone are almost purely glucocorticoid, dexamethasone being far more potent and longer acting. Fludrocortisone has strong mineralocorticoid action with some glucocorticoid effect. Desoxycorticosterone pivalate (DOCP) is a long-acting injectable that is essentially mineralocorticoid only.

Cushing disease: reducing cortisol

Hyperadrenocorticism in dogs is most often due to a pituitary tumour secreting ACTH (pituitary-dependent), and less often an adrenal tumour. Long-term glucocorticoid therapy produces a similar picture, called iatrogenic Cushing. In horses the equivalent is pituitary pars intermedia dysfunction, managed with a dopamine agonist such as pergolide because the affected cells lose dopamine inhibition.

Two main drugs are used in dogs.

- **Trilostane** is an enzyme inhibitor that blocks steroid synthesis in the adrenal, decreasing cortisol output. The effect is reversible and the drug is usually given with food. The main concerns are over-suppression, a transient hypocortisolism that can be missed on routine testing, reversible mineralocorticoid deficiency, and rarely adrenal necrosis with permanent insufficiency. Therapy is monitored by clinical signs and by cortisol testing.
- **Mitotane (o,p'-DDD)** is an adrenolytic: it selectively damages the cortical zones that make cortisol. It is given as an induction phase followed by maintenance and needs careful monitoring. Side effects include vomiting, lethargy, ataxia and, if overdone, hypoadrenocorticism, which requires stopping the drug and giving glucocorticoids.

Neither drug cures a pituitary tumour. The aim is to control clinical signs, not to normalise every laboratory value. Surgery is the usual choice for an operable adrenal tumour.

Addison disease: replacing what is lost

Hypoadrenocorticism is deficiency of adrenocortical hormones, most commonly immune-mediated destruction in dogs. Signs are vague: lethargy, vomiting,

weakness, weight loss, sometimes collapse. In crisis, hyperkalaemia and hypovolaemia threaten the heart and circulation.

Emergency (Addisonian crisis). Intravenous fluids are the mainstay. Hypoglycaemia and hyperkalaemia are treated directly. A rapid-acting glucocorticoid is given, and dexamethasone is often preferred because it does not interfere with a diagnostic ACTH stimulation test. Mineralocorticoid is added when electrolytes indicate deficiency.

Maintenance. Two parts are needed: a mineralocorticoid (DOCP by periodic injection, or daily fludrocortisone) and a glucocorticoid (low-dose prednisolone or prednisone, tapered to the lowest level that controls signs). Dogs with atypical disease, where only glucocorticoids are lacking at first, still need electrolyte checks because mineralocorticoid deficiency can appear later.

Overtreatment mimics Cushing: increased thirst, urination, appetite and infections.

Iatrogenic suppression and stress dosing

Giving glucocorticoids for more than a short course suppresses CRH and ACTH. The adrenal cortex then atrophies. If the drug is stopped abruptly, the animal cannot make cortisol and may collapse. The remedy is a gradual tapering, and a recognition that recovery can take weeks.

Stress dosing is the idea that a normal animal increases cortisol output during illness, surgery, anaesthesia or trauma. An animal with Addison disease, or one on long-term steroids, cannot do this, so the dose must be increased temporarily during stress. Concerning signs include unexplained collapse, hypotension, hypoglycaemia and vomiting after a stressful event.

Remember also that topical, ocular and injectable depot steroids can suppress the axis. Progestins such as megestrol have glucocorticoid-like activity and cause adrenal suppression as well.

Mineralocorticoids and other uses

Mineralocorticoids have little use outside Addison disease in small animals. Fludrocortisone's sodium retention can cause hypertension and oedema if overdosed, and its effect on potassium is the monitoring target.

In ruminants, glucocorticoids have specific uses. A potent glucocorticoid given late in gestation can induce parturition because it mimics the fetal cortisol surge that triggers labour. This also explains why such drugs are a risk for abortion in pregnant animals. Prolonged use in livestock may raise glucose and suppress immunity. Check withdrawal periods and the current regulatory position before use in food animals.

Concept cleared

Negative feedback
Cortisol suppresses CRH and ACTH. Exogenous steroid does the same, which is why long-term therapy atrophies the adrenal cortex.

ACTH controls cortisol, not aldosterone
Aldosterone is controlled mainly by renin-angiotensin and potassium, so secondary adrenal failure spares electrolytes.

Trilostane inhibits; mitotane destroys
Trilostane reversibly blocks steroid synthesis. Mitotane damages adrenal cortex tissue, so over-treatment can be more lasting.

Stress dosing
Animals that cannot raise cortisol need a temporary dose increase during illness or surgery to avoid adrenal crisis.

Memory aid: Cushing is Cortisol Crowded
Excess cortisol gives thirst, hunger, thin skin, pot belly and infections. Addison is the opposite: low sodium, high potassium, shock.

Compare and contrast

Cushing drugs in dogs

Drug	Mechanism	Key risk
Trilostane	Reversible adrenal enzyme inhibition	Over-suppression, rarely adrenal necrosis
Mitotane	Adrenolytic damage to cortex	GI and CNS effects, iatrogenic Addison

Corticosteroid activity

Drug	Glucocorticoid	Mineralocorticoid	Use
Hydrocortisone	Yes	Some	Crisis, replacement
Prednisolone	Yes	Little	Maintenance and anti-inflammatory
Dexamethasone	Very potent	Almost none	Emergency, testing-friendly
Fludrocortisone	Some	Strong	Addison maintenance
DOCP	Minimal	Yes	Addison maintenance

Species notes

Dogs
Both Cushing and Addison disease are common. Trilostane is the usual drug for Cushing and DOCP with a glucocorticoid for Addison.

Cats
Spontaneous Cushing and Addison disease are uncommon. Cats are relatively resistant to the side effects of glucocorticoids but fragile skin and diabetes can occur.

Horses
Pituitary pars intermedia dysfunction causes hirsutism and laminitis. Dopamine agonist therapy is used, not adrenal enzyme inhibitors.

Cattle and sheep
Corticosteroids can induce parturition, and may cause abortion in pregnancy. Check withdrawal periods and local rules for food animals.

Clinical pearls

Self-test: 10 questions

1. Which hormone mainly stimulates cortisol release from the adrenal cortex?

ACTH from the pituitary drives cortisol secretion.

2. Aldosterone secretion is controlled mainly by:

ACTH has only a minor effect on aldosterone.

3. Trilostane acts by:

It is an adrenal enzyme inhibitor.

4. Mitotane is best described as:

It damages adrenal cortical tissue.

5. A dog on mitotane develops anorexia, vomiting and diarrhoea. The best action is to:

These signs suggest hypoadrenocorticism.

6. A long-acting injectable mineralocorticoid for Addison disease is:

Desoxycorticosterone pivalate replaces aldosterone-type activity.

7. Why is dexamethasone often chosen in an Addisonian crisis before testing?

Dexamethasone does not cross-react with the cortisol assay.

8. Overtreatment of Addison disease with prednisolone causes signs resembling:

Excess glucocorticoid produces iatrogenic hyperadrenocorticism.

9. Stress dosing is needed in an animal with Addison disease because it:

Normal animals boost cortisol under stress; these animals cannot.

10. Equine pituitary pars intermedia dysfunction is usually treated with:

Loss of dopaminergic inhibition drives the disease, so a dopamine agonist is used.

Key points to revise

1. Cortisol release follows CRH to ACTH to adrenal cortex with negative feedback.
2. Aldosterone is controlled mainly by renin-angiotensin and potassium.
3. Glucocorticoid excess produces PU/PD, polyphagia, muscle wasting and infection risk.
4. Trilostane is a reversible adrenal enzyme inhibitor used for canine Cushing.
5. Mitotane is adrenolytic and needs careful monitoring.
6. Addison disease needs mineralocorticoid plus glucocorticoid replacement.
7. Addisonian crisis is treated with fluids, glucocorticoid and correction of metabolic derangements.
8. Prolonged steroid use causes adrenal atrophy and requires tapering and stress cover.

Go deeper on this site

- Ch 30. Sex hormones, anabolics and growth promoters (in this book)
- Ch 28. Pancreatic hormones and antidiabetic drugs (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index

- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Addison disease (hypoadrenocorticism) in animals
- Merck Veterinary Manual: Cushing disease (pituitary-dependent hyperadrenocorticism) in animals
- Merck Veterinary Manual: Cushing syndrome (hyperadrenocorticism) in animals

CHAPTER 30 OF 33

Sex hormones, anabolics and growth promoters

The actions, uses and hazards of oestrogens, progestins, androgens and anabolic steroids in animals, with emphasis on pyometra and bone marrow toxicity, and on why hormonal growth promoters and doping are regulated.

After this chapter you can

- Describe the main actions of oestrogens, progestins and androgens
- Explain why oestrogens and progestins predispose to pyometra
- Recognise oestrogen-induced bone marrow suppression and species sensitivity
- Describe uses and adverse effects of anabolic steroids
- Explain the regulatory and ethical issues in hormonal growth promotion and misuse

Sex steroids: one family, many effects

Oestrogens, progestins and androgens are steroid hormones made from cholesterol in the gonads, adrenal cortex and placenta. They act like other steroids: they enter the cell, bind intracellular receptors and change gene transcription. Effects are slow in onset and often long in duration.

Natural hormones are largely destroyed in the liver when swallowed, so drug forms are usually modified for oral activity, esterified for depot injection, or implanted. These changes alter potency and duration but not the basic receptor action.

A key idea for this chapter is that these drugs are not simple tools for one organ. They act on the uterus, mammary gland, prostate, bone marrow, liver, pituitary and behaviour all at once. Most serious adverse effects come from this wide action.

Oestrogens

Oestrogens such as oestradiol, and the synthetic diethylstilbestrol, promote development of the female tract, mammary tissue and secondary sex characteristics, and sensitise the uterus to progesterone.

Uses in small animals are now narrow. A weak oestrogen is used for urethral sphincter incompetence in spayed bitches, because oestrogen increases the sensitivity of the urethral smooth muscle to adrenergic stimulation. Oestrogen has also been used for mismating, but this is **not advised**: injectable oestrogens can cause pyometra and fatal bone marrow suppression, and oral oestrogen given during diestrus raises pyometra risk and is unreliable. Safer alternatives such as prostaglandins or antiprogestins are preferred where available.

Bone marrow toxicity is the dangerous effect. Oestrogens can cause bone marrow hypoplasia, with an initial rise and then a fall in neutrophils, followed by thrombocytopenia and anaemia. The effect may be delayed and is not always dose-predictable. Cats are especially sensitive. Weekly blood counts are needed if oestrogens are used.

Other effects include induced oestrus, hepatotoxicity, prostatic changes in male dogs and abortion.

Progestins and the pyometra problem

Progesterone maintains pregnancy by quietening the myometrium and promoting uterine gland secretion. Synthetic progestins (megestrol acetate, medroxyprogesterone) have been used to suppress oestrus, treat some behavioural and skin conditions, and in some prostatic or mammary disorders.

The problem is the uterus. Progesterone thickens and secretes from the endometrium, closes the cervix and reduces local immune defence. Repeated or prolonged exposure leads to **cystic endometrial hyperplasia**, which fills with fluid and becomes an ideal site for bacterial growth. This is **pyometra**. Oestrogen primes

the uterus to respond, so oestrogen followed by progestin or diestrus is the worst combination.

Other adverse effects of progestins include mammary hyperplasia and tumours, diabetes mellitus in cats, adrenal suppression, acromegaly-like growth hormone excess in dogs, and behavioural change. Because of these risks, they are generally avoided where alternatives exist.

Pyometra patients are acutely ill and often need surgery. A drug history of oestrogen or progestin should always be asked for.

Androgens

Testosterone and its derivatives drive male sexual development and behaviour, spermatogenesis and sex accessory glands, and also have anabolic effects on muscle and bone. Clinical uses are limited, for example in some libido or hormone-responsive conditions, and drugs must be chosen carefully.

Adverse effects include aggression, greasy coat, prostatic enlargement in dogs, suppression of the animal's own gonadal function (feedback inhibition of LH and FSH), and liver toxicity, especially with oral 17-alpha-alkylated forms. Liver function should be checked during treatment. Androgens given to a female can virilise her, and they can harm a pregnant female's fetuses.

Anabolic steroids

Anabolic steroids (nandrolone, stanozolol, boldenone) are androgen derivatives chosen for greater protein-building effect relative to male-type effects. Receptor activation increases nitrogen retention and muscle mass and may stimulate red cell production by enhancing erythropoietin response.

Veterinary uses are limited and include convalescence, debilitation and some anaemias. Evidence is variable and these are not substitutes for nutrition, treating the cause, or adequate calories.

The separation of anabolic and androgenic effects is incomplete. Hepatotoxicity, behavioural change, and fluid retention occur. They are subject to doping control in racing and sport animals and are controlled substances in many places.

Growth promoters, regulation and misuse

Some countries allow implants of sex-steroid or anabolic agents (for example trenbolone, zeranol, oestradiol) in beef cattle to increase growth and feed efficiency. Others, including the European Union, prohibit them. The concern is residues in meat and public-health effects, together with trade barriers and welfare issues.

For India, rules on hormonal growth promoters, hormone use in dairy animals, and maximum residue limits (MRLs) are set through national notifications and food-safety regulations. Check the current notification before advising on any use in food animals.

Misuse includes using anabolic steroids to improve appearance of show or racing animals, giving hormones to hasten maturity, and using hormones to increase milk. These are ethically and legally problematic, and some are harmful to the animal. A student should also know that residues carry a withdrawal period issue, and that clinical use must follow label and legal requirements.

Remember: a drug being available is not the same as being permitted for a given species or purpose.

Concept cleared

Oestrogen primes, progesterone promotes
Oestrogen sensitises the uterus and progesterone creates the secretory, immunologically weak environment. Together they predispose to pyometra.

Marrow toxicity is delayed
Oestrogen bone marrow suppression may appear after the drug has been given, so monitoring continues beyond the treatment.

Anabolic is not safe
Anabolic steroids retain androgenic and liver effects. Their benefits are modest and the risks real.

Residues and regulation

Hormonal growth promoters are restricted or banned in many jurisdictions to prevent residues in food and for trade and ethical reasons.

Memory aid: Oestrogen: B-P-L

Bone marrow, Pyometra, Liver. The three serious oestrogen hazards.

Compare and contrast

Sex hormone classes

Class	Examples	Main concern
Oestrogens	Oestradiol, diethylstilbestrol	Bone marrow suppression, pyometra, hepatotoxicity
Progestins	Megestrol, medroxyprogesterone	Pyometra, mammary tumours, diabetes in cats, adrenal suppression
Androgens and anabolics	Testosterone, nandrolone, stanozolol	Liver toxicity, behaviour, prostatic effects, doping

Mismating: choices

Option	Comment
Oestrogens	Not advised: pyometra and marrow risk
Prostaglandin analogues	Effective, with systemic effects to manage
Antiprogestins	Effective, availability limited in some countries

Species notes

Dogs

Pyometra follows diestrus and is made likelier by oestrogens and progestins. Oestrogen for

Cats

Highly sensitive to oestrogen toxicity. Megestrol can cause diabetes, adrenal suppression and mammary disease.

incontinence is used with blood monitoring.

Cattle
Hormonal growth implants are allowed in some countries and banned in others. Check the current Indian notification and withdrawal rules.

Horses
Anabolic steroids and sex hormones are prohibited substances in competition. Always check the rules of the governing body.

Poultry and pigs
Hormone growth promotion is not an accepted practice in most regulatory systems. Ask for current guidance.

Clinical pearls

Self-test: 10 questions

1. Which is the most serious haematological effect of oestrogens?

Oestrogen can cause marrow suppression with thrombocytopenia and anaemia.

2. Pyometra is promoted mainly by:

Oestrogen sensitises, progesterone drives glandular secretion and lowers defences.

3. Which species is especially sensitive to oestrogen toxicity?

Cats are highly sensitive to oestrogen-induced marrow toxicity.

4. A known adverse effect of megestrol in cats is:

Progestins have glucocorticoid-like activity and can cause diabetes in cats.

5. Oral 17-alpha-alkylated androgens are notable for:

This chemical modification increases liver toxicity.

6. Why are oestrogens not advised for mismating?

Injectable oestrogens carry a great risk of serious adverse effects.

7. The anabolic effect of these drugs is mainly:

They increase protein synthesis and nitrogen retention.

8. Why are hormonal growth promoters controversial?

Residue and public health concerns drive regulation, and rules differ between countries.

9. Prolonged progestin use may cause which uterine change?

Progestins stimulate endometrial glands, creating a setting for infection.

10. Before advising hormone use in a dairy cow in India, you should:

Regulations and MRLs change and must be checked.

Key points to revise

1. Sex steroids act through intracellular receptors and change gene expression.
2. Oestrogens can cause bone marrow suppression, pyometra and hepatotoxicity.
3. Cats are very sensitive to oestrogen toxicity.

4. Progestins predispose to cystic endometrial hyperplasia and pyometra.
5. Progestins can cause mammary disease, diabetes in cats and adrenal suppression.
6. Androgens and anabolics can be hepatotoxic and alter behaviour.
7. Hormonal growth promoters are restricted or banned in many countries.
8. Misuse in sport, show or food animals has legal, ethical and welfare consequences.

Go deeper on this site

- Ch 31. Calcium, phosphorus, vitamin D and bone drugs (in this book)
- Ch 29. Adrenal hormones and the glucocorticoid axis (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Prevention or termination of pregnancy in bitches and queens
- Merck Veterinary Manual: Hormonal treatment for integumentary disease in animals
- Merck Veterinary Manual: Hormonal control of the estrous cycle in dogs

CHAPTER 31 OF 33

Calcium, phosphorus, vitamin D and bone drugs

How parathyroid hormone, vitamin D and calcitonin hold blood calcium steady, and how calcium salts, vitamin D analogues and bisphosphonates are used. The chapter explains the treatment concepts for milk fever in cows and eclampsia in bitches.

After this chapter you can

- Explain how PTH, vitamin D and calcitonin regulate calcium and phosphorus
- Describe the activation steps of vitamin D and the therapeutic use of its analogues
- Explain how bisphosphonates work and where they are used in animals
- Describe the treatment principles and safety rules of intravenous calcium in milk fever

- Explain how prepartum diet prevents hypocalcaemia in dairy cows

Calcium balance in outline

Calcium is needed for nerve conduction, muscle contraction, clotting and bone strength. Blood ionised calcium is held in a narrow range, because even small falls cause tremor, weakness and seizures, and rises cause weakness, polyuria and kidney damage. Three organs defend the level: bone (the store), the intestine (absorption) and the kidney (excretion and activation of vitamin D).

Phosphorus moves in the opposite direction of calcium in many controls. Raised blood phosphate drives calcium down, and the body also tries to remove excess phosphate through the kidney. This is why kidney failure upsets calcium and phosphorus together.

Three hormones do the work: **parathyroid hormone** (PTH), **calcitriol** (active vitamin D) and **calcitonin**.

Parathyroid hormone and calcitonin

PTH is released from the parathyroid glands when ionised calcium falls. It raises blood calcium in three ways: it increases bone resorption, it increases calcium reabsorption in the distal kidney tubule while promoting phosphate loss in urine, and it stimulates the kidney enzyme 1-alpha hydroxylase to make calcitriol, which then raises intestinal calcium absorption.

PTH is a hormone for minute-to-minute and day-to-day defence of calcium. Continuous excess, as in primary hyperparathyroidism or renal secondary hyperparathyroidism, causes bone loss. This distinction matters in therapy: in humans, intermittent PTH analogues can build bone, but they are not standard veterinary drugs.

Calcitonin comes from the C cells of the thyroid and lowers calcium by inhibiting osteoclasts. Its physiological role in adult animals is minor, and its clinical use in veterinary medicine is limited. Calcitonin has a possible role in cows during early lactation, though it is not the main defence in milk fever, where PTH and vitamin D response matter more.

Vitamin D and its analogues

Vitamin D is a hormone precursor. Cholecalciferol (D3) comes from the skin by sunlight in many species, or from the diet. The liver adds a hydroxyl group to make 25-hydroxyvitamin D, the storage form. The kidney then adds a second hydroxyl group through 1-alpha hydroxylase to make **calcitriol**, the active hormone. This last step is controlled by PTH, low calcium and low phosphate.

Calcitriol acts on nuclear receptors and increases intestinal absorption of calcium and phosphate, supports bone mineralisation and helps PTH action. Dogs and cats make little vitamin D in the skin and depend on the diet.

Therapeutic uses include:

- **Calcitriol** for hypoparathyroidism (with calcium) and sometimes in chronic kidney disease to reduce secondary hyperparathyroidism.
- Dietary vitamin D to prevent rickets in growing animals and osteomalacia in adults.

Toxicity is important. Excess vitamin D causes hypercalcaemia, mineralisation of soft tissues including the kidney, and kidney failure. In dogs, a frequent cause is ingestion of cholecalciferol-based rodenticides or human vitamin D skin creams such as calcipotriol, so owners should be asked about household products.

Bisphosphonates

Bisphosphonates are stable analogues of pyrophosphate that bind strongly to bone mineral at sites of active remodelling. When an osteoclast resorbs this bone, it takes in the drug. Nitrogen-containing agents such as pamidronate, zoledronate and alendronate inhibit an enzyme (farnesyl pyrophosphate synthase) needed for osteoclast function, which causes the cell to lose activity or die.

The result is reduced bone resorption and a lower blood calcium. Uses in animals include:

- Hypercalcaemia of malignancy and other causes of severe hypercalcaemia, usually given by slow intravenous infusion with fluids.
- Pain from bone tumours in dogs, as part of a wider plan.
- Bone-related disease in horses, such as navicular disease, with tiludronate approved in some countries. Check the product status locally.

Oral absorption is poor and the drugs irritate the oesophagus, so oral forms need care. They are excreted by the kidney, so kidney function should be considered. Rare risks include low blood calcium and jaw bone necrosis with long use. Their effects persist for long periods because they stay in bone.

Milk fever and intravenous calcium

Milk fever (parturient paresis) is a fall in blood calcium in dairy cows around calving. A sudden demand for calcium in colostrum and milk exceeds the supply, and the cow's PTH and vitamin D response has not yet risen. Signs progress from restlessness and tremor to inability to rise, cold extremities, a weak pulse, a cow lying with her head turned to the flank, and eventually coma.

Treatment is calcium given by intravenous injection, using calcium borogluconate or similar salts. Many products also contain magnesium and phosphorus, which helps when those minerals are also low. The key safety rules are:

- Give the solution **slowly** and listen to the heart. Rapid injection can cause arrhythmia, bradycardia and cardiac arrest. If the rhythm changes, stop the infusion.
- Keep the solution warm and avoid leakage around the vein, which causes severe tissue damage. Subcutaneous routes are used for some products, with attention to local reactions.
- Expect relapse in some cows, and do not assume that the cow that stood up is cured.
- A cow that does not respond may have low phosphorus or magnesium, mastitis, or muscle damage from lying, and needs reassessment.

Prevention relies on diet. A low calcium diet before calving prompts the cow to mobilise bone calcium in advance. Alternatively, a diet with a negative dietary cation-anion difference, using anionic salts, makes the blood slightly acidic and increases PTH effectiveness. Both need feed analysis, since high potassium forages raise the risk.

Similar treatment principles apply to **eclampsia** in lactating bitches, where calcium is given slowly with monitoring of heart rhythm, and puppies are weaned or supplemented. In bitches the main cause is high milk calcium loss, not a fall in

dietary calcium before whelping, and calcium supplementation during pregnancy is generally discouraged.

Phosphate binders and avoiding errors

In chronic kidney disease, phosphate builds up, which lowers calcium and stimulates PTH. Dietary phosphate restriction is the first step. If needed, oral phosphate binders such as aluminium hydroxide, calcium carbonate or lanthanum are mixed with food to bind phosphate in the gut. Aluminium products carry a toxicity concern in long-term use, and calcium products can raise blood calcium.

Common errors to avoid:

- Treating a low total calcium without considering albumin or ionised calcium.
- Giving calcium and vitamin D together without monitoring, which risks hypercalcaemia.
- Giving rapid intravenous calcium to a cow because she is critically ill.
- Giving calcium to an animal that is already hypercalcaemic.

Treatment of mild hypercalcaemia centres on the cause, intravenous fluids and stopping contributing drugs. Bisphosphonates and other options come later.

Concept cleared

Concept cleared: Why milk fever happens
Think of a bank account where a huge withdrawal (colostrum) is made suddenly while deposits (PTH and vitamin D response) have not yet been set up. The balance drops before the system adapts.

Concept cleared: Why low-calcium dry cow diets prevent it
A cow fed little calcium before calving is already forced to run her PTH system hard, so when milk demand begins her bone and gut mechanisms are ready.

Concept cleared: Why rapid calcium is dangerous

Calcium raises heart muscle excitability and contractility. A sudden surge can push the heart into abnormal rhythm or stop it in systole, so the injection must be slow.

Concept cleared: Bisphosphonates stick to bone

They are like glue that coats the bone surface where osteoclasts are working. The osteoclast eats the coated bone and is poisoned, so resorption stops.

Memory aid: Remembering the calcium trio

PTH pulls calcium UP from bone, kidney and gut (via D). Calcitonin takes it DOWN, 'tone it down'. For calcium injections remember: Slow and Listen, because fast calcium stops the heart.

Compare and contrast

Calcium-regulating hormones

Hormone	Source	Trigger	Net effect on blood calcium
PTH	Parathyroid gland	Low calcium	Raises it: bone, kidney, activates vitamin D
Calcitriol	Kidney (from vitamin D)	PTH, low phosphate	Raises it: gut absorption
Calcitonin	Thyroid C cells	High calcium	Lowers it: inhibits osteoclasts

Drugs for calcium and bone disorders

Drug	Mechanism	Main use	Key caution
Calcium borogluconate	Replaces calcium	Milk fever, eclampsia	Give slowly with cardiac monitoring
Calcitriol	Active vitamin D	Hypoparathyroidism, renal hyperparathyroidism	Hypercalcaemia
Bisphosphonates	Inhibit osteoclasts	Hypercalcaemia, bone pain	Renal excretion, oesophagitis
Phosphate binders	Bind dietary phosphate	Chronic kidney disease	Aluminium toxicity, hypercalcaemia

Species notes

Cattle

Milk fever occurs in high-yielding dairy cows soon after calving, and treatment is slow intravenous calcium with heart monitoring. Prevention uses prepartum diet management.

Buffalo

Hypocalcaemia is reported in dairy buffalo around calving, and the same treatment principles apply. Practical feeding in India often relies on locally available forages, so mineral content should be checked.

Dog

Eclampsia occurs in lactating bitches, especially small breeds with large litters. Calcium is given slowly with monitoring, and puppies are fed separately. Cholecalciferol rodenticides cause severe hypercalcaemia and kidney injury.

Cat

Cats can develop hypocalcaemia after thyroidectomy through parathyroid injury. Dietary vitamin D is essential. Check ionised calcium after surgery.

Horse

Lactation tetany can occur in mares, usually with stress or transport. Tiludronate is used for some bone

conditions in countries where it is approved.

Clinical pearls

Self-test: 10 questions

1. Which organ activates vitamin D to calcitriol?

The kidney 1-alpha hydroxylase makes calcitriol. The liver makes 25-hydroxyvitamin D.

2. Which of the following is a PTH action?

PTH increases phosphate excretion and calcium reabsorption and stimulates vitamin D activation.

3. The main danger of rapid intravenous calcium is:

Rapid calcium excites the myocardium and can cause bradycardia, arrhythmia or arrest.

4. Bisphosphonates act by:

They bind to bone and impair osteoclast function.

5. A negative DCAD diet before calving helps prevent milk fever by:

Mild metabolic acidosis increases tissue response to PTH.

6. Which cause of hypercalcaemia is typical in dogs?

Cholecalciferol and calcipotriol cause severe vitamin D toxicity.

7. Calcitonin is produced by:

Calcitonin comes from thyroid C (parafollicular) cells.

8. A cow with milk fever stands after treatment and then relapses. What is the best interpretation?

Relapse occurs in some cows, and other minerals or complications may be involved.

9. Which agent is used to lower raised blood phosphate in chronic kidney disease?

Oral phosphate binders reduce intestinal phosphate absorption.

10. In bitches, which is generally discouraged to prevent eclampsia?

Supplementing calcium in pregnancy can suppress parathyroid response and increase risk.

Key points to revise

1. PTH raises blood calcium by acting on bone and kidney and by activating vitamin D.
2. Calcitriol is made by 1-alpha hydroxylation in the kidney and raises intestinal calcium absorption.
3. Calcitonin lowers calcium by inhibiting osteoclasts, but plays a minor role in adults.
4. Bisphosphonates inhibit osteoclasts and treat hypercalcaemia and bone pain.
5. Milk fever is treated with slow intravenous calcium, with the heart monitored.
6. Prepartum low calcium or negative DCAD diets help prevent milk fever.
7. Eclampsia in bitches is treated with slow calcium and puppies are removed from nursing.
8. Phosphate binders are used in chronic kidney disease along with dietary restriction.

Go deeper on this site

- Ch 32. Drugs in reproduction (in this book)
- Ch 30. Sex hormones, anabolics and growth promoters (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Parturient paresis (milk fever) in cows
- Merck Veterinary Manual: Hypocalcemia in small animals
- University of Minnesota Libraries: Principles of Pharmacology

CHAPTER 32 OF 33

Drugs in reproduction

How hormones and related drugs are used to time oestrus, support or end pregnancy, control uterine activity and lactation, and treat infertility. The chapter links each drug class to the physiology it borrows.

After this chapter you can

- Explain the physiological basis of oestrus synchronisation with prostaglandins, progestogens and GnRH
- Distinguish uterotonics, abortifacients and tocolytics by mechanism and clinical purpose
- Describe how lactation is stimulated or suppressed pharmacologically
- Outline drug approaches to common infertility problems
- State the main cautions and species differences in reproductive drug use

Why reproductive drugs work

Reproduction is run by a hormone chain: the hypothalamus releases GnRH, the pituitary releases FSH and LH, the ovary makes oestrogen and progesterone, and the uterus releases prostaglandin F2-alpha (PGF2a) when the cycle must end. Reproductive drugs copy, block or time one link of this chain.

If you can draw the chain, you can predict the drug. A drug that mimics GnRH pushes LH release. A drug that mimics PGF2a destroys a functional corpus luteum. A drug that mimics progesterone holds the animal in the luteal phase. Most exam questions are really questions about this chain.

A second idea is timing. The same drug can be useful or useless depending on the day of the cycle or the stage of gestation, so always ask where the animal is in the cycle before choosing a drug.

Oestrus synchronisation

The aim is to bring many females into oestrus, or ovulation, at a predictable time so that artificial insemination can be planned. There are two basic strategies.

- **Shorten the luteal phase.** PGF2a and its analogues cause regression of the corpus luteum (luteolysis). Progesterone then falls and the animal returns to oestrus after a few days. The key limitation is that it works only when a mature, functional corpus luteum is present. In a cow in the early days after ovulation, or one that is not cycling, it does nothing.
- **Extend the luteal phase artificially.** Progestogens given as intravaginal devices, implants or feed additives hold the animal under progesterone. When the source is withdrawn, the animals come into heat together.
- **Control follicular waves.** GnRH given at the start of a protocol makes a new follicular wave emerge by causing ovulation or luteinisation of the dominant follicle. A later PGF2a injection removes the corpus luteum, and a second GnRH synchronises the ovulation. Protocols of this type are called fixed-time AI programmes, with Ovsynch as the best-known example.

Equine chorionic gonadotropin (eCG) is often added in anoestrous animals because it has FSH-like and LH-like activity and stimulates follicle growth. In small ruminants, progestogen sponges with eCG are widely used to bring out-of-season animals into breeding.

Common confusion: PGF2a does not induce oestrus by acting on the ovary directly as a stimulant; it removes the progesterone brake. Also, PGF2a is of no use for synchronisation in the bitch, because the dog has a different luteal control system.

Uterotonics

Uterotonics increase uterine contraction. The main drugs are **oxytocin**, **ergot alkaloids** such as ergometrine, and **prostaglandins**.

Oxytocin acts on oxytocin receptors in the myometrium, which increase in number near term. This is why the same drug is weak in early gestation but powerful at parturition. It is used to hasten delivery in uterine inertia, to expel retained fetal membranes or uterine contents, to control postpartum haemorrhage and to help milk let-down.

The most important safety rule is to **exclude obstruction first**. If the fetus is malpositioned or the pelvis is too narrow, a uterotonic can rupture the uterus. Oxytocin is also less effective if the animal is hypocalcaemic, because calcium is needed for muscle contraction. In bitches with weak labour, calcium is often considered together with oxytocin.

Ergot alkaloids give sustained contraction, so they are used only after the fetus and placenta are out. Their sustained tone would trap a fetus if given earlier.

Prostaglandins also contract the uterus, which is why they help empty the uterus in pyometra and retained contents. Do not confuse this with the milk let-down action of oxytocin.

Abortifacients and pregnancy termination

Abortifacients end an unwanted pregnancy, for example in mis-mating, or empty the uterus in disease. The mechanisms differ.

- **PGF2a** is luteolytic, and in species where the corpus luteum maintains pregnancy it ends gestation. This applies strongly to cattle in the first half and to mares in early pregnancy. In the later stages of cattle pregnancy the placenta also makes progesterone, so effects vary with stage.
- **Glucocorticoids** such as dexamethasone can trigger abortion or parturition in late-gestation cattle because they mimic the fetal cortisol signal that begins normal birth.
- **Progesterone receptor blockers** such as aglepristone terminate pregnancy in bitches by removing progesterone action.
- **Dopamine agonists** such as cabergoline lower prolactin, which supports the corpus luteum in the bitch, and are used for termination alone or combined with

a prostaglandin.

Prostaglandins can cause vomiting, salivation, diarrhoea and abdominal discomfort, especially in dogs and cats. They must also be handled carefully by pregnant women and by people with asthma, because skin absorption can cause effects.

Tocolytics and holding pregnancy

A **tocolytic** relaxes the uterus or reduces its contraction. Beta-2 agonists such as clenbuterol and terbutaline relax uterine smooth muscle through cAMP-mediated pathways. In practice they are used to relax the uterus before obstetric manipulation or caesarean preparation in cattle and horses. They are not used to hold a normal pregnancy for long.

For maintaining pregnancy in mares with placentitis or a threatened loss, a synthetic progestogen such as altrenogest is used to support progesterone activity. The benefit comes only when the cause of progesterone failure is understood; extra progesterone does not cure infection.

Side effects of beta agonists include tachycardia and tremor. Because clenbuterol is also a misused growth promoter in food animals, it is a drug where legal status must always be checked before use. This is discussed in the next chapter.

Lactation control and infertility concepts

Stimulating milk. Oxytocin causes milk ejection by contracting the myoepithelial cells, not by making more milk. Prolactin, in turn, drives milk synthesis. Dopamine antagonists such as domperidone raise prolactin and are sometimes used to promote milk in dams.

Suppressing milk. Dopamine agonists (cabergoline, bromocriptine) inhibit pituitary prolactin release. They are used in false pregnancy of the bitch and after weaning to dry off a bitch or queen. Bromocriptine has more vomiting than cabergoline.

Infertility. Treat the cause, not the symptom. Common concepts follow.

- Anoestrus due to a persistent corpus luteum or pyometra: PGF2a to remove luteal tissue.
- Follicular cysts: GnRH or hCG to induce luteinisation and ovulation.

- Luteal insufficiency: progesterone support, or GnRH after insemination to improve luteal function.
- Delayed ovulation in mares: hCG or a GnRH agonist to time ovulation.
- Pyometra in the bitch: PGF2a or aglepristone with antibiotics, only where the cervix is open and the animal is stable, because spillage of pus is a serious risk.

Always combine drugs with good management. Nutrition, body condition, heat detection and uterine infection matter more than any injection.

Concept cleared

Luteolysis needs a corpus luteum
PGF2a analogues act only when a mature functional corpus luteum exists. If there is none, there is nothing to lyse.

Receptor density decides response
Myometrial oxytocin receptors rise near term, so the same oxytocin dose has little effect early in pregnancy and a strong effect at parturition.

Remove the brake or press the pedal
Synchronisation either removes progesterone (PGF2a, progestogen withdrawal) or stimulates the cascade (GnRH, eCG, hCG). Knowing which one is used explains the protocol.

Oxytocin ejects milk but does not make it
Milk synthesis depends on prolactin; oxytocin only triggers let-down. Prolactin is controlled by dopamine, which is why dopamine agonists dry off milk.

Memory aid: Reproductive drug triad: G-P-O
GnRH starts the chain, Prostaglandin ends the luteal phase, Oxytocin empties the uterus and milk gland. Check the chain order when you are unsure which drug fits.

Compare and contrast

Uterotonics compared

Drug	Main action	Typical use	Key caution
Oxytocin	Rhythmic myometrial contraction, milk ejection	Uterine inertia, retained membranes, let-down	Exclude obstruction; check calcium
Ergometrine	Sustained contraction	After placenta is delivered, haemorrhage	Never before fetal delivery
PGF2a	Luteolysis and contraction	Pyometra, abortion, synchronisation	Adverse effects in dogs; handler safety

Synchronisation approaches

Approach	Example drugs	How it works	Limitation
Luteolytic	PGF2a, cloprostenol	Destroys corpus luteum	Needs functional corpus luteum
Progestogen	Intravaginal device, altrenogest	Holds luteal phase, then withdrawal	Needs device or feeding for days
GnRH based	GnRH, Ovsynch	Controls follicular wave and ovulation	Needs strict timing

Species notes

Cattle
Prostaglandin and GnRH based fixed-time AI programmes are central to dairy herd reproduction. Dexamethasone can induce late-gestation abortion or parturition.

Horses
PGF2a is used to shorten dioestrus, hCG or GnRH agonists to time ovulation, and altrenogest to suppress oestrus or support pregnancy.

Dogs and cats
The bitch does not respond to PGF2a for simple synchronisation.

Sheep and goats
Progestogen sponges with eCG are used to bring ewes and does into

Cabergoline and aglepristone are the key concept drugs, and prostaglandin side effects are marked.

breeding outside the natural season.

Buffalo

Buffaloes show weak oestrus signs and seasonal anoestrus, so synchronisation with fixed-time AI is of special practical interest; response depends on nutrition and season.

Clinical pearls

Self-test: 10 questions

1. A PGF2a analogue will induce oestrus in a cow only if she has:

PGF2a acts by luteolysis, so a mature functional corpus luteum is required.

2. Which drug is a progesterone receptor blocker used to terminate pregnancy in bitches?

Aglepristone blocks progesterone receptors.

3. Before giving oxytocin to a bitch with delayed labour, the most important step is to:

Uterotonics can rupture the uterus if there is obstruction.

4. Ergot alkaloids should be used:

Sustained contraction would trap the fetus.

5. Oxytocin helps lactation by:

Oxytocin causes let-down, not synthesis.

6. Cabergoline is used to suppress lactation because it:

Dopamine inhibits prolactin release.

7. In Ovsynch type programmes the first GnRH injection mainly:

It induces ovulation or luteinisation of the dominant follicle.

8. eCG is added to progestogen protocols in anoestrous animals because it:

It stimulates follicular growth.

9. Which agent can be used as a tocolytic before obstetric manipulation?

Beta-2 agonists relax uterine smooth muscle.

10. Which statement about prostaglandin handling is correct?

Skin absorption can cause effects in these people.

Key points to revise

1. Reproductive drugs copy, block or time the GnRH-FSH/LH-steroid-prostaglandin chain.
2. PGF2a needs a functional corpus luteum.
3. Progestogen withdrawal brings animals into heat together.

4. GnRH based protocols time follicular waves and ovulation.
5. Oxytocin is a uterotonic and milk ejection drug; obstruction must be excluded.
6. Ergot alkaloids are used only after delivery.
7. Abortifacient choice depends on species and pregnancy stage.
8. Dopamine agonists suppress prolactin and milk.

Go deeper on this site

- Ch 33. Hormone misuse and Indian regulation (in this book)
- Ch 31. Calcium, phosphorus, vitamin D and bone drugs (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual
- Food Safety and Standards Authority of India (FSSAI)
- Codex Alimentarius (FAO/WHO)

CHAPTER 33 OF 33

Hormone misuse and Indian regulation

Why hormones such as oxytocin and anabolic agents are misused in animals, what harm this does to animals and to food safety, and how residues and legal controls are approached. Regulatory details change often, so students must check current notifications.

After this chapter you can

- Explain why oxytocin is misused in dairy animals and the harm to animals
- Describe illegal use of anabolic agents and growth promoters in food animals
- Explain how milk and meat residues arise and what withdrawal periods and MRLs mean
- State the role of regulators and the reporting route in broad terms
- Describe the veterinarian's professional responsibility

The problem in perspective

Hormones are legitimate and valuable drugs. The problem is not the molecule but the use: giving a drug to change production or appearance of a healthy animal, without a diagnosis, outside the legal route, or without respecting withdrawal times.

This chapter explains the concepts. Laws, bans and limits in India are revised by notification, so all regulatory statements here are general. **Always check the current notification** from the competent authority before you advise or act.

Three questions help in every case. Is there a diagnosis? Is the drug being used by a lawful route? Will the animal's milk or meat enter the food chain before residues have fallen?

Oxytocin misuse in dairy animals

Oxytocin triggers milk let-down. Some dairy keepers inject it routinely to draw out more milk quickly, or to make a buffalo or cow release milk without her calf. This is a misuse of a drug whose real indications are obstetric.

The harms are concrete.

- **Animal welfare.** Repeated injections are painful and stressful. Animals can become dependent on the injection for let-down, a learned and hormonal response that makes hand milking without the injection difficult.
- **Reproduction.** Chronic exposure is thought to disturb the reproductive cycle and may contribute to fertility problems. The strength of evidence differs among reports.
- **Udder health.** Forced emptying can raise the risk of teat and udder injury and cause incomplete milk let-down in the long term.
- **Human health.** Oxytocin given to milking animals is not the main concern for the consumer, because it is a peptide broken down in the gut; the larger concern is the pattern of unsupervised drug use and its hygiene. Do not overstate residue risk from oxytocin itself.

India has restricted the manufacture, sale and supply of oxytocin through drug-control notifications and court proceedings in recent years, with controls on who may produce and distribute it. The details, including any veterinary provisions, have changed over time, so check the current notification.

A practical approach for the veterinarian is to treat the underlying reason for poor let-down, such as stress, pain, an unfamiliar milker or a missing calf, and to teach calm milking routines. Teat preparation and a short, consistent routine stimulate the animal's own oxytocin release.

Illegal anabolics and growth promoters

Growth promoters are drugs that increase weight gain or leanness. In some countries certain anabolic hormones are permitted under regulation for beef production; in others they are banned. For students, the key points are these.

- **Anabolic steroids** (androgenic, oestrogenic and similar compounds) and **beta-agonists such as clenbuterol** may be abused to improve carcass leanness or growth.
- **Stilbenes** such as diethylstilbestrol were once used as growth promoters, but they are carcinogenic and are widely banned in food animals.
- In India, use of hormonal growth promoters in food animals is controlled under drug and food laws; check the current notification for what is prohibited.
- Because of safety concerns, use of drugs on **extra-label or growth-promotion grounds** in food animals is professionally unacceptable.

Use in companion animals and in sport animals raises separate issues, such as doping control in racing horses, where banned substances and testing rules apply.

Hormones used in sport or in companion animals are not exempt from rules. A veterinarian should know whether a drug is permitted for the species and purpose, and should never supply a drug when the stated purpose is growth promotion in food animals.

How residues arise

A **residue** is the drug or its metabolites that remain in edible tissue, milk or eggs after treatment. Residues depend on dose, route, formulation, animal age, liver and kidney function, and time since treatment. Milk is a special route because many drugs are secreted into it, and milk is consumed daily by the very young and the sick.

Two terms are essential.

- **Withdrawal period (withholding time)**: the minimum time between the last dose and slaughter, or the use of milk or eggs, so that residues fall to a safe level.
- **Maximum residue limit (MRL)**: the highest concentration of a residue legally accepted in a food, set from toxicology and exposure data. International reference values are developed under Codex, and national authorities set their own limits.

Withdrawal times given on a label apply to the licensed dose and route. Extra-label use, higher dose or longer treatment can make the label time unsafe, which is why the veterinarian must advise a longer period when required.

Some substances have no safe level at all and cannot be used in food animals. For these, regulators set zero tolerance or ban use.

Milk from treated animals must also be kept out of the supply for calves that will later be sold for meat. Mixed bulk milk can dilute a residue, but dilution is never an acceptable plan for handling treated animals.

Detection, enforcement and reporting

In India, food safety limits and testing are the responsibility of the food safety regulator, the Food Safety and Standards Authority of India (FSSAI), with state food authorities. Drug licensing and sale are governed by drug-control authorities. Animal husbandry departments and veterinary councils play their own roles.

Residue monitoring uses laboratory methods such as chromatographic and immunoassay screening. Positive samples can lead to action against the producer or supplier.

If you find or suspect illegal hormone use, the broad route is as follows. Details of the competent office differ by state, so confirm locally.

1. Record what you saw: animal, product, drug, source, dates and persons involved.
2. Do not sell or supply the milk or meat from treated animals during withdrawal.
3. Report to the local authority as required, which may include the state animal husbandry department, the drug controller or the food safety officer.
4. Keep copies of records and follow your professional council's code.

Check the current notification for the correct reporting channel and forms.

Good records make tracing possible: animal identity, drug, batch, dose, route, date and the withdrawal end date. Without records neither the farmer nor the veterinarian can show compliance.

The veterinarian's responsibility

The veterinarian is the gatekeeper. Prescribing only for a diagnosed condition, keeping treatment records, giving clear withdrawal advice in writing and refusing to supply drugs for production enhancement protect animals, farmers and consumers.

Education of farmers is as important as enforcement. Many farmers use oxytocin because they believe it is necessary; showing safe milking practice and calf-at-foot stimulation reduces the demand.

Finally, remember that law follows science and politics, so it changes. Reading the current notification is a professional habit, not a one-time task.

Concept cleared

Use, not molecule, is the issue
The same hormone is a drug in disease and a misuse in a healthy animal. Indication, route and record keeping decide legality and ethics.

Withdrawal period
The label time only protects consumers when the licensed dose and route are followed.

MRL
A maximum residue limit is a science-based legal ceiling, and zero tolerance applies to substances with no safe level.

Verify the notification
Indian orders on hormones change. State the principle and look up the current notification.

Memory aid: D-R-W-R

Diagnose, Record, Withdrawal advice, Report. Four duties of a veterinarian handling hormones in food animals.

Compare and contrast

Legitimate versus misuse

Drug	Legitimate use	Misuse
Oxytocin	Obstetric indications and defined clinical needs	Routine injection to force milk let-down
Anabolic steroid	Defined therapy where lawful	Growth promotion in food animals
Clenbuterol	Bronchodilator or tocolytic where permitted	Leanness enhancer in meat animals

Withdrawal period and MRL

Term	Meaning	Who sets it
Withdrawal period	Time to wait before milk or meat use	Label, regulator and veterinarian advice
MRL	Maximum residue concentration allowed in food	Regulators, with Codex as an international reference

Species notes

Cattle

Oxytocin misuse is a welfare and herd reproduction issue, and milk withdrawal periods apply to any treatment.

Buffalo

Buffalo milk letdown is strongly linked to the calf and handling, and this is a common setting for oxytocin misuse; check local control orders.

Sheep and goats

Poultry

Treated animals entering the meat chain need withdrawal respect; hormonal growth promotion is not acceptable.

Hormone use for growth is not an accepted practice, and residue concern extends to eggs and meat; check current rules.

Horses
Racing and sport horses fall under doping control, a separate regulatory field from food safety.

Clinical pearls

Self-test: 10 questions

1. The main reason oxytocin is misused in dairy animals is to:

It triggers milk ejection.

2. A withdrawal period is:

It allows residues to fall to safe levels.

3. An MRL is:

It is a ceiling concentration.

4. Which class is banned widely as a carcinogenic growth promoter?

Diethylstilbestrol is a stilbene.

5. Clenbuterol misuse in food animals aims at:

It is a beta agonist used as repartitioning agent.

6. Which statement about Indian regulation is most appropriate?

Rules are revised by notification.

7. Which body is the national food safety regulator?

FSSAI sets food safety standards.

8. Extra-label higher dose in a dairy cow means the label withdrawal time is:

The veterinarian must advise a longer period.

9. A harm of repeated oxytocin injection includes:

Animals can come to depend on injection for let-down.

10. On suspecting illegal hormone use, a veterinarian should first:

Documentation and reporting are the duties.

Key points to revise

1. Misuse means use without diagnosis, outside the legal route or ignoring withdrawal.
2. Oxytocin misuse harms welfare, udder and fertility.
3. Clenbuterol and anabolic agents are abused as growth promoters.
4. Residues depend on dose, route, species and time.
5. Withdrawal periods protect consumers.
6. MRLs are legal ceilings; some substances have zero tolerance.
7. FSSAI and drug control authorities have different roles.
8. The veterinarian keeps records, advises, and reports.

Go deeper on this site

- Ch 32. Drugs in reproduction (in this book)
- Ch 31. Calcium, phosphorus, vitamin D and bone drugs (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual
- Food Safety and Standards Authority of India (FSSAI)
- Codex Alimentarius (FAO/WHO)

How to use Book 2: a short discussion

Book 1 explained how drugs behave in general. Book 2 applies those ideas to the drugs themselves, organised the way the body is organised: nerves, brain, inflammation, heart and blood vessels, blood and kidney, lungs and gut, and finally hormones and reproduction. Learning drugs by body system is the method most veterinary colleges follow, because a drug is easiest to remember when you know the organ it acts on and the problem it is used to solve.

Why the autonomic chapters come first

The first five chapters cover the autonomic nervous system and the drugs that mimic or block it. They are the key to the whole book. Atropine, neostigmine, adrenaline, the alpha-2 sedatives and the muscle relaxants all work by changing the signals carried by acetylcholine and noradrenaline. If you understand which receptor sits in which organ, you can predict the effect of a drug you have never met, and you can also predict its side effects. Students who skip these chapters usually find the cardiovascular, respiratory and gut chapters harder than they need to be.

Three questions for every drug

Each chapter is built around three questions. What does the drug do at the cell or receptor level? What does that mean for the animal in front of you? And what changes between species? The third question matters more in veterinary medicine than in human medicine. A drug that is routine in a dog can be dangerous in a cat, and a medicine that is safe in a cow may leave residues in milk. The Species section of each chapter collects those differences in one place so that you do not have to hunt for them.

Concepts, not dose tables

You will not find dose tables in this book. Doses change with the product, the formulation and the country, and a number copied from a study book is a poor guide at the bedside. Instead the book explains the reasoning that sits behind a dose: why a drug needs a loading phase, why a narrow safety margin demands monitoring, why a long half-life makes accumulation likely. For actual doses use the product label, a current formulary or a clinical pharmacologist. Statements about Indian regulation are marked with a reminder to check the current notification, because notifications and bans change.

A study plan that works

Read the Learn section once for the story, then move to Concepts and Compare, which turn the story into a few clear ideas and side-by-side tables. Take the quiz before you read the Revise points, not after. Getting a question wrong and reading the explanation teaches more than getting it right by guessing. Return to a chapter after a week and repeat the quiz; the progress bar at the top of the book records which chapters you have already tested on this device.

Many chapters link onward to related chapters and to other guides on this site, such as the veterinary drugs list, the Drug Index and the dose calculation guide. Following those links is the quickest way to connect a mechanism to a real product and a real case. Book 3 continues the series with chemotherapy: antibacterials, antiparasitic drugs, antifungals, anticancer drugs and the stewardship ideas that protect them.

If you are preparing for an examination, use the search box above the chapter list to jump to a term, then read the chapter around it so the term stays attached to its

mechanism. Short revision sessions of one chapter a day, each ending with the quiz, are far more effective than a single long session before the paper.

This material is written for education. It does not replace the judgement of a registered veterinarian, and it must not be used to treat an animal without professional advice.

BVSC & AH STUDY BOOK 3 OF 7

Chemotherapy: Antimicrobial, Antiparasitic and Anticancer Drugs

Nineteen chapters on the drugs that kill or control microbes, parasites and cancer cells, together with resistance, residues and food safety. Each chapter explains the mechanism, the clinical meaning and the species cautions, and ends with a 10-question self-test.

19 chapters | **190** practice questions | **No** dose tables

By Dr. Rameez Bloch, BVSc & AH, MVSc

Start here

Pick a chapter from the list on the left (or the top bar on a phone). Chapters 1 and 9 are the thinking chapters: how to choose an antibiotic and how to protect it. Chapters 2 to 8 cover the antibacterial classes, chapters 10 and 11 cover residues and mastitis, chapters 12 to 16 cover antifungal, antiviral and antiparasitic drugs, and chapters 17 to 19 cover disinfectants, cancer drugs and immune drugs. Each chapter has six parts: Learn, Concepts, Compare, Species, Quiz and Revise. Your quiz progress is saved on this device only.

CHAPTER 1 OF 19

Principles of chemotherapy and antibiotic selection

The reasoning behind choosing an antibacterial drug: spectrum, killing versus inhibiting, the PK/PD indices that predict success, laboratory sensitivity testing, biofilms, combinations and the rules for prophylaxis. It builds the stewardship mindset used in every later chemotherapy chapter.

After this chapter you can

- Define spectrum and explain why narrow spectrum is preferred when the pathogen is known
- Distinguish bactericidal from bacteriostatic action and state when the difference matters
- Explain concentration-dependent and time-dependent killing as PK/PD concepts
- Interpret MIC and disc diffusion results and their limits
- Describe how biofilms, combinations and prophylaxis affect antibiotic choice

Selective toxicity and the logic of choice

Chemotherapy means using chemicals that harm an invader more than the host. This property is called **selective toxicity**. Antibacterials achieve it by attacking structures or pathways that bacteria have and animal cells lack or have in a different form, such as the cell wall, the bacterial ribosome or folate synthesis.

Choosing an antibiotic is therefore a chain of questions. Is there really a bacterial infection? Which organism is likely? Will the drug reach the infected site at a useful concentration? Is the drug safe in this species and this production class? Finally, is the choice defensible in terms of resistance and residues?

A common student error is to start from the drug name. Start from the patient and the site of infection, then work towards the drug.

Spectrum of activity

The **spectrum** is the range of bacteria a drug can act against. A *narrow-spectrum* drug acts on a limited group, for example mainly Gram-positive organisms. A *broad-spectrum* drug acts on many groups, including Gram-positive, Gram-negative and sometimes anaerobes or atypical organisms.

Broad spectrum sounds attractive but has costs. It disturbs the normal flora, particularly in the gut, which can cause diarrhoea, overgrowth of resistant organisms and loss of colonisation resistance. It also exerts selection pressure on many bacterial species at once, so it favours resistance more widely.

The principle is to use the **narrowest spectrum that covers the likely or proven pathogen**. Spectrum is not fixed forever: acquired resistance can remove a species

from a drug's useful spectrum, so a textbook spectrum is only a starting guide.

Gram-negative bacteria have an outer membrane that many large or hydrophilic molecules cannot cross, which is one reason some Gram-positive-active drugs fail against them.

Bactericidal and bacteriostatic action

A **bactericidal** drug kills bacteria. A **bacteriostatic** drug stops multiplication and relies on host defences to clear the organisms. Examples usually placed in the first group are beta-lactams and aminoglycosides; in the second, tetracyclines and macrolides at ordinary concentrations. Many drugs sit between the two depending on concentration and organism.

The distinction is laboratory-defined, based on the relation between the MIC and the minimum bactericidal concentration. It is a spectrum, not a strict label.

Clinically the difference matters most when host defences are weak: neutropenia, endocarditis, meningitis, severe sepsis or infection in poorly perfused tissue. In such cases a bactericidal drug is preferred. In a healthy animal with a localised infection, a bacteriostatic drug usually works well.

Common confusion: never combine a drug that needs actively dividing bacteria to kill (such as a beta-lactam) with one that halts growth without good reason, since the second may blunt the first. This is a theoretical antagonism that has real support in some infections but is not universal.

Pharmacokinetic and pharmacodynamic principles

Pharmacokinetics describes what the body does to the drug, and **pharmacodynamics** what the drug does to the bacteria. **PK/PD** links the two so that we can predict success.

Antibacterials follow two broad killing patterns:

- **Concentration-dependent killing.** Higher peak concentration relative to MIC gives faster, greater killing. Aminoglycosides and fluoroquinolones are classic examples. The useful indices are peak to MIC and area under the curve to MIC. These drugs often have a post-antibiotic effect, meaning bacterial growth stays suppressed after levels fall.

- **Time-dependent killing.** Killing depends on how long the concentration stays above the MIC, because the effect saturates at a few multiples of MIC. Beta-lactams are the standard example. The useful index is the time above MIC.

This is why dosing schedules differ between classes. We do not need numbers here; the idea is that peak matters for the first group and duration matters for the second.

The drug must also reach the **site of infection**. Fluoroquinolones and macrolides penetrate cells and tissues, while beta-lactams and aminoglycosides stay mostly in extracellular fluid. Pus, necrotic tissue and low oxygen reduce the activity of some drugs, notably aminoglycosides.

Culture, sensitivity, MIC and biofilms

Whenever practical, take a sample *before* starting treatment and send it for **culture and sensitivity**. Poor sampling and prior antibiotic use are the commonest reasons for misleading results.

The **minimum inhibitory concentration (MIC)** is the lowest drug concentration that prevents visible growth in a standard test. A lower MIC means the organism is more susceptible, but MICs of different drugs cannot be compared directly. A result is read against *breakpoints* set by a standards body, giving the categories susceptible, intermediate or resistant. The breakpoint takes into account the drug's achievable concentration, so it is drug-, species- and often site-specific.

In **disc diffusion** (Kirby-Bauer), a disc of drug is placed on an inoculated agar plate. The drug diffuses outward and the diameter of the clear zone around the disc is measured and interpreted against published zone breakpoints. A larger zone is not always a better drug, because diffusion depends on molecular size.

Laboratory sensitivity does not guarantee a cure. Penetration, host immunity and drug toxicity still decide the outcome.

Biofilms are communities of bacteria embedded in a self-made matrix on tissue or devices such as catheters, implants and necrotic bone. Bacteria within are slow-growing, protected from immune cells and far less affected by antibiotics, often needing concentrations many times the standard MIC. Standard tests use free-floating bacteria and so miss this tolerance. Management usually requires removal or debridement of the foreign or dead material, not just a longer drug course.

Combinations and prophylaxis

Single-drug therapy is the default. Combinations are justified for specific reasons:

- Severe infection before the pathogen is known, to widen cover.
- Polymicrobial infection, for example mixed aerobes and anaerobes.
- Synergy, as with a beta-lactam plus an aminoglycoside, or a sulfonamide plus a diaminopyrimidine.
- Delaying resistance, as in tuberculosis in human medicine.

Combinations carry outcomes of *synergy* (greater than the sum), *additivity* or *antagonism*. They also increase toxicity, cost and selection pressure, so they should not be used merely for comfort.

Prophylaxis means giving an antibiotic to prevent infection. It is justified when there is a predictable pathogen, a defined short risk period and proven benefit, for example around certain clean-contaminated or implant surgery, given so that tissue levels are present at the time of contamination. It is not justified as a substitute for hygiene, routine post-operative cover in clean procedures, or to prevent viral disease. Prophylactic or growth-promoting use of antibiotics in herds is a major driver of resistance, and national rules on it change, so check the current notification of the relevant Indian authority.

Finally, follow the stewardship rule: right drug, right dose, right duration, reviewed when culture results return, and stopped when no longer needed. Antibiotics are a shared resource for animal and human health.

Concept cleared

Narrowest effective spectrum
Pick the drug that covers the likely pathogen and no more. Broad spectrum disturbs normal flora and selects resistance widely.

Peak versus time
Concentration-dependent drugs need a high peak relative to MIC; time-dependent drugs need levels above MIC for as long as possible.

In vitro is not in vivo

A susceptible report shows the organism is inhibited in a test, not that the drug reaches the site or that the host will clear the infection.

Biofilm tolerance

Bacteria in biofilms survive concentrations that kill free-floating cells, so source control matters as much as the drug.

Memory aid: Selecting an antibiotic: SPASS

Site of infection, Pathogen likely, Activity (spectrum and killing pattern), Safety in this species, Stewardship and residues. Run through the five before naming a drug.

Compare and contrast

Bactericidal versus bacteriostatic

Feature	Bactericidal	Bacteriostatic
Effect	Kills bacteria	Halts multiplication
Dependence on host defences	Lower	Higher
Typical examples	Beta-lactams, aminoglycosides	Tetracyclines, macrolides (usually)
Preferred when	Immunocompromised, endocarditis, sepsis	Healthy host, localised infection

Concentration-dependent versus time-dependent killing

Feature	Concentration-dependent	Time-dependent
Key driver	High peak relative to MIC	Time above MIC
PK/PD index	Peak/MIC or AUC/MIC	Time above MIC
Post-antibiotic effect	Usually prolonged	Short or absent for most
Examples	Aminoglycosides, fluoroquinolones	Beta-lactams

Species notes

Cattle

Food-producing animal: every choice must consider milk and meat withdrawal and residue rules. Rumen flora can be disturbed by oral antibiotics, so route matters.

Poultry

Flock-level treatment through water or feed makes consistent dosing difficult and favours resistance. Egg residues and withdrawal need attention in layers.

Dogs and cats

Culture is practical and should guide chronic or recurrent infections such as pyoderma and urinary tract infection. Some drug classes are riskier in cats.

Horses

Oral antibiotics can upset hindgut flora and cause colitis, so route and class need care.

Sheep and goats

Small ruminants have few licensed products; extra-label use needs veterinary justification and a cautious withdrawal approach.

Clinical pearls

Self-test: 10 questions

1. Selective toxicity means that a drug:

Antibacterials exploit targets absent or different in host cells.

2. Which is generally a time-dependent antibacterial?

Beta-lactam efficacy tracks time above MIC; aminoglycosides and fluoroquinolones are concentration-dependent.

3. The MIC is best defined as the:

Killing is the MBC, not the MIC.

4. Bactericidal therapy is most preferred in:

When host defences are weak, killing is needed.

5. A drawback of broad-spectrum therapy is:

Broad spectrum disturbs flora and broadens selection pressure.

6. Biofilm infections are difficult to treat mainly because bacteria in them:

Tolerance is a physiological and structural protection.

7. In disc diffusion testing, the result is read from the:

Zone diameter is compared with breakpoints.

8. Which is a legitimate reason for combination therapy?

Combinations need a reason such as spread of cover or synergy.

9. Appropriate prophylaxis is:

Prophylaxis should be targeted and brief.

10. The post-antibiotic effect is usually most notable with:

Concentration-dependent drugs often suppress growth after levels fall.

Key points to revise

1. Selective toxicity means the drug harms bacteria more than the host.
2. Spectrum is the range of organisms a drug acts on; prefer the narrowest that is adequate.
3. Bactericidal drugs kill; bacteriostatic drugs inhibit and need host defences.
4. Concentration-dependent drugs depend on peak to MIC; time-dependent drugs on time above MIC.
5. MIC is the lowest concentration that prevents visible growth and is read against breakpoints.
6. Disc diffusion zone size must be interpreted against standard zone breakpoints.
7. Biofilms are tolerant to antibiotics and usually need source control.
8. Prophylaxis needs a defined risk and a short course; combinations need a clear reason.

Go deeper on this site

- Ch 2. Sulfonamides and diaminopyrimidines (in this book)
- Ch 3. Beta-lactam antibiotics (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- WHO: Antimicrobial resistance fact sheet
- Merck Veterinary Manual: Penicillins
- Merck Veterinary Manual: Cephalosporins and cephamycins

CHAPTER 2 OF 19

Sulfonamides and diaminopyrimidines

Sulfonamides block folate synthesis and diaminopyrimidines block its next step, which is why the combination is synergistic and often bactericidal. The chapter covers resistance, crystalluria, coccidiosis and mastitis uses, and residue concerns.

After this chapter you can

- Explain how sulfonamides and diaminopyrimidines block sequential steps of folate synthesis
- Describe why potentiated sulfonamides show synergy
- Explain the mechanism and prevention of crystalluria
- List uses in coccidiosis and mastitis and the limits of each
- Describe resistance, adverse effects and residue considerations

Why folate is the target

Bacteria and protozoa must make their own folic acid, because they generally cannot take up the finished vitamin. Folate is needed to make thymidine, purines and some amino acids, so without it DNA synthesis stops. Mammals take folate from the diet, so a drug that blocks folate *synthesis* shows **selective toxicity**.

The practical lesson is that these drugs are old, cheap and widely available, which is exactly why they are overused and why resistance is common. Treat them as useful drugs that now need a susceptibility check and a clear indication.

This is the central idea of the chapter: two drug groups block two different steps of the same pathway, and each alone is weak but together they are strong.

Sulfonamides: mechanism and properties

Sulfonamides are structural analogues of **para-aminobenzoic acid (PABA)**. The bacterial enzyme *dihydropteroate synthase* normally joins PABA to a pteridine to form dihydropteroic acid. Sulfonamides compete with PABA for this enzyme and block the step. This is competitive antagonism, so excess PABA, such as that released from pus, necrotic tissue or procaine breakdown, reduces their effect.

Used alone, they are mainly **bacteriostatic**. They have a broad but now unreliable spectrum covering some Gram-positive and Gram-negative bacteria, and some protozoa such as coccidia and Toxoplasma.

The sulfonamide group is large. In practice we sort members by behaviour: *systemic* agents absorbed well and used for infections in tissues, *gut-active* agents that stay in the lumen, and *topical* agents for skin and eye. The behaviour, not the name, tells you the use.

Sulfonamides differ in absorption and excretion. Some are well absorbed and excreted in urine, some are poorly absorbed from the gut and act locally, and some are used topically. They are usually weak acids, widely distributed, and cross into most body fluids including the CSF. Metabolism is mainly by acetylation, with species differences: dogs do not acetylate sulfonamides well, which affects their handling in that species.

Diaminopyrimidines and potentiation

Trimethoprim and related drugs such as ormetoprim and pyrimethamine inhibit **dihydrofolate reductase (DHFR)**, the next enzyme, which converts dihydrofolate to tetrahydrofolate. They are selective because bacterial DHFR is far more sensitive than the mammalian enzyme. Pyrimethamine is used against protozoa.

When a sulfonamide and a diaminopyrimidine are given together, the sequential block makes the effect much greater than either alone: **synergy**, also called potentiation. The combination is often **bactericidal**, has a broader spectrum, and delays resistance. These are called **potentiated sulfonamides**, for example trimethoprim-sulfadiazine and trimethoprim-sulfamethoxazole.

The best synergy occurs when the two components reach the site in an effective ratio, which is a reason to use licensed combinations rather than improvised mixtures. Trimethoprim is lipophilic, widely distributed and a weak base, and it can concentrate in prostate and in tissues, while the sulfonamide partner is a weak acid.

Resistance

Resistance is widespread. Mechanisms include altered dihydropteroate synthase with low affinity for the drug, increased PABA production, and acquired resistant enzymes carried on plasmids. Resistance genes for sulfonamides spread easily and often travel together with those for other classes.

Because resistance is so common, the usual rule is to confirm susceptibility rather than assume it, and to avoid long unsupervised courses in herds or flocks, which select resistant bacteria and resistant coccidia. Mixing feed or water medication also carries a risk of uneven intake by sick animals.

Cross-resistance occurs between members of the sulfonamide group, so a resistant organism is resistant to the whole group. Resistance to trimethoprim arises through resistant DHFR enzymes. The combination retains activity against some organisms resistant to either component, but this advantage is not guaranteed. Bacteria may also bypass the block when pus supplies thymidine, which is another reason these drugs work poorly in abscesses.

Adverse effects and crystalluria

Sulfonamides and their acetylated metabolites may be poorly soluble in acidic urine and can precipitate in the kidney tubules and urinary tract. This is **crystalluria**. It may cause haematuria, tubular damage and obstruction. Risk factors are dehydration, acidic urine, high doses and poorly soluble agents. Prevention is straightforward: keep the animal well hydrated, avoid in dehydrated or oliguric patients, and favour more soluble products or alkaline urine when needed.

Other effects include hypersensitivity reactions, and in dogs, keratoconjunctivitis sicca (dry eye), immune-mediated polyarthritis, and drug fever, particularly with potentiated products, with certain breeds such as Doberman pinschers reported as predisposed. Folate-deficiency effects such as bone marrow suppression can occur with prolonged use or in animals with poor folate status. Trimethoprim combinations may suppress thyroid function in dogs on longer use. Intravenous potentiated sulfonamide given rapidly to horses can cause collapse, so route and rate matter. Cats may be sensitive to some effects.

Uses in coccidiosis and mastitis, and residues

Coccidiosis. Sulfonamides such as sulfaquinoxaline and sulfadimidine act on the asexual stages of *Eimeria*, notably the schizont stage, and work best when given early. Because they are not fully coccidiocidal, host immunity develops while the drug suppresses multiplication. Dosing in water is common in poultry and young ruminants. Whether a sulfonamide is permitted in laying birds varies, and egg residue rules apply; check the current notification.

Mastitis. Sulfonamides and potentiated products have been used for mastitis, mostly by injection. Udder pus and debris blunt their action, resistance is common, and the drug must reach the infected quarter at an effective level, so they are not an automatic first choice. Susceptibility testing and the current label for milk withdrawal guide use. In every case treat mastitis as a herd problem: milking hygiene and dry-cow management matter more than any single drug.

Common confusions. Students often think trimethoprim and sulfonamides compete with each other. They do not: they act on different enzymes in one pathway. Another confusion is that sulfonamides are antimetabolites that harm the host. They do not harm the host folate pathway because the host does not synthesise folate. Finally, *bacteriostatic alone but bactericidal together* is a statement about the combination, not about each component.

Other uses. Potentiated sulfonamides treat a range of respiratory, urinary, enteric and soft-tissue infections and some protozoal infections.

Residues. Sulfonamides are among the residues most often detected in animal products, because of long use and slow clearance at times. Withdrawal periods and maximum residue limits apply; check the current notification and product label for India.

Concept cleared

Sequential block
Sulfonamides stop PABA being used; diaminopyrimidines stop DHFR. Two blocks in one pathway give synergy.

Selective toxicity by dependence

Microbes must synthesise folate while mammals take it from food, so the pathway is safe to attack.

PABA competition

Pus and tissue debris contain PABA and thymidine, weakening the effect of these drugs in abscesses.

Solubility and crystals

Poorly soluble drugs and acidic, concentrated urine lead to crystals, which hydration prevents.

Memory aid: Folate steps: PABA then DHFR

Sulfonamides Stop the first step (PABA to dihydropteroate); Trimethoprim Terminates the Tetrahydrofolate step (DHFR). S for first, T for second.

Compare and contrast

Sulfonamide versus diaminopyrimidine

Feature	Sulfonamide	Diaminopyrimidine
Target enzyme	Dihydropteroate synthase	Dihydrofolate reductase
Mimics	PABA	Folate substrate (inhibitor)
Alone	Bacteriostatic	Bacteriostatic
Examples	Sulfadiazine, sulfadimidine	Trimethoprim, ormetoprim, pyrimethamine

Sulfonamide alone versus potentiated sulfonamide

Feature	Alone	Potentiated
Action	Bacteriostatic	Often bactericidal
Spectrum	Narrower	Broader
Resistance	High	Somewhat delayed
Effect in pus	Poor	Still reduced

Species notes

Dogs

Dry eye, polyarthritis and hypersensitivity are noted with potentiated sulfonamides; dogs acetylate poorly, so crystalluria and effects need monitoring.

Horses

Rapid intravenous potentiated products can cause collapse; oral use can disturb hindgut flora.

Poultry

Used for coccidiosis and some bacterial disease; egg and meat residue rules and toxicity at high water levels are concerns.

Cattle and calves

Used for scours, respiratory disease and coccidiosis; milk and meat withdrawal must be observed.

Cats

May show greater sensitivity to adverse effects; use carefully and with hydration.

Clinical pearls

Self-test: 10 questions

1. Sulfonamides are structural analogues of:

They compete with PABA for dihydropteroate synthase.

2. Trimethoprim inhibits:

DHFR is the second step.

3. Synergy between a sulfonamide and trimethoprim arises from:

Two different steps are blocked.

4. Crystalluria is best prevented by:

Dilute, less acidic urine keeps drugs soluble.

5. Why do sulfonamides work poorly in abscesses?

Debris supplies PABA and thymidine.

6. Sulfonamides in coccidiosis mainly act on the:

They suppress asexual multiplication.

7. A known adverse effect in dogs given potentiated sulfonamides is:

Dry eye is well described.

8. Sulfonamide alone is typically:

Combination with a diaminopyrimidine often becomes bactericidal.

9. Resistance to sulfonamides commonly involves:

Resistant enzymes are plasmid carried.

10. Pyrimethamine is mainly used against:

It is a diaminopyrimidine used for protozoal infection.

Key points to revise

1. Sulfonamides inhibit dihydropteroate synthase by mimicking PABA.
2. Diaminopyrimidines inhibit DHFR.
3. The combination is synergistic and often bactericidal.
4. Folate synthesis is a selective target because mammals use dietary folate.
5. Crystalluria occurs in acidic, concentrated urine with poorly soluble drugs.
6. Resistance is plasmid-mediated and common.
7. Sulfonamides act on early asexual stages of Eimeria.
8. Residues in food are an ongoing concern; check current rules.

Go deeper on this site

- Ch 3. Beta-lactam antibiotics (in this book)
- Ch 1. Principles of chemotherapy and antibiotic selection (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Sulfonamides
- WHO: Antimicrobial resistance fact sheet
- Merck Veterinary Manual: Penicillins

CHAPTER 3 OF 19

Beta-lactam antibiotics

Beta-lactams block cell wall synthesis and kill growing bacteria. The chapter covers penicillin groups, cephalosporin generations, beta-lactamase inhibitors and why carbapenems are kept for human medicine and reserve use.

After this chapter you can

- Explain how beta-lactams inhibit peptidoglycan cross-linking and why this kills growing bacteria
- Classify penicillins and describe the spectrum of each group
- Describe cephalosporin generations and the trend in spectrum
- Explain how beta-lactamase inhibitors restore activity
- Explain why carbapenems are reserved and the stewardship rationale

Mechanism: attacking the cell wall

The bacterial cell wall is built from **peptidoglycan**, a mesh of sugar chains cross-linked by short peptides. The cross-linking is done by **penicillin-binding proteins (PBPs)**, which are transpeptidase enzymes. Beta-lactams, named for the four-membered beta-lactam ring, mimic the end of the peptide and bind PBPs irreversibly. Cross-linking stops.

The cell keeps growing but the wall is weak. Autolytic enzymes then break the wall and the cell bursts from internal osmotic pressure. This explains three key facts. Beta-lactams are **bactericidal**, they act only on **actively growing** bacteria, and they are **time-dependent** drugs. Mammalian cells have no cell wall, so toxicity to the host is low.

Beta-lactams are weak acids, mostly stay in extracellular fluid, are excreted largely by the kidney through tubular secretion, and do not easily enter cells. Mycoplasma lacks a cell wall and is naturally resistant.

Common confusion: a bacteriostatic drug that stops growth can antagonise a beta-lactam, because the beta-lactam needs growing cells. Also, Gram-negative bacteria have an outer membrane, so a drug must pass porin channels before it reaches PBPs, which is why spectrum differs between members.

Resistance to beta-lactams

There are three main mechanisms.

1. **Beta-lactamases** hydrolyse the ring. This is the commonest mechanism. Gram-positive bacteria release the enzyme outside the cell, and Gram-negative bacteria hold it in the periplasmic space.
2. **Altered PBPs** with low affinity for the drug. The classic example is the *mecA* gene in methicillin-resistant staphylococci, which makes them resistant to practically all beta-lactams except specially designed ones. This is why MRSA and MRSP are a serious problem.
3. **Reduced entry or increased efflux** in Gram-negative bacteria through changes in porin channels.

Extended-spectrum beta-lactamases (ESBLs) and carbapenemases in Gram-negative bacteria are a global concern because they remove many options at once.

Penicillins

All penicillins share the 6-aminopenicillanic acid core. They are grouped by spectrum.

- **Natural penicillins** (benzylpenicillin, penicillin V). Active against Gram-positive organisms, anaerobes and a few Gram-negatives. Destroyed by beta-lactamase. Benzylpenicillin is acid-labile, so oral absorption is poor. Procaine and benzathine forms are depot preparations that give prolonged levels after injection, but they also lead to long residue periods in food animals.
- **Penicillinase-resistant penicillins** (cloxacillin, dicloxacillin, oxacillin). Active against staphylococci that produce beta-lactamase. They are used mainly in mastitis intramammary products. They are not effective against MRSA.
- **Aminopenicillins** (ampicillin, amoxicillin). Wider spectrum including some Gram-negative organisms such as certain *E. coli* and *Salmonella*, but still destroyed by beta-lactamase. Amoxicillin is acid-stable and better absorbed orally than ampicillin. Because these drugs are mostly excreted by the kidney, urine concentrations are high, which suits urinary infection, but dose adjustment thinking is needed in renal failure.
- **Extended-spectrum penicillins** (carboxypenicillins and ureidopenicillins such as ticarcillin and piperacillin). Added *Pseudomonas* activity; used mainly with an inhibitor and mostly in companion animal or hospital practice.

The main toxic problem is **hypersensitivity**, which can be severe, and cross-allergy exists among penicillins and, to a lesser extent, cephalosporins. Oral use can disturb gut flora, notably in rodents, rabbits, guinea pigs and ruminants.

Cephalosporins by generation

Cephalosporins share a cephem nucleus and are more resistant to many staphylococcal beta-lactamases than natural penicillins. They are grouped into **generations**. The pattern is a rough guide, not a rigid rule.

- **First generation** (cefazolin, cephalexin, cefadroxil). Good against Gram-positive cocci including staphylococci, with limited Gram-negative cover. Used for skin infections and surgical prophylaxis. Oral first-generation agents are absorbed well in monogastric animals.
- **Second generation** (cefoxitin, cefuroxime). A little more Gram-negative activity, and cefoxitin (technically a cephamycin) has anaerobe cover.
- **Third generation** (ceftiofur, cefovecin, cefpodoxime, ceftriaxone). Stronger Gram-negative activity and better tissue penetration, with somewhat less Gram-positive activity than first generation. Ceftriaxone and similar drugs reach the CSF.
- **Fourth generation** (cefquinome, cefepime). Broad cover including Gram-positives and many Gram-negatives and some resistance to beta-lactamases.

In general, moving from first to later generations increases Gram-negative activity. Cephalosporins are **not active** against enterococci, and are poor against MRSA. Third and later generations are classed by international bodies among important antimicrobials for human medicine, so use them only when justified, ideally after culture. Check the current Indian policy on their use in animals.

Beta-lactamase inhibitors

Clavulanic acid, sulbactam and tazobactam have little antibacterial activity of their own. They bind beta-lactamases and inactivate them, acting as **suicide inhibitors**. When combined with a penicillin, the partner drug is protected and its spectrum is restored. Amoxicillin-clavulanate is the best-known veterinary example, extending cover to many beta-lactamase-producing staphylococci, *E. coli* and anaerobes.

Inhibitors have limits. They do not help when resistance is due to altered PBPs, as in MRSA, and they do not inactivate all beta-lactamases, such as ESBLs of certain classes. Combination drugs should therefore be used where beta-lactamase producers are genuinely likely, not as a default for every infection. Gastrointestinal upset is a recognised effect.

Remember the logic: an inhibitor combination answers the question *is an enzyme destroying my drug?* It does not answer *is the target changed?* or *is the drug kept out?* When culture shows a plain penicillin-susceptible organism, an inhibitor combination adds spectrum and selection pressure without benefit, and the narrower drug is the better stewardship choice.

Carbapenems and why they are reserved

Carbapenems (imipenem, meropenem, ertapenem) have the widest spectrum of the beta-lactams, covering Gram-positives, Gram-negatives and anaerobes, and are stable against most beta-lactamases including ESBLs. They are usually the last line for serious multi-drug-resistant Gram-negative infections in human hospitals.

They are reserved for these reasons:

- They are among the few options left when ESBL-producing organisms cause severe infection in people.
- Use in animals could select carbapenemase producers, which can spread to humans, and resistance genes are often on mobile elements carrying other resistance too.
- Many authorities restrict or prohibit their use in food animals, and recommend that any companion-animal use be only after culture shows no alternative. Check the current Indian notification and veterinary council guidance.

Stewardship principle: protect drugs that human medicine cannot do without. Even when a species is not a food animal, hospital-acquired resistant bacteria can pass between animals and people, so the same restraint applies to companion animals. Beta-lactam residues in milk also cause allergic reactions and interfere with dairy fermentation, so withdrawal periods must be respected.

Concept cleared

Cell wall as the target

Blocking PBP cross-linking weakens the wall; growing bacteria burst. Hence bactericidal, time-dependent, and inactive on non-dividing cells or cell-wall-less Mycoplasma.

Beta-lactamase protection

Enzymes cut the ring; inhibitors block the enzymes. The inhibitor protects the penicillin, it does not widen the drug beyond enzyme-mediated resistance.

Altered target resistance

MRSA has a PBP with low affinity, so all standard beta-lactams and inhibitor combinations fail.

Reserve drugs

Carbapenems are kept to protect human treatment of resistant Gram-negative infection.

Memory aid: Beta-lactam features: C-T-G

Cell wall target, Time-dependent, Growing cells only. Each point helps answer questions on mode of action and combination logic.

Compare and contrast

Penicillin groups

Group	Examples	Main spectrum	Beta-lactamase stable?
Natural	Benzylpenicillin	Gram-positive, anaerobes	No
Penicillinase-resistant	Cloxacillin	Staphylococci	Yes
Aminopenicillins	Amoxicillin, ampicillin	Plus some Gram-negatives	No (unless with inhibitor)
Extended-spectrum	Piperacillin	Plus Pseudomonas	No (with inhibitor)

Cephalosporin generations

Generation	Examples	Trend
First	Cefazolin, cephalexin	Gram-positive focus
Second	Cefoxitin, cefuroxime	More Gram-negative, anaerobes with cefoxitin
Third	Ceftiofur, cefovecin, ceftriaxone	Strong Gram-negative, CSF entry for some
Fourth	Cefquinome, cefepime	Broad, more enzyme stable

Species notes

Cattle
Intramammary penicillinase-resistant penicillins and cephalosporins are widely used; milk and meat withdrawal and discard of milk must be followed.

Dogs and cats
First-generation cephalosporins and amoxicillin-clavulanate are common for skin and urinary infections; hypersensitivity can occur.

Horses
Procaine penicillin can cause reactions if inadvertently given

Rabbits, guinea pigs, hamsters
Oral penicillins and some cephalosporins can cause fatal

intravenously; oral beta-lactams may disturb hindgut flora.

dysbiosis; avoid unless a specialist advises.

Poultry and pigs
Used in flock and herd treatment; check residue rules and the current policy on cephalosporin use in food animals.

Clinical pearls

Self-test: 10 questions

1. Beta-lactams act by inhibiting:

They bind penicillin-binding proteins.

2. Beta-lactams are ineffective against Mycoplasma because:

No peptidoglycan means no target.

3. Cloxacillin is mainly valued for:

It resists staphylococcal penicillinase.

4. Clavulanic acid works by:

It is a suicide inhibitor of beta-lactamase.

5. MRSA is resistant mainly because of:

A low-affinity PBP makes beta-lactams ineffective.

6. Which pair is correct?

Gram-negative activity rises with generation.

7. Which is the main reason carbapenems are reserved?

Stewardship protects them for human use.

8. Beta-lactams show killing that is:

Time above MIC is the driver.

9. The most important adverse effect class of penicillins is:

Allergic reactions are the main concern.

10. Amoxicillin differs from benzylpenicillin in being:

Aminopenicillins are orally absorbed and broader.

Key points to revise

1. Beta-lactams bind PBPs and block peptidoglycan cross-linking.
2. They are bactericidal and time-dependent and need growing bacteria.
3. Beta-lactamase is the commonest resistance mechanism.
4. mecA gives altered PBP and MRSA, resistant to most beta-lactams.
5. Penicillins are grouped as natural, penicillinase-resistant, amino and extended-spectrum.
6. Gram-negative activity generally rises from first to later cephalosporin generations.
7. Clavulanic acid, sulbactam and tazobactam inhibit beta-lactamases.
8. Carbapenems are reserved for resistant Gram-negative infection and protected for human use.

Go deeper on this site

- Ch 4. Aminoglycosides and aminocyclitols (in this book)
- Ch 2. Sulfonamides and diaminopyrimidines (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Penicillins
- Merck Veterinary Manual: Cephalosporins and cephamycins
- WHO: Antimicrobial resistance fact sheet

CHAPTER 4 OF 19

Aminoglycosides and aminocyclitols

Aminoglycosides are bactericidal, concentration-dependent drugs that act on the 30S ribosome and are used mainly against aerobic Gram-negative bacteria. Their narrow safety margin (kidney, inner ear, neuromuscular junction) and long tissue residues shape every clinical decision.

After this chapter you can

- Explain how aminoglycosides enter bacteria, bind the ribosome and kill
- State the spectrum and why anaerobes are naturally resistant
- Describe the mechanisms and risk factors for nephrotoxicity, ototoxicity and neuromuscular blockade
- Explain why gentamicin, amikacin and streptomycin differ in use and resistance
- Explain why aminoglycoside residues persist in kidney and what this means for withdrawal and stewardship

Chemistry and mechanism of action

Aminoglycosides are polycationic sugars joined to an aminocyclitol ring. Gentamicin, amikacin, tobramycin, kanamycin and neomycin carry a 2-

deoxystreptamine ring. **Streptomycin** carries a streptidine ring, and **spectinomycin** is a related aminocyclitol without amino sugars, which is why it is only bacteriostatic and gentler.

The drug first crosses the outer membrane of Gram-negative bacteria, then is taken across the inner membrane by an **energy-dependent, oxygen-requiring** process driven by the membrane electrical potential. Inside, it binds the **30S ribosomal subunit**, distorts the A site and causes misreading of mRNA. Faulty proteins insert into the cell membrane, make it leaky and allow still more drug to enter. This positive feedback explains why, unlike most protein synthesis inhibitors, aminoglycosides are **bactericidal**.

Killing is **concentration-dependent**, and a **post-antibiotic effect** continues after levels fall. Bacteria also show temporary adaptive resistance after exposure. For these reasons the modern approach favours a high peak followed by a long drug-free interval rather than frequent small exposures. This is a concept, not a dose, and the label or a formulary must be used for the actual regimen.

Spectrum and common confusions

The useful spectrum is aerobic Gram-negative rods (Escherichia coli, Klebsiella, Pseudomonas, Proteus, Salmonella) and some staphylococci. Because uptake needs oxygen, **anaerobes are intrinsically resistant**. The same logic explains poor activity in abscess pus, necrotic tissue and low pH, where oxygen is low and the drug binds to debris. Streptococci and enterococci are only weakly susceptible alone, but a cell-wall active drug such as a penicillin damages the wall and lets aminoglycosides in, giving **synergy**.

Individual agents differ. Gentamicin is the workhorse for Gram-negative sepsis, uterine and ocular uses. Amikacin is a semi-synthetic kanamycin derivative that resists many bacterial inactivating enzymes, so it is kept for gentamicin-resistant organisms and should be protected by restricted use. Streptomycin is used for mycobacteria, Brucella (with a tetracycline) and some Leptospira work, and in veterinary practice it often appears as dihydrostreptomycin. Neomycin is poorly absorbed orally and is used locally in the gut and on skin. Spectinomycin is used in poultry and pigs for Mycoplasma and enteric infections.

A frequent confusion: aminoglycosides are not absorbed from the gut after oral dosing, so they are given by injection for systemic infection. A drug that stays in the gut after oral use is not a failure, it is a feature for enteric infections, but absorption can rise in a damaged intestine.

Pharmacokinetics

Aminoglycosides are highly polar. They distribute mainly in **extracellular fluid**, so the dose reflects lean body weight and fat is not a useful reservoir. Penetration into CSF, bone, prostate and the eye is poor. Protein binding is low. Excretion is by **glomerular filtration** of unchanged drug, so renal disease, dehydration and neonatal immaturity prolong the half-life.

A small fraction is taken up by proximal tubular cells and by hair cells of the inner ear and is released very slowly. This tissue binding explains both toxicity and the long residue persistence described below. Plasma levels can look safe while the kidney cortex is holding a large load.

Nephrotoxicity, ototoxicity and neuromuscular block

Nephrotoxicity. Filtered drug binds to the brush border of proximal tubule cells, is taken in by receptor-mediated endocytosis and concentrates in lysosomes. Lysosomal damage, mitochondrial injury and cell death follow. Early signs are enzymuria and casts, then loss of concentrating ability, and later a rise in creatinine. Injury is often non-oliguric and can be reversible because tubule cells regenerate. Risk rises with dehydration, pre-existing renal disease, older age, sepsis, repeated or prolonged dosing, and combination with other nephrotoxins such as NSAIDs, amphotericin B and loop diuretics. Giving the same total as one large dose reduces uptake because the transport process saturates, which is another reason for the extended-interval approach.

Ototoxicity. The drug accumulates in perilymph and kills sensory hair cells, which do not regenerate. Cochlear damage causes deafness. Vestibular damage causes ataxia, head tilt and nystagmus. Gentamicin and streptomycin tend to affect the vestibular system, whereas neomycin and amikacin are more cochlear. Cats are particularly sensitive to vestibular effects. Loop diuretics add risk. Topical gentamicin or neomycin in a perforated ear drum can reach the inner ear.

Neuromuscular blockade. Aminoglycosides reduce presynaptic acetylcholine release and postsynaptic sensitivity by competing with calcium. The effect is rapid after fast intravenous injection or intraperitoneal instillation and is worse with anaesthetics, muscle relaxants, magnesium and in hypocalcaemia. Calcium salts and neostigmine can partly reverse it. Do not give these drugs as a fast intravenous bolus.

Monitoring means keeping the patient hydrated, checking urine for casts and specific gravity, and avoiding combinations with other nephrotoxic drugs.

Resistance and interactions

The commonest mechanism is **enzymatic modification** by acetyl-, phosphoryl- or adenylyl-transferases, usually plasmid-carried and transferable between species. Each enzyme attacks a defined set of drugs, which is why gentamicin resistance does not always predict amikacin resistance. Other mechanisms are reduced uptake, efflux, and ribosomal methylation by 16S rRNA methyltransferases, which gives high-level resistance to nearly the whole class. Mutation of the ribosomal target is important for streptomycin in single-step resistance, for example in mycobacteria.

An important *in vitro* interaction: carbenicillin and other penicillins can inactivate aminoglycosides if mixed in the same syringe or infusion bag. This is a pharmaceutical incompatibility and differs from the helpful in vivo synergy. Aminoglycosides are also inactivated in acidic or high-salt, high-divalent-cation environments, and they are less active in pus.

Residues, withdrawal and stewardship

Because kidney tissue retains aminoglycosides for a long time, residues can be found in kidney and, to a lesser extent, liver long after plasma levels disappear. **Withdrawal times are therefore long** and kidney is usually the limiting tissue in meat. Withdrawal is also longer in animals with renal damage. For these reasons, extra-label use in food animals is hazardous. Milk residues occur after intramammary or parenteral use, and the licensed withdrawal for milk must be respected. Maximum residue limits and the list of permitted products in India are set by national authorities. Check the current notification from FSSAI and the relevant veterinary authority before applying any figure.

Stewardship points: aminoglycosides are valuable against multidrug-resistant Gram-negatives, and amikacin in particular is a reserve drug. Use culture and sensitivity, avoid prophylactic or routine use, avoid sub-therapeutic exposure that selects resistance, and follow national and WOAH or WHO guidance on categories of importance. In human medicine streptomycin and amikacin are important for tuberculosis and resistant infections, so animal use should be restricted accordingly.

Concept cleared

Oxygen-dependent entry
Aminoglycosides need an energised, oxygenated bacterial membrane to enter, so anaerobes and bacteria in necrotic, low-oxygen, acidic pus are poorly affected.

Concentration-dependent killing
Higher peak relative to MIC gives faster kill and a post-antibiotic effect, so a large dose with a long interval is both effective and less toxic than frequent small doses.

Tissue trapping
Uptake into proximal tubule cells and inner-ear hair cells explains toxicity and long residues even when plasma levels are low.

Synergy with cell-wall drugs
Penicillins damage the wall and allow aminoglycosides into Gram-positive cells, giving synergy that is helpful in vivo but must not be mixed in one syringe.

Memory aid: Aminoglycoside cautions: NOW
Nephro, Oto, neuromuscular Weakness. Also remember they are Ineffective without Oxygen, so anaerobes escape.

Compare and contrast

Aminoglycosides compared

Drug	Main use	Resistance point	Key caution
Gentamicin	Gram-negative sepsis, local ocular and uterine use	Common modifying enzymes	Nephrotoxic, vestibular
Amikacin	Gentamicin-resistant Gram-negatives	Resists many enzymes, ribosomal methylases	Reserve drug, nephrotoxic
Streptomycin / dihydrostreptomycin	Mycobacteria, Brucella with tetracycline, Leptospira	Single-step ribosomal mutation	Vestibular and cochlear damage, esp. cats
Neomycin	Oral gut or topical use	Modifying enzymes	Not for systemic use, toxic if absorbed
Spectinomycin	Poultry and pig Mycoplasma and enteric infections	Ribosomal mutation, enzymes	Mainly bacteriostatic, less toxic

Toxicity of aminoglycosides

Target	Mechanism	Reversible?	Risk modifiers
Kidney	Proximal tubule uptake, lysosomal injury	Often yes	Dehydration, NSAIDs, age, sepsis
Cochlea	Hair cell death	No	Loop diuretics, long courses
Vestibular system	Hair cell death	Partly by compensation	Cats, streptomycin and gentamicin
Neuromuscular junction	Reduced ACh release, calcium competition	Yes with calcium, neostigmine	Anaesthetics, fast IV, low calcium

Species notes

Cattle

Very long kidney withdrawal and milk residue concerns. Extra-label use is risky, so rely on the label and the current national rules.

Dogs

Nephrotoxicity is the main concern, especially in dehydrated or older dogs and with concurrent NSAIDs. Keep the patient hydrated.

Cats

Prone to vestibular toxicity, particularly with streptomycin and dihydrostreptomycin. Use with great care.

Horses

Gentamicin and amikacin are used for Gram-negative infections, including intra-articular and regional perfusion. Monitor kidney, and note risk with NSAIDs and in foals with sepsis.

Poultry and pigs

Neomycin, apramycin, spectinomycin and others are used for gut infections. Check current approvals and withdrawal periods for each product.

Clinical pearls

Self-test: 10 questions

1. Why are anaerobic bacteria intrinsically resistant to aminoglycosides?

Entry is an oxygen-dependent, energy-driven process, so anaerobes do not take up the drug.

2. Which ribosomal subunit do aminoglycosides bind?

They bind the 30S subunit and cause mRNA misreading.

3. Which statement about killing pattern is correct?

High peaks give greater kill, and the effect persists after levels fall.

4. Which factor most increases the risk of nephrotoxicity?

Reduced renal perfusion and other nephrotoxins increase tubular accumulation and injury.

5. Ototoxicity of aminoglycosides is mainly caused by:

Drug accumulates in perilymph and destroys sensory hair cells, which do not regenerate.

6. Aminoglycoside-induced neuromuscular weakness is best treated with:

Calcium opposes the reduced acetylcholine release.

7. Why is amikacin kept for resistant Gram-negative infections?

Its structure protects it from many enzymes, so it should be preserved as a reserve drug.

8. Which tissue most often determines the withdrawal time of aminoglycosides in food animals?

Kidney retains the drug for a long time after plasma levels fall.

9. Which species is especially prone to vestibular toxicity from streptomycin?

Cats are particularly sensitive to vestibular effects of this group.

10. The synergy between a penicillin and an aminoglycoside against streptococci depends on:

Wall damage allows more aminoglycoside inside. Mixing in a syringe inactivates the aminoglycoside.

Key points to revise

1. Aminoglycosides bind the 30S subunit and are bactericidal.
2. Uptake needs oxygen, so anaerobes are resistant.
3. Killing is concentration-dependent with a post-antibiotic effect.
4. They are not absorbed from the gut and reach mainly extracellular fluid.
5. Excretion is by glomerular filtration, and renal failure prolongs half-life.
6. Toxicities are nephrotoxicity, ototoxicity and neuromuscular blockade.
7. Resistance is mainly by plasmid-borne modifying enzymes, and amikacin resists many of them.
8. Residues persist in kidney, so withdrawal times are long and national limits must be checked.

Go deeper on this site

- Ch 5. Tetracyclines and phenicols (in this book)
- Ch 3. Beta-lactam antibiotics (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- FDA Center for Veterinary Medicine: Judicious use of antimicrobials
- FDA Animal Antibiotic Stewardship Plan
- WHO Antimicrobial resistance fact sheet

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Tetracyclines and phenicols

Tetracyclines and phenicols are broad-spectrum, mainly bacteriostatic protein synthesis inhibitors. This chapter explains how they act, why they chelate calcium, how resistance spreads, and why chloramphenicol is restricted while florfenicol is used in food animals.

After this chapter you can

- Describe the ribosomal targets and bacteriostatic action of tetracyclines and phenicols
- Explain the spectrum, including intracellular and vector-borne pathogens
- Explain calcium chelation and its effects on absorption, teeth and intravenous safety
- Compare oxytetracycline and doxycycline
- Explain chloramphenicol hazards, why florfenicol differs, and the main resistance mechanisms

Tetracyclines: mechanism and spectrum

Tetracyclines have a four-ring structure. They enter bacteria by passive diffusion through porins and by an energy-dependent transport, and bind the **30S ribosomal subunit**. There they block the A site so that aminoacyl-tRNA cannot attach, and protein synthesis stops. The effect is **bacteriostatic**, so host defences must clear the organism.

The spectrum is broad. It includes many Gram-positive and Gram-negative bacteria, but the clinical value today lies mainly in organisms that live inside cells or need special handling: *Rickettsia*, *Anaplasma*, *Ehrlichia*, *Chlamydia*, *Mycoplasma*, *Borrelia*, *Brucella* and *Leptospira*. Their good tissue and cell penetration help here. Because resistance is now widespread among common enteric and respiratory bacteria, tetracyclines should not be chosen blindly for these infections.

Tetracyclines also affect mammalian mitochondrial ribosomes slightly and have non-antibacterial effects such as matrix metalloproteinase inhibition and anti-inflammatory activity. These are the basis for some uses of doxycycline in skin and periodontal disease, but they are secondary to the antibacterial action.

Calcium chelation and its consequences

Tetracyclines bind divalent and trivalent cations (calcium, magnesium, iron, aluminium and zinc). This single chemical property explains several clinical points.

- **Absorption.** Oral tetracycline given with milk, antacids, iron or mineral supplements forms insoluble chelates and absorption falls. Doxycycline is less affected because it is more lipophilic.
- **Teeth and bone.** The drug deposits in developing teeth and growing bone as a calcium complex, causing yellow-brown discolouration and sometimes enamel hypoplasia. It is avoided in pregnant animals and in the young during tooth development unless the benefit is clear.
- **Intravenous safety.** Rapid intravenous injection binds plasma calcium and can cause hypotension, collapse and arrhythmia, particularly in cattle. Injection should be slow and, for some products, diluted, as the label requires.
- **Intramuscular depots.** Long-acting oxytetracycline products are irritant. They can cause painful swelling, tissue damage and a persistent injection-site residue that spoils meat.

A common confusion: chelation is one chemical property with several different clinical faces. In the gut it lowers absorption, in the plasma it can depress the heart if given fast, and in growing tissues it leaves a permanent stain. None of these is a therapeutic benefit.

Pharmacokinetics: oxytetracycline versus doxycycline

Oxytetracycline is the classic veterinary tetracycline. It is usually given by injection to food animals, and oral absorption in ruminants is poor and may disturb rumen flora. It is excreted largely unchanged by the kidney, and also in bile. Long-acting forms prolong exposure but also prolong residues.

Doxycycline is more lipophilic. It is well absorbed orally in monogastric animals, has better tissue and intracellular penetration, a longer half-life, and is eliminated mainly by non-renal routes (bile and gut), so it is safer in renal disease. Its important adverse effect in cats is **oesophageal injury and stricture** if a dry tablet or capsule lodges in the oesophagus. Give tablets followed by water or a small amount of food. In horses, oral doxycycline has been used but the intestinal flora can be disturbed.

Doxycycline is also the common choice for canine ehrlichiosis, anaplasmosis, leptospirosis and some Chlamydia and Mycoplasma infections in companion animals.

Minocycline, a related lipophilic tetracycline, is occasionally used in small animals, and tigecycline-type newer agents are reserved for human medicine. Dosing for every agent must come from the product label or a current formulary, since absorption and tissue binding differ between drugs and species.

Tetracycline adverse effects

Beyond teeth, chelation and injection-site reactions, important adverse effects include gastrointestinal upset, **antibiotic-associated colitis in horses** (disruption of hindgut flora), hepatotoxicity at high doses, photosensitisation, and renal tubular injury with out-of-date or degraded tetracycline, which produces a Fanconi-like syndrome. Tetracyclines can worsen azotaemia through their anti-anabolic effect, and some forms are nephrotoxic in dehydrated animals. Intravenous overdose and some solvent vehicles can cause cardiac depression. Rapid IV injection in cattle is the best-known acute risk.

Phenicols: chloramphenicol and florfenicol

Phenicols bind the **50S subunit** at the peptidyl transferase centre and block peptide bond formation. They are broad-spectrum and mainly bacteriostatic, with activity against many anaerobes, Gram-positive and Gram-negative bacteria and intracellular organisms, and good penetration into CSF, eye and brain.

Chloramphenicol cautions. It has two types of bone marrow toxicity: a dose-related, reversible suppression of erythroid, myeloid and platelet precursors, and a rare idiosyncratic aplastic anaemia described in humans, which is unrelated to dose and can be fatal. Because of the human hazard, it is **prohibited in food-producing animals** in many countries, and Indian rules should be confirmed from the current notification. People handling it should avoid contact and wear gloves. Cats metabolise it slowly because glucuronidation is poor, so dosing intervals must be longer and toxicity is more likely. Neonates share this weakness. It inhibits hepatic cytochrome P450 enzymes and prolongs the effect of drugs such as phenobarbital and some anaesthetics.

Florfenicol is a fluorinated derivative of thiamphenicol. It lacks the nitro group linked to human aplastic anaemia and is not inactivated by the acetyltransferase that destroys chloramphenicol. It is licensed in some countries for respiratory disease in cattle and pigs and for fish. It can still cause reversible dose-related marrow effects, gastrointestinal upset, injection-site lesions and a long tissue withdrawal. Check the label and current rules for milk, dairy cows and calves.

Resistance and stewardship

Tetracycline resistance is commonly by **efflux pumps** encoded by tet genes, or by **ribosomal protection proteins** that dislodge the drug. A third mechanism is enzymatic inactivation. These genes sit on plasmids and transposons and spread between species, so a bacterium resistant to oxytetracycline is often cross-resistant to other older tetracyclines, though doxycycline and minocycline may sometimes remain active. Because older uses were widespread, resistance in farm bacteria is high.

Phenicol resistance includes chloramphenicol acetyltransferase (cat genes), efflux pumps (for example floR, which affects both chloramphenicol and florfenicol) and the *cfr* gene, which methylates 23S rRNA and gives combined resistance to phenicols, lincosamides, oxazolidinones, pleuromutilins and streptogramin A. This is why florfenicol use is of concern for linezolid-related resistance.

Stewardship points: do not use tetracyclines for viral diarrhoea or as routine feed additives, avoid prophylaxis, and use culture where possible. The use of antimicrobial growth promoters has been restricted in many countries. Check the current Indian notifications about permitted use and about chloramphenicol, and follow national policy for residues and MRLs.

Concept cleared

Bacteriostatic does not mean weak

Both classes stop protein synthesis without killing directly, but with a competent immune system, they cure many infections. They are poor choices in severely immunocompromised animals.

Chelation

Binding of calcium and other cations explains reduced oral absorption, tooth staining, IV hypotension and cautions with dairy and minerals.

Lipophilicity

Doxycycline's lipophilicity gives better absorption, intracellular penetration and non-renal clearance than oxytetracycline.

Structure explains safety

Florfenicol lacks the nitro group of chloramphenicol and is not destroyed by acetyltransferase, which is why it is used in food animals while chloramphenicol is not.

Memory aid: Tetracycline cautions: TEETH CA

Teeth staining, Esophageal stricture (doxy in cats), Entry with calcium lowers absorption, Tissue irritation at injection, Hypotension if IV fast, Colitis in horses, Azotaemia and nephrotoxicity.

Compare and contrast

Oxytetracycline versus doxycycline

Feature	Oxytetracycline	Doxycycline
Lipophilicity	Lower	Higher
Effect of cations on oral absorption	Marked	Smaller
Main elimination	Kidney and bile	Mostly non-renal
Use in renal disease	More caution	Preferred of the two
Typical use	Food animal injectables	Companion animals, vector-borne disease
Special hazard	Injection-site residue, IV collapse	Oesophageal stricture in cats

Chloramphenicol versus florfenicol

Feature	Chloramphenicol	Florfenicol
Nitro group	Present	Replaced by fluorine
Aplastic anaemia link in humans	Yes, rare	Not reported
Inactivation by acetyltransferase	Yes	No
Food animal use	Prohibited in many countries	Licensed for some food species
Cats	Slow glucuronidation, caution	Not a main concern

Species notes

Cattle

Oxytetracycline long-acting injections cause injection-site residues and lesions. Rapid IV injection can cause collapse. Florfenicol is licensed in some countries for respiratory disease but has restrictions in dairy cows.

Cats

Doxycycline tablets can cause oesophageal stricture if given dry. Chloramphenicol is cleared slowly, so intervals must be longer.

Dogs

Doxycycline is the common choice for ehrlichiosis, leptospirosis and some respiratory pathogens. Chloramphenicol is used cautiously because of marrow effects.

Horses

Tetracyclines can cause enterocolitis. Chloramphenicol is rarely used in food-producing horses, and its status should be checked locally.

Fish and poultry

Oxytetracycline and florfenicol are used in aquaculture and poultry in

some countries, so withdrawal and national limits must be checked.

Clinical pearls

Self-test: 10 questions

1. Which ribosomal subunit do tetracyclines bind?

They block the A site on the 30S subunit.

2. Which statement about phenicols is correct?

They block peptide bond formation at the peptidyl transferase centre.

3. Why should oral tetracycline not be given with antacids or milk?

Divalent and trivalent cations bind the drug.

4. A recognised hazard of dry doxycycline tablets in cats is:

Tablets can lodge in the oesophagus and cause injury, so follow with water or food.

5. Rapid intravenous oxytetracycline in cattle may cause:

Chelation of plasma calcium depresses the heart.

6. Why is doxycycline safer than oxytetracycline in renal disease?

Biliary and intestinal elimination reduce dependence on the kidney.

7. Why is florfenicol acceptable in some food animals when chloramphenicol is not?

Structural differences remove the human aplastic anaemia concern, though residue rules still apply.

8. Why is chloramphenicol more toxic in cats?

Slow glucuronide conjugation prolongs the half-life.

9. Which gene can give combined resistance to phenicols, lincosamides and pleuromutilins?

cfr methylates 23S rRNA, affecting several 50S-binding classes.

10. The commonest tetracycline resistance mechanisms are:

tet genes encode efflux pumps and ribosomal protection proteins.

Key points to revise

1. Tetracyclines bind the 30S subunit and block aminoacyl-tRNA attachment.
2. Phenicols bind the 50S subunit and inhibit peptidyl transferase.
3. Both classes are mainly bacteriostatic and broad spectrum.
4. Tetracyclines chelate calcium, magnesium, iron and aluminium.
5. Chelation explains tooth staining, reduced absorption and IV hypotension.
6. Doxycycline is lipophilic, with non-renal elimination.
7. Chloramphenicol can cause marrow toxicity and human aplastic anaemia, and is banned in food animals in many countries.
8. Tetracycline resistance is by efflux and ribosomal protection, and phenicol resistance includes floR and cfr.

Go deeper on this site

- Ch 6. Macrolides, lincosamides and pleuromutilins (in this book)
- Ch 4. Aminoglycosides and aminocyclitols (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- FDA Center for Veterinary Medicine: Judicious use of antimicrobials
- FDA Animal Antibiotic Stewardship Plan
- WHO Antimicrobial resistance fact sheet

CHAPTER 6 OF 19

Macrolides, lincosamides and pleuromutilins

These three classes bind the 50S ribosomal subunit at overlapping sites and are mainly bacteriostatic. The chapter covers spectrum, tissue concentration, shared resistance, important drug interactions and the serious species-specific toxicities that every veterinary student must know.

After this chapter you can

- Describe how macrolides, lincosamides and pleuromutilins inhibit the 50S ribosome
- Explain the spectrum and tissue distribution of erythromycin, tylosin, clindamycin and tiamulin
- Explain MLS-B cross-resistance and the cfr mechanism
- Identify the main drug interactions, including tiamulin with ionophores
- Recall species-specific toxicities such as lincosamide enterocolitis and tilmicosin cardiotoxicity

Mechanism of action

All three classes bind the **50S ribosomal subunit** near the peptidyl transferase centre, but at slightly different positions.

- **Macrolides** (erythromycin, tylosin, tilmicosin, tulathromycin, gamithromycin) sit in the nascent peptide exit tunnel of the 23S rRNA. They block the growing peptide chain and cause premature release of incomplete peptides.
- **Lincosamides** (lincomycin, clindamycin, pirlimycin) bind at the peptidyl transferase region and interfere with peptide bond formation and tRNA positioning.
- **Pleuromutilins** (tiamulin, valnemulin) bind the peptidyl transferase centre and distort the site where the tRNA is placed, preventing peptide bond formation.

Effects are mainly **bacteriostatic**, though high concentrations can be bactericidal against some organisms. Because the binding sites overlap, a macrolide and a lincosamide given together can compete and lose activity, so the combination is not rational unless a product is specifically licensed for it.

Macrolides: spectrum and pharmacology

Macrolides are active against Gram-positive cocci, *Mycoplasma*, *Campylobacter*, *Lawsonia*, *Rhodococcus* (with rifampin), and respiratory pathogens such as *Pasteurella* and *Mannheimia* for the newer agents. Most Enterobacteriaceae are resistant because the drug does not cross their outer membrane well.

They are lipophilic weak bases. In acidic compartments they become ionised and trapped, a process called **ion trapping**, so tissue and intracellular levels, especially in lung and phagocytes, far exceed plasma levels. White cells carry the drug to the infection site. This explains why newer long-acting macrolides such as tulathromycin give prolonged lung exposure after a single injection, and why plasma levels are a poor guide to efficacy. Milk, being slightly more acidic than plasma, also concentrates the drug, which affects milk withdrawal.

Erythromycin is also a **motilin receptor agonist**, which explains its gastrointestinal prokinetic effect and its tendency to cause cramping, diarrhoea or vomiting. It is also a potent inhibitor of CYP3A and of P-glycoprotein. Tylosin is used widely in pigs and poultry for mycoplasmal and enteric disease and in dogs for chronic colitis. Tilmicosin and tulathromycin are used mainly for bovine and swine respiratory disease.

Lincosamides and pleuromutilins

Lincomycin and clindamycin are active against Gram-positive cocci, many **anaerobes**, *Toxoplasma*, *Mycoplasma* and some protozoa. Gram-negative aerobes are resistant. Clindamycin is better absorbed and more potent than lincomycin. Both penetrate **bone, abscesses and tissues** well and are concentrated in phagocytes, which is why clindamycin is a common choice in dental disease, osteomyelitis and deep skin infection in dogs and cats. They do not cross the blood-brain barrier well in the absence of inflammation.

Elimination is mostly hepatic, with partial biliary and renal excretion. Lincosamides can cause a mild neuromuscular blocking effect, so caution with anaesthetics and relaxants is sensible. In cats, clindamycin capsules can cause oesophagitis if not washed down. Rapid intravenous injection should be avoided because of cardiovascular depression.

Tiamulin and valnemulin are used almost exclusively in pigs and poultry. Their spectrum covers *Mycoplasma*, *Brachyspira* (swine dysentery and spirochaetal colitis), *Lawsonia*, *Actinobacillus pleuropneumoniae* and many Gram-positive bacteria and anaerobes. They accumulate in lung tissue. Resistance develops by stepwise ribosomal mutation, and for Brachyspira this is an important concern. Because pleuromutilins are used in animals but not widely as first-line in people, they are regarded as valuable for animal health. Rules on their use should be checked in the current national notification.

Resistance mechanisms

The key mechanism is methylation of 23S rRNA by **Erm methylases**, which blocks all three drug groups at once and gives the **MLS-B phenotype** (macrolide, lincosamide and streptogramin B). It can be constitutive or **inducible**. In inducible resistance, only a macrolide switches on the gene, so a bacterium may appear sensitive to clindamycin in routine testing but fail in treatment. Laboratories detect this by placing erythromycin and clindamycin discs close together, and a flattened inhibition zone (the D-test) shows induction.

Other mechanisms are efflux pumps (mef, msr), which affect macrolides but not lincosamides, drug inactivation by esterases and phosphotransferases, and ribosomal mutation. The cfr gene gives broad cross-resistance across phenicols, lincosamides, pleuromutilins, oxazolidinones and streptogramin A. Any macrolide use in a herd can therefore select resistance to lincosamides and vice versa.

Interactions and species toxicities

Lincosamides in the wrong species. Lincosamides and, to a lesser extent, macrolides given orally to rabbits, guinea pigs, hamsters, horses and ruminants can wipe out protective gut flora and allow overgrowth of *Clostridium* species, causing fatal enterocolitis. Use is avoided in these species. In dogs and cats diarrhoea is milder.

Erythromycin in horses. In foals it is used for *Rhodococcus equi* pneumonia, but may cause hyperthermia and diarrhoea, and in adults it risks severe colitis. Mares can pass it through milk to foals. Foals receiving macrolides need temperature monitoring in hot weather.

Tilmicosin. It is cardiotoxic. Injection in pigs can be fatal, and it should not be given intravenously. Accidental self-injection in humans has caused deaths. It is also dangerous in horses and goats. Handle with extreme care and check the label.

Tiamulin and ionophores. Tiamulin inhibits hepatic cytochrome P450 and slows metabolism of monensin, salinomycin and narasin. This produces ionophore toxicity (muscle damage, ataxia, paralysis, growth depression and death) even at normal ionophore intake. The two should not be given together, and a withdrawal gap is required by the label. Horses are very sensitive to ionophores.

Other interactions. Erythromycin and some other macrolides inhibit CYP3A and P-glycoprotein and can raise levels of drugs such as cyclosporine, digoxin, theophylline and some opioids. Lincosamides add to neuromuscular blockade of anaesthetics and aminoglycosides.

Residues and stewardship

Macrolides concentrate in tissues and milk, and tulathromycin and tilmicosin persist in lung and fat, which gives long withdrawal periods in some labels. Tiamulin has a withdrawal in pig meat. Always apply the labelled withdrawal and consult the current FSSAI and veterinary authority notifications for Indian MRLs and permitted products.

Stewardship points: reserve newer long-acting macrolides for confirmed or high-risk respiratory disease rather than blanket group treatment. Do not use lincosamides or macrolides in species at risk of fatal enterocolitis. Culture and test for inducible resistance where relevant. Macrolides are also critically important in

human medicine, so veterinary use should follow national and WHO or WOAH advice.

Remember that residue behaviour depends on the product, route and species, so a withdrawal period learned for one macrolide cannot be transferred to another.

Concept cleared

Overlapping binding sites
Macrolides, lincosamides and pleuromutilins all bind near the peptidyl transferase region of the 50S subunit, so they compete with each other and share resistance mechanisms.

Ion trapping
Weakly basic macrolides concentrate in acidic tissues, lung and phagocytes, so tissue concentrations are much higher than plasma concentrations.

Inducible MLS-B resistance
Erm methylase can be switched on by a macrolide, so a clindamycin-susceptible isolate may fail. The D-test detects it.

Enzyme inhibition drives toxicity
Erythromycin and tiamulin inhibit hepatic enzymes, so partner drugs such as ionophores or cyclosporine accumulate.

Memory aid: MLS and friends share a site
Macrolide, Lincosamide, Streptogramin B and pleuromutilin all sit on the same 50S region: one methylase, many problems. Remember D for D-test and Diarrhoea (lincosamides in rabbits and horses).

Compare and contrast

Three 50S-binding classes

Class	Examples	Main spectrum	Key caution
Macrolides	Erythromycin, tylosin, tilmicosin, tulathromycin	Gram-positive, Mycoplasma, Pasteurella, Lawsonia	Tilmicosin cardiotoxicity, GI upset, colitis in horses
Lincosamides	Lincomycin, clindamycin, pirlimycin	Gram-positive, anaerobes, Toxoplasma	Fatal enterocolitis in rabbits, rodents, horses, ruminants
Pleuromutilins	Tiamulin, valnemulin	Mycoplasma, Brachyspira, Lawsonia	Ionophore toxicity

Resistance mechanisms

Mechanism	Macrolides	Lincosamides	Pleuromutilins
erm methylation (MLS-B)	Resistant	Resistant	Usually not the main route
Efflux (mef, msr)	Resistant	Usually susceptible	Not the main route
Ribosomal mutation	Possible	Possible	Stepwise, important in Brachyspira
cfr methylation	Not the main route	Resistant	Resistant

Species notes

Rabbits, guinea pigs, hamsters

Lincosamides and many macrolides given orally can cause fatal clostridial enterocolitis. Avoid.

Horses and foals

Erythromycin or newer macrolides are used for Rhodococcus equi in foals with a risk of hyperthermia and diarrhoea. Lincosamides are dangerous in adults. Horses are also very sensitive to ionophores.

Pigs

Cattle and small ruminants

Tylosin, lincomycin, tiamulin and tilmicosin are used for enteric and respiratory disease. Tilmicosin injection can be fatal. Do not combine tiamulin with ionophores.

Tulathromycin, tilmicosin and gamithromycin are used for respiratory disease. Oral lincosamides are dangerous in ruminants. Tilmicosin is hazardous to goats and humans on self-injection.

Dogs and cats

Clindamycin is used for dental, bone and skin infection and toxoplasmosis. Give capsules to cats with water to avoid oesophagitis. Tylosin is used for chronic colitis in dogs.

Clinical pearls

Self-test: 10 questions

1. Which ribosomal subunit do macrolides bind?

They bind the 23S rRNA of the 50S subunit in the peptide exit tunnel.

2. Why do macrolide concentrations in lung exceed plasma levels?

Ion trapping concentrates lipophilic weak bases in acidic tissues and cells.

3. What is the clinical importance of inducible MLS-B resistance?

A macrolide can induce erm expression, which the D-test detects.

4. Which action of erythromycin explains its prokinetic effect?

Erythromycin mimics motilin and stimulates gastric and intestinal motility.

5. Which species is at greatest risk of fatal enterocolitis from oral lincosamides?

Rabbits and other hindgut fermenters lose protective flora and develop Clostridium overgrowth.

6. Which macrolide is notably cardiotoxic and dangerous on accidental human self-injection?

Tilmicosin has caused fatal cardiac effects, so extreme care is required.

7. Tiamulin combined with monensin leads to:

Tiamulin inhibits hepatic CYP enzymes and raises ionophore exposure.

8. Which drug group is a good choice for Brachyspira hyodysenteriae in pigs?

Tiamulin and valnemulin are important for swine dysentery, though resistance should be monitored.

9. Why is combining a macrolide with a lincosamide generally irrational?

Both bind close sites on the 50S subunit, so one can reduce the effect of the other.

10. In cats, clindamycin capsules should be followed by water to avoid:

Capsules can lodge in the oesophagus and cause local injury.

Key points to revise

1. Macrolides, lincosamides and pleuromutilins bind the 50S subunit and are mainly bacteriostatic.
2. Macrolides concentrate in lung, phagocytes and milk by ion trapping.
3. Erythromycin is a motilin agonist and a CYP3A and P-glycoprotein inhibitor.
4. Clindamycin has good anaerobic, bone and Toxoplasma activity.
5. Tiamulin and valnemulin are used for Brachyspira, Mycoplasma and Lawsonia in pigs and poultry.
6. Erm methylation gives MLS-B cross-resistance and can be inducible.
7. Lincosamides and some macrolides can cause fatal enterocolitis in sensitive species.
8. Tilmicosin is cardiotoxic, and tiamulin with ionophores causes toxicity.

Go deeper on this site

- Ch 7. Fluoroquinolones and other synthetic antibacterials (in this book)
- Ch 5. Tetracyclines and phenicols (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- FDA Center for Veterinary Medicine: Judicious use of antimicrobials
- FDA Animal Antibiotic Stewardship Plan
- WHO Antimicrobial resistance fact sheet

CHAPTER 7 OF 19

Fluoroquinolones and other synthetic antibacterials

How fluoroquinolones such as enrofloxacin and marbofloxacin kill bacteria by blocking DNA gyrase and topoisomerase IV, why they must be used sparingly, and how nitroimidazoles and nitrofurans differ. The chapter stresses spectrum, resistance, residue concerns and responsible use.

> **After this chapter you can**

- Explain how fluoroquinolones block DNA gyrase and topoisomerase IV and why killing is concentration-dependent
- Describe the spectrum, main adverse effects and key interactions of enrofloxacin and marbofloxacin
- Explain how resistance to fluoroquinolones arises and why it spreads easily
- Describe the mechanism, spectrum and cautions for nitroimidazoles and nitrofurans
- Apply the principles of responsible use of critically important antibacterials in practice

Where these drugs fit

Fluoroquinolones, nitroimidazoles and nitrofurans are **synthetic** antibacterials. They are made in the laboratory, not derived from moulds or soil bacteria like penicillins or tetracyclines. Because they have no natural parent molecule, bacteria had less prior exposure to them, but resistance has still appeared quickly once they were widely used.

The three groups have little in common except origin. Fluoroquinolones are broad-spectrum drugs for aerobic bacteria. Nitroimidazoles are mainly for anaerobic bacteria and protozoa. Nitrofurans are older drugs now largely withdrawn from food animal use. Keep these three mechanisms separate in your mind and the chapter becomes simple.

Fluoroquinolone mechanism and spectrum

DNA in a bacterial cell is tightly coiled. To copy or read it, the cell must cut, unwind and rejoin the strands. Two enzymes do this work: **DNA gyrase** (topoisomerase II) and **topoisomerase IV**. Fluoroquinolones lock these enzymes onto the DNA after the strand has been cut. The cut cannot be sealed, DNA breaks accumulate and the cell dies. This is why the drugs are **bactericidal**.

In Gram-negative bacteria the main target is gyrase. In Gram-positive bacteria it is mainly topoisomerase IV. Mammalian topoisomerases are different enough that the drugs are selectively toxic, though not perfectly.

Killing is **concentration-dependent**. The higher the peak concentration relative to the MIC, the faster and more complete the kill, and the drugs also show a useful post-antibiotic effect. This is why the aim is a high peak at an appropriate interval, not frequent small exposures.

The spectrum covers many Gram-negative rods (E. coli, Salmonella, Pasteurella, Pseudomonas to a variable degree), Mycoplasma, and some Gram-positive cocci. Activity against **anaerobes is poor**, so these drugs are not a stand-alone choice for deep abscesses or mixed infections with anaerobes. Newer veterinary agents differ in how well they cover Gram-positives, so check the product literature.

Enrofloxacin and marbofloxacin in practice

Both drugs are well absorbed after oral and parenteral use, distribute widely and reach high levels in tissues such as prostate, lung, bone and skin, and are lipid-soluble enough to penetrate cells. This helps against intracellular organisms.

A frequent point of confusion: **enrofloxacin is partly de-ethylated in the liver to ciprofloxacin**, which is itself active. Marbofloxacin is not handled this way. When you read a susceptibility report, remember that the parent drug and its active metabolite both contribute to the effect.

Important adverse effects and cautions:

- **Cartilage damage in young, rapidly growing animals.** Joint erosions are well recognised in puppies, so these drugs are generally avoided during the growth period. Large breeds are most at risk.
- **Retinal toxicity in cats** linked to enrofloxacin at high exposure, which can cause blindness. This is the reason for strict dose limits on the label.
- **Lowered seizure threshold.** Use caution in epileptic animals.
- **Chelation.** Divalent and trivalent cations (calcium, magnesium, iron, aluminium, zinc) bind the drug in the gut and reduce absorption. Do not mix with antacids, mineral supplements or dairy at the same time.
- Gastrointestinal upset, and local tissue reaction after injection.

Fluoroquinolones can also raise theophylline levels by reducing its clearance, a useful example of a metabolic interaction.

Resistance and responsible use

Fluoroquinolone resistance is built up in steps. **Point mutations** in the genes for gyrase and topoisomerase IV (the quinolone resistance-determining regions) reduce drug binding. **Efflux pumps** and reduced porin entry lower the concentration inside the cell. Plasmid-borne genes, such as the *qnr* family, protect the target and can pass between bacteria, which allows low-level resistance to spread sideways. Several small steps together produce clinical failure.

Resistance to one fluoroquinolone usually means resistance to all of them. Exposure of gut bacteria to sub-lethal drug levels selects resistant E. coli and Campylobacter, which can reach people through food or direct contact.

For this reason the major regulators and WHO treat fluoroquinolones as **critically important** for human medicine. Responsible use means:

- Keep them for infections where culture and sensitivity, or clear clinical judgement, show that first-line drugs will not work.
- Never use them for routine prophylaxis, mass medication or growth promotion.
- Use the right dose for the full intended course. Under-dosing selects resistance.
- Avoid use in food animals unless the label allows it, and observe the withdrawal period. Rules on fluoroquinolone use in food-producing animals differ between countries and have changed over time. For India, check the current notification of the relevant authority and the label.

Nitroimidazoles

Metronidazole is the standard example, with others such as tinidazole, ronidazole and dimetridazole. These are **prodrugs**. In an anaerobic cell, low-redox-potential proteins donate electrons to the nitro group. The reduced form is a reactive radical that damages DNA and kills the organism. In aerobic cells, oxygen removes the electron again, so the drug stays inactive. That explains the **selective toxicity for anaerobes** and protozoa such as Giardia, Trichomonas and Entamoeba.

In dogs and cats metronidazole is used for anaerobic infections, giardiasis and some inflammatory bowel conditions. It penetrates tissues, bone and abscesses well and crosses the blood-brain barrier. Resistance is uncommon but increasing.

The main toxicity concern is **neurotoxicity**, usually seen with prolonged or excessive exposure, with signs such as ataxia, head tilt, nystagmus and seizures. Treatment is stopping the drug and supportive care. Nitroimidazoles are also considered potentially carcinogenic and mutagenic from laboratory evidence. For that reason they are prohibited in food-producing animals in many countries. Check the current Indian notification before any use in a food species.

Nitrofurans and common confusions

Nitrofurans include furazolidone, nitrofurazone and nitrofurantoin. Like nitroimidazoles they are reduced inside the bacterial cell to reactive intermediates that attack DNA and ribosomal proteins, so resistance develops slowly. They have a wide spectrum against Gram-positive and Gram-negative bacteria and some protozoa.

The important residue concept: nitrofuran parent drugs vanish quickly, but their **tissue-bound metabolites** persist for a long time and can be detected in meat, eggs and fish long after treatment. Because of concern about carcinogenicity of these residues, nitrofurans are banned in food animals in many countries, and testing programmes look for the metabolites. Whether and how they are permitted in India is a matter of current notification, so confirm before use. Nitrofurantoin remains a human urinary antiseptic, and in pets it is occasionally used for urinary infection because it concentrates in urine.

Common confusions to avoid:

- Fluoroquinolones act on DNA enzymes, but nitroimidazoles and nitrofurans damage DNA through reduction. Both end in DNA damage, but by different routes.
- Metronidazole is not effective against aerobes, and enrofloxacin is not reliable against anaerobes. Together they cover different gaps, but combination should be justified, not routine.
- A drug with good in vitro activity is not automatically safe in the species. Always check species and age limits.

Concept cleared

Trapped DNA breaks

Fluoroquinolones freeze gyrase and topoisomerase IV on cut DNA, so strand breaks cannot be repaired and the bacterium dies.

Concentration-dependent killing

The peak concentration relative to the MIC drives effect, so the aim is a high peak, not frequent small doses.

Prodrug activation in anaerobes

Nitroimidazoles become toxic only when reduced in low-oxygen cells, which gives anaerobe and protozoal selectivity.

Bound metabolite residues

Nitrofuran metabolites bind to tissue proteins and persist, so a short withdrawal period cannot be trusted and many countries ban the group in food animals.

Memory aid: Fluoroquinolone cautions: CART

Cartilage in young animals, Absorption blocked by cations, Retina in cats, Threshold for seizures lowered.

Compare and contrast

Fluoroquinolones vs nitroimidazoles vs nitrofurans

Feature	Fluoroquinolones	Nitroimidazoles	Nitrofurans
Main target	DNA gyrase and topoisomerase IV	DNA damage after reduction in anaerobes	DNA and protein damage after reduction
Spectrum	Aerobic Gram-negatives, Mycoplasma, some Gram-positives	Anaerobes and protozoa	Broad, includes some protozoa
Key concern	Cartilage damage, feline retinopathy, resistance	Neurotoxicity, carcinogenicity concern	Persistent residues, carcinogenicity concern
Food animal use	Restricted; check current rules	Prohibited in many countries; check Indian rules	Prohibited in many countries; check Indian rules

Enrofloxacin vs marbofloxacin

Feature	Enrofloxacin	Marbofloxacin
Active metabolite	Partly converted to ciprofloxacin	Not converted to ciprofloxacin
Feline retinal risk	Recognised at high exposure	Not a recognised concern at label use
Class concern	Critically important antibacterial	Critically important antibacterial
Interaction with cations	Chelation lowers absorption	Chelation lowers absorption

Species notes

Dogs

Avoid during the rapid growth period, especially in large breeds, because of cartilage damage. Metronidazole can cause neurological signs with prolonged exposure.

Cats

Enrofloxacin can cause retinal damage and blindness at excess exposure, so label limits matter. Marbofloxacin is often chosen when a quinolone is justified.

Poultry

Cattle and buffalo

Fluoroquinolone use in poultry is closely linked to resistant E. coli and Campylobacter reaching people, so rules are strict in many countries. Check the current notification for India.

Use in food animals depends on the label and local law. Withdrawal period for milk and meat must be observed and recorded.

Horses

Fluoroquinolones carry a risk of joint cartilage damage in foals, so they are generally avoided in young animals.

Clinical pearls

Self-test: 10 questions

1. The main target of fluoroquinolones in Gram-negative bacteria is:

Gyrase is the primary target in Gram-negatives, and topoisomerase IV in Gram-positives.

2. Which statement about fluoroquinolone killing is correct?

The peak concentration relative to MIC drives the bactericidal effect.

3. A classic toxicity of enrofloxacin in cats is:

Retinal toxicity and blindness are linked to high exposure in cats.

4. Why are fluoroquinolones avoided in growing puppies of large breeds?

Joint cartilage erosion is seen in growing animals.

5. Which co-administered product reduces fluoroquinolone absorption?

Divalent and trivalent cations chelate the drug in the gut.

6. Which fluoroquinolone is partly converted to ciprofloxacin?

Enrofloxacin is partly de-ethylated to ciprofloxacin; marbofloxacin is not.

7. Metronidazole is selectively toxic to anaerobes because:

Oxygen reverses the activation, so aerobes are spared.

8. A sign of metronidazole neurotoxicity in dogs is:

Central vestibular signs follow prolonged or excessive exposure.

9. Why do nitrofurans cause special residue concern?

Bound metabolites can be found in tissues long after the parent drug has gone.

10. Which practice is NOT responsible fluoroquinolone use?

Routine prophylaxis with critically important drugs selects resistance.

Key points to revise

1. Fluoroquinolones inhibit DNA gyrase and topoisomerase IV and are bactericidal.
2. They have poor activity against anaerobes.
3. Cartilage damage in young animals and retinal damage in cats are the classic toxicities.

4. Cations chelate fluoroquinolones and reduce absorption.
5. Resistance arises by target mutations, efflux and plasmid-borne protection genes.
6. Nitroimidazoles are prodrugs activated in anaerobes and are neurotoxic when overexposed.
7. Nitrofurans leave persistent tissue-bound residues, and many countries ban them in food animals.
8. Responsible use means reserving critically important drugs for proven need and following local rules, which for India must be checked in the current notification.

Go deeper on this site

- Ch 8. Polypeptide and miscellaneous antibiotics (in this book)
- Ch 6. Macrolides, lincosamides and pleuromutilins (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Wikipedia: Fluoroquinolone
- Wikipedia: Nitroimidazole
- FDA Center for Veterinary Medicine: Antimicrobial resistance

CHAPTER 8 OF 19

Polypeptide and miscellaneous antibiotics

Polymyxins (colistin), bacitracin, glycopeptides such as vancomycin and the ionophore antibiotics each work by an unusual mechanism and each carries a distinct stewardship message. The chapter covers why colistin is protected as a last-resort drug and why ionophores are dangerous to non-target species.

After this chapter you can

- Explain how polymyxins disrupt the Gram-negative outer membrane and why they are nephrotoxic
- Describe the status of colistin in food animals and the problem of plasmid-borne resistance, with hedged Indian rules

- Explain the mechanism and use of bacitracin and why it is applied topically
- Describe how vancomycin works and how vancomycin resistance arises
- Explain how ionophores act, their uses in poultry and ruminants, and why they are toxic to horses and dogs

Why these drugs are grouped together

The drugs in this chapter do not belong to one family. They are grouped because each is either a peptide in structure or acts by an unusual mechanism, and because most are poorly absorbed or too toxic for general systemic use. Their value lies in narrow roles: topical use, gut-restricted use, last-resort treatment of resistant Gram-negative infection, or coccidiosis control.

Ask three questions for each drug. What does it attack? Why is it not used like penicillin? What is the stewardship message? The answers follow from the mechanism.

Polymyxins and colistin

Polymyxin B and polymyxin E (**colistin**) are cationic peptides with a fatty tail. The outer membrane of Gram-negative bacteria carries negatively charged lipopolysaccharide (LPS). The positively charged polymyxin binds LPS, displaces the calcium and magnesium that stabilise it, and disrupts the membrane. The cell leaks and dies. The effect is **bactericidal** and does not need the cell to be dividing.

Because the target is the Gram-negative outer membrane, the spectrum is limited to **Gram-negative bacteria** including Pseudomonas, Klebsiella, E. coli and Acinetobacter. Gram-positive bacteria, anaerobes and some naturally resistant genera such as Proteus are not covered.

Absorption from the gut is negligible. This has two consequences. Oral colistin acts in the gut lumen, which made it popular for enteric colibacillosis in young animals. By injection, however, the drug causes **nephrotoxicity and neurotoxicity**, so systemic use is limited to serious infections where other drugs have failed. Polymyxins can also cause neuromuscular blockade, which is worsened by anaesthetics or muscle relaxants.

Colistin is now valued in human medicine as a **last-resort drug** against carbapenem-resistant Gram-negative infection. A plasmid gene, *mcr-1*, was found in bacteria from animals and people, and it moves between bacteria and species. Because heavy use in livestock was seen as driving this resistance, many countries restricted colistin in food animals. India has taken a regulatory step to prohibit colistin in food-producing animals, including as a growth promoter, but you should check the current notification for exact scope, dates and exceptions.

Bacitracin

Bacitracin is a polypeptide produced by *Bacillus subtilis*. It blocks the recycling of a lipid carrier that moves cell wall building blocks across the membrane. Without the carrier, peptidoglycan cannot be completed. The target is a different step from penicillin, so there is no cross-resistance with beta-lactams.

Spectrum is mainly Gram-positive cocci and rods. Bacitracin is **too nephrotoxic for systemic use**, so it is used topically, often in ointments combined with neomycin and polymyxin to widen the spectrum, in eye and skin preparations.

Zinc bacitracin and similar salts have been used in feed as growth promoters because they are poorly absorbed and act in the gut. Growth promotion with antibiotics is increasingly restricted worldwide for stewardship reasons. For India, check the current notification and label for any permitted feed use.

Vancomycin and the glycopeptides

Vancomycin is a large glycopeptide. It binds the **D-alanyl-D-alanine** end of the peptidoglycan precursor and physically blocks the transpeptidase and transglycosylase enzymes from using it. The mechanism is different from beta-lactams, which bind the enzyme itself.

It is active against Gram-positive bacteria including methicillin-resistant staphylococci and Clostridioides difficile, but it cannot cross the Gram-negative outer membrane, so Gram-negatives are not covered. It is not absorbed orally, so it is given intravenously for systemic infection and orally only for gut infections. Adverse effects include nephrotoxicity and ototoxicity, and rapid infusion can cause histamine-mediated flushing.

Resistance in enterococci arises when the terminal D-Ala-D-Ala is replaced by **D-Ala-D-lactate**, which vancomycin binds poorly. The genes (van genes) can spread between bacteria. A famous lesson: avoparcin, a related glycopeptide once used as a growth promoter, was linked to vancomycin-resistant enterococci in farm animals, and it was withdrawn in several regions. Vancomycin itself is not a routine veterinary drug and is held in reserve for resistant infections in companion animals where culture supports its use.

Stewardship lessons and common confusions

Each drug in this chapter teaches a stewardship point. Colistin shows how a drug used for convenience in animals can threaten a human last-resort option, because the resistance gene sits on a plasmid and crosses species. Vancomycin and avoparcin show how a related drug used in feed can select resistance to the human drug. Bacitracin shows how a drug can be useful precisely because it stays on the surface or in the gut. Ionophores show that a drug with no human use can still be dangerous in the wrong animal.

Common confusions:

- **Poor absorption does not mean no resistance.** Gut-restricted drugs still expose the huge bacterial population of the intestine and can select resistant bacteria.
- **Bacitracin and vancomycin both affect cell wall synthesis** but at different steps, and neither is a beta-lactam. There is no cross-resistance with penicillins.
- **Ionophores are called antibiotics but are used mainly as coccidiostats and production aids.** Their rules and their toxicity profile differ from antibiotics used for treatment.
- **Polymyxin B and colistin** are closely related and cross-resistant, so resistance to one predicts resistance to the other.

In practice, record every medicated feed, check the species on the label, and treat any ban or restriction notified by the Indian authorities as binding. Look up the current notification for the exact scope.

Ionophore antibiotics

Monensin, salinomycin, lasalocid and narasin are produced by *Streptomyces*. They are lipid-soluble molecules that bind positive ions (sodium, potassium, calcium) and

carry them across membranes, destroying the ion gradients that cells need. Organisms with high ion demands, such as Gram-positive bacteria and coccidial protozoa, are affected. Gram-negatives are protected by the outer membrane.

Uses in veterinary medicine:

- **Poultry:** coccidiostats in feed. Resistance develops slowly, since the mechanism is physical and not a single enzyme target.
- **Ruminants:** improve feed efficiency. They shift rumen fermentation toward propionate, reduce lactic acid and methane production, and help prevent coccidiosis and bloat in some systems.

Ionophores are not used in human medicine, so concern about cross-resistance to human drugs is smaller than for other classes. The real concern is **toxicity**. Horses are extremely sensitive and develop cardiac and skeletal muscle damage from contaminated feed. Dogs, cats and some birds such as turkeys can also be poisoned. Cattle are tolerant at label levels but are poisoned by feed-mixing errors. Signs include anorexia, weakness, dyspnoea and sudden death. Mixing errors and wrong species feeding are the commonest causes.

Ionophores also interact with drugs such as tiamulin, which can raise toxicity because tiamulin slows their metabolism. Never mix them in feed meant for horses, and always keep records of which feed went to which flock or herd.

Concept cleared

Membrane attack on Gram-negatives
Cationic polymyxins bind LPS and break the outer membrane, so they act only on Gram-negative bacteria and are toxic to kidney and nerve.

Poor absorption decides the use
Bacitracin and oral colistin and vancomycin stay in the gut or on the skin, which is both their purpose and the reason systemic toxicity limits injection.

Binding the substrate, not the enzyme

Vancomycin binds D-Ala-D-Ala so cell wall enzymes cannot use it, and resistance swaps the terminal to D-Ala-D-lactate.

Ionophore selectivity and danger

Ionophores wreck ion gradients, helping against Gram-positives and coccidia, but the same action poisons horses and dogs.

Memory aid: Four P-B-V-I roles

Polymyxin breaks the outer membrane, Bacitracin blocks the carrier, Vancomycin binds the D-Ala tail, Ionophores wreck the ion gradient.

Compare and contrast

Polypeptide and glycopeptide antibiotics

Drug	Target	Spectrum	Main limitation
Colistin / polymyxin B	LPS and outer membrane	Gram-negative	Nephrotoxic, neurotoxic, last-resort status
Bacitracin	Lipid carrier in cell wall synthesis	Gram-positive	Nephrotoxic, topical use only
Vancomycin	D-Ala-D-Ala of peptidoglycan precursor	Gram-positive	Not absorbed orally, resistance via D-Ala-D-Lac
Ionophores	Ion gradients across membranes	Gram-positive and coccidia	Toxic to horses, dogs and turkeys

Oral colistin vs injectable colistin

Feature	Oral	Injectable
Absorption	Negligible	Complete by route
Site of action	Gut lumen	Systemic
Toxicity	Low	Kidney and nerve toxicity
Stewardship	Food animal use restricted in many countries; check Indian notification	Reserve for resistant infection under veterinary control

Species notes

Poultry

Ionophores are used as coccidiostats. Never feed these medicated feeds to other species and observe withdrawal periods. Colistin use as a feed additive is a stewardship concern, so check current Indian rules.

Horses

Extremely sensitive to ionophores. Accidental feeding of poultry or cattle feed has caused fatal cardiac and muscle damage.

Dogs and cats

Susceptible to ionophore poisoning from poultry feed or cattle feed. Topical bacitracin combinations are used for skin and eye problems.

Cattle and buffalo

Ionophores improve rumen efficiency at label levels, but mixing errors cause toxicity. Colistin was used for enteric disease in calves but is restricted in food animals in many places.

Pigs

Oral polymyxins have been used for post-weaning E. coli diarrhoea, which is the type of use now under scrutiny because of mcr resistance.

Clinical pearls

Self-test: 10 questions

1. Polymyxins act by:

Their cationic structure binds LPS and breaks the Gram-negative outer membrane.

2. Which organisms are covered by colistin?

The target is found only on Gram-negative cells.

3. The main toxicity of injected colistin is:

Kidney and nerve toxicity limits systemic use.

4. The plasmid gene linked with transferable colistin resistance is:

mcr-1 modifies LPS and spreads between bacteria.

5. Why is bacitracin used topically?

It is nephrotoxic when absorbed, so topical use is safer.

6. Vancomycin binds to:

This blocks cell wall enzymes from using the substrate.

7. Vancomycin resistance in enterococci involves:

The altered terminus binds vancomycin poorly.

8. Ionophores act by:

They collapse ion gradients in susceptible cells.

9. Which species is most sensitive to ionophore poisoning?

Horses develop cardiac and skeletal muscle damage from small exposure.

10. Ionophores are not effective against Gram-negative bacteria because:

The outer membrane blocks entry of these molecules.

Key points to revise

1. Polymyxins bind LPS and disrupt the outer membrane of Gram-negative bacteria.
2. Injected polymyxins are nephrotoxic and neurotoxic.
3. Plasmid-borne mcr resistance threatens colistin as a last-resort drug.
4. Check the current Indian notification for colistin and feed additive rules.
5. Bacitracin inhibits cell wall synthesis and is used topically.
6. Vancomycin binds D-Ala-D-Ala and is active against Gram-positives only.
7. Ionophores carry ions across membranes and are used as coccidiostats and rumen modifiers.
8. Ionophores are highly toxic to horses and also to dogs and turkeys.

Go deeper on this site

- Ch 9. Antimicrobial resistance and stewardship (in this book)
- Ch 7. Fluoroquinolones and other synthetic antibacterials (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Wikipedia: Polymyxin
- Wikipedia: Ionophore
- FDA Center for Veterinary Medicine: Antimicrobial resistance

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Antimicrobial resistance and stewardship

How bacteria become resistant, how resistance spreads between animals, people and the environment, and what a veterinarian does about it. Covers the WHO AWaRe idea, withdrawal periods and residue limits, and why treatment records matter.

After this chapter you can

- Describe the main biochemical mechanisms of antimicrobial resistance
- Explain how resistance genes spread between bacteria and between species
- Explain the AWaRe classification idea and how it guides drug choice
- Explain withdrawal period, MRL and why FSSAI limits (hedged) matter for food safety
- List the elements of good stewardship and treatment record keeping

What resistance means

A bacterium is **resistant** when it can grow at drug concentrations that would normally stop it. In the laboratory this is measured by the **minimum inhibitory concentration (MIC)** and compared with a breakpoint set by expert committees. Treatment fails when the concentration that can safely be reached in the patient is not high enough relative to the MIC.

Resistance can be **intrinsic**, a natural feature of the species (for example, Gram-negatives are naturally protected from vancomycin by the outer membrane), or **acquired**, through mutation or gene transfer. Antimicrobial resistance is recognised by WHO as a major global health threat. Use in animals, in people and in the environment all contribute, which is the **One Health** view.

An important idea: antimicrobials do not create resistance genes in most cases. They **select** bacteria that already carry them. Every exposure, particularly to low or inadequate concentrations, gives the resistant survivors room to multiply.

Mechanisms of resistance

Bacteria use a small number of strategies, and each links to a drug class you already know.

- **Enzymatic inactivation.** Beta-lactamases break the beta-lactam ring. Other enzymes modify aminoglycosides or chloramphenicol.
- **Target change.** The binding site is altered so the drug no longer fits. Examples: altered penicillin-binding protein in MRSA, gyrase mutation for fluoroquinolones, ribosomal methylation for macrolides, D-Ala-D-Lac for vancomycin.
- **Reduced entry.** Loss or narrowing of porins in Gram-negative outer membranes.
- **Efflux.** Pumps remove the drug as fast as it enters, which is common with tetracyclines and fluoroquinolones.
- **Bypass.** The cell uses another pathway or makes extra target, as with resistance to trimethoprim or sulphonamides.

Other protective states are not genetic. **Biofilms** embed bacteria in a matrix where drug penetration is poor and cells grow slowly, and **persister** cells survive without being genetically resistant. This is why infections on implants, in the udder or in chronic wounds often relapse.

How resistance spreads

Resistance spreads by **vertical** inheritance when a resistant cell divides, and by **horizontal gene transfer** between cells. The three routes are conjugation (direct transfer of plasmids through contact), transduction (carried by bacteriophage) and transformation (uptake of free DNA).

Plasmids can carry several resistance genes at once. This gives **co-selection**: using one drug selects bacteria that are also resistant to other drugs on the same plasmid. A farm using tetracycline may thereby maintain resistance to other classes as well.

Resistant bacteria travel on food, water, manure, hands, hospital surfaces and wildlife. A dog with a resistant skin infection can share the organism with its owner. A resistant E. coli from poultry can colonise people who handle the birds. Residues of antibiotics in manure and water can keep selecting resistance in the environment.

Stewardship and the AWaRe idea

Stewardship means using antimicrobials so that they cure the patient and stay effective for the future. The WHO **AWaRe** framework sorts antibiotics into three groups for human medicine:

- **Access:** first- and second-choice drugs with narrower spectrum and lower resistance potential, which should be widely available.
- **Watch:** drugs with higher resistance potential, whose use should be limited to specific indications and monitored.
- **Reserve:** last-resort drugs for multi-resistant infections, used with strict oversight.

Veterinary medicine borrows the same logic: start with narrow, first-line drugs, restrict the critically important ones such as fluoroquinolones, third-generation cephalosporins and colistin, and keep last-resort drugs for people. The exact lists for animals differ, so use the current WOAH or national list.

Practical stewardship steps:

1. Confirm that the condition is bacterial and needs treatment. Viral and many self-limiting conditions do not.
2. Take samples for culture and sensitivity before treatment where possible, especially in recurrent or serious cases.
3. Choose the narrowest effective drug and a route that reaches the site.
4. Use the correct dose and duration, and avoid sub-therapeutic exposure.
5. Do not use antibiotics for growth promotion or routine prophylaxis.
6. Prevent disease through vaccination, hygiene, nutrition and biosecurity.
7. Review the response and stop when appropriate.

Withdrawal periods, residue limits and food safety

When a drug is given to a food-producing animal, residues can remain in milk, meat, eggs and honey. The **withdrawal period** is the minimum time that must pass between the last dose and the collection of milk or slaughter of the animal so that residue levels have fallen below the legal limit. It depends on the drug, formulation, route, species and product. The label of the product is the authority, and the period

may be longer if the animal has liver or kidney disease or if the product is used outside the label.

The legal limit is the **maximum residue limit (MRL)**: the highest residue concentration of a substance accepted in a food. In India the Food Safety and Standards Authority (FSSAI) regulates antibiotic and pharmacologically active substance limits in food. Limits, listed substances and the regulations are amended from time to time, so check the current FSSAI notification and the label.

Why residues matter: they can cause allergy in sensitive consumers, disturb human gut bacteria, select resistant bacteria and, in milk, interfere with fermentation in dairy products. Milk from treated animals during withdrawal must be discarded, not mixed in the bulk tank. Using a drug extra-label, for example a drug prohibited in food animals, can make residues illegal regardless of the interval.

Records are the tool that makes all this work. A **treatment record** should note the animal identity, date, diagnosis, drug and batch, dose, route and duration, the person treating, and the earliest date for milk or slaughter. Good records let you trace a residue violation, check compliance, review which drugs are used most, and justify decisions. Keep culture reports and prescriptions with them.

Surveillance, One Health and the veterinarian's role

Resistance cannot be managed by one clinic alone. **Surveillance** programmes collect resistance data from animals, food, people and the environment so that trends can be seen and policy can be set. Veterinary laboratories contribute by reporting culture and sensitivity results accurately and by following standard methods and breakpoints.

The veterinarian has several roles. As a prescriber, you decide whether an antimicrobial is needed, which one and for how long. As an adviser, you explain to farmers why completing a course matters, why leftover tablets must not be shared or reused, and why a milk discard period is not optional. As a record keeper, you provide the data that makes surveillance and food safety checks possible.

Common confusions:

- **A resistant bacterium does not make the animal resistant.** The resistance belongs to the microbe, not the patient.

- **Stopping a course early is not the main cause of resistance.** The bigger drivers are unnecessary use and exposure to inadequate drug levels. Duration should be as short as is effective.
- **Rotating drugs does not by itself fix resistance.** Reducing total use and choosing correctly does more.
- **A sensitive result in the laboratory does not guarantee cure.** Site of infection, drug penetration and host defence still matter.

Farmers should be advised to follow only the veterinarian's prescription, to avoid buying antibiotics over the counter for self-medication, and to keep the treatment record on the farm.

Concept cleared

Selection, not creation
Antimicrobials usually select resistant bacteria already present, so every unnecessary or under-dosed course increases the resistant share.

Five resistance mechanisms
Inactivating enzymes, altered targets, reduced entry, efflux and bypass explain nearly all acquired drug resistance.

Horizontal transfer and co-selection
Plasmids move between bacteria and often carry several genes, so one drug can maintain resistance to many.

Withdrawal period and MRL
The withdrawal period is the time needed for residues to fall below the MRL, and recorded treatment dates make it enforceable.

Memory aid: Resistance mechanisms: DREAM
Destroy the drug, Reduce entry, Efflux it, Alter the target, bypass by Making another pathway.

Compare and contrast

AWaRe groups

Group	Idea	Veterinary translation
Access	First-line, narrow spectrum	Preferred starting choices
Watch	Higher resistance potential, limited indications	Use after sensitivity evidence; restrict critically important drugs
Reserve	Last resort for multi-resistant infections	Keep for people; avoid in food animals

Intrinsic vs acquired resistance

Feature	Intrinsic	Acquired
Origin	Natural trait of the species	Mutation or gene transfer
Predictability	Predictable from species	Needs testing
Example	Gram-negatives and vancomycin	ESBL-producing E. coli
Spread	Not transferable	Can spread horizontally

Species notes

Dairy cattle and buffalo
Milk withdrawal must be observed and recorded. Mastitis treatment should follow culture where possible, and dry-cow therapy should not be routine for every quarter.

Poultry
Flock-level treatment and prophylaxis drive resistance in E. coli and Salmonella. Biosecurity and vaccination are preferred. Eggs and meat have separate withdrawal rules.

Pigs
In-feed medication for groups raises co-selection risk. Follow label and avoid routine prophylaxis.

Dogs and cats
Resistant skin and urinary pathogens such as MRSP and ESBL E. coli can be shared with owners. Culture

before using critically important drugs.

Horses
Hospital-acquired resistant infections occur, so hygiene and surgical prophylaxis protocols matter. Check rules on equine use in the food chain.

Clinical pearls

Self-test: 10 questions

1. Resistance by beta-lactamase is an example of:

The enzyme breaks the beta-lactam ring.

2. Which mechanism is typical of tetracycline resistance?

Efflux pumps are a common mechanism for tetracyclines.

3. Transfer of plasmid DNA through direct cell contact is:

Conjugation uses direct contact.

4. Transfer of DNA by bacteriophage is called:

Phages carry bacterial DNA between cells.

5. In AWaRe, Reserve antibiotics are:

They are kept for infections that no other drug can treat.

6. The withdrawal period is:

It lets residues fall below the MRL.

7. MRL stands for:

It is the highest accepted residue concentration in food.

8. Co-selection occurs when:

Selecting for one gene retains the others on the same element.

9. Which is NOT a stewardship step?

Routine prophylaxis selects resistance and is discouraged.

10. Relapse of udder or implant infection despite a susceptible organism may be explained by:

Biofilms limit drug penetration and protect slow-growing cells.

Key points to revise

1. Resistance is measured by MIC against a breakpoint.
2. Mechanisms: enzyme inactivation, target change, reduced entry, efflux and bypass.
3. Horizontal transfer occurs by conjugation, transduction and transformation.
4. Resistance in animals, people and the environment is linked through One Health.
5. AWaRe groups antibiotics as Access, Watch and Reserve.
6. Withdrawal period is the time for residues to fall below the MRL.
7. FSSAI regulates antibiotic residue limits in India, so check the current notification.

8. Treatment records, culture reports and narrow-spectrum first-line choices are the base of stewardship.

Go deeper on this site

- Ch 10. Drug residues, MRLs and food safety (in this book)
- Ch 8. Polypeptide and miscellaneous antibiotics (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Concepts
- Veterinary Drug Concepts Clearly Explained

Sources

- WHO: Antimicrobial resistance fact sheet
- FDA Center for Veterinary Medicine: Antimicrobial resistance
- Wikipedia: Antimicrobial resistance

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Drug residues, MRLs and food safety

Why traces of veterinary drugs persist in milk, meat, eggs and honey, how maximum residue limits and withdrawal periods protect the consumer, and how the Indian food-safety system, testing and farm practice fit together. Written for the veterinarian who prescribes the drug and therefore owns the residue risk.

After this chapter you can

- Explain why residues occur and which animal products are affected
- Define ADI, MRL and withdrawal period and describe how they relate to each other
- Explain why withdrawal periods differ between milk, meat, eggs and honey
- Outline the Indian food-safety framework for residues, with appropriate hedging
- Describe screening and confirmatory testing and the farm practices that prevent violations

What a residue is and why it matters

A **drug residue** is the parent drug, its metabolites, or related substances that remain in an edible product after treatment. The animal's body does not clear a drug at the moment treatment stops. Elimination follows the pharmacokinetics you studied earlier, so some drug stays in blood and tissues for a time, and a part of it enters milk, eggs or honey.

Residues matter for several reasons. Some people are sensitised to drugs such as penicillins, and a trace in milk can trigger a reaction. Sub-inhibitory antibiotic exposure through food may favour resistant gut bacteria. Some drugs are toxic or carcinogenic to humans and have no place in food animals at all. Finally, antibiotic in milk has a technological cost: it inhibits the starter cultures used for curd, yoghurt and cheese, so processors reject such milk.

Residue control is a food-safety duty shared by the farmer, the veterinarian, the processor and the regulator. The veterinarian is the key person because the treatment decision, and the advice on withholding the product, starts with the prescription.

Residues in milk, meat, eggs and honey

Each product behaves differently, and this is why one drug can carry several different withdrawal times.

- **Milk.** Many drugs reach milk by passive diffusion. Weak bases are trapped in milk because milk is slightly more acidic than plasma (ion trapping), and lipid-soluble drugs concentrate in milk fat. Intramammary products leave high local concentrations in the udder. Milk is consumed fresh and pooled, so one treated cow can contaminate a whole tank.
- **Meat and offal.** Residues persist in tissues. Kidney and liver often hold the highest levels because they handle elimination, and injection sites can keep drug for a long time. Tissue binding and depot formulations lengthen the stay.
- **Eggs.** Drug may be deposited in yolk or albumen during egg formation, and the effect lasts until the follicles that formed during treatment have been laid. Many drugs are not approved for layers whose eggs are for human consumption.
- **Honey.** Bees are food-producing animals too. Antibiotics put in hives for brood disease can remain in honey for a long period because honey does not

metabolise them. Honey is therefore a well-known problem product in international trade.

Remember that residues are not only antibiotics. Anthelmintics, anti-inflammatories such as NSAIDs, hormones, coccidiostats and pesticides used as ectoparasiticides can all appear.

ADI, MRL and the logic of the safe limit

Regulators work backwards from human safety, in steps.

1. Toxicology studies identify a level with no observed adverse effect. A safety factor is applied to give the **acceptable daily intake (ADI)**, the amount a person can consume every day for life without appreciable risk.
2. Using typical food consumption, the ADI is divided among the foods that may contain the drug. This gives the **maximum residue limit (MRL)**, the highest concentration of residue legally accepted in a specified food (for example muscle, liver, kidney, milk, eggs).
3. Studies of how fast residues fall in the target tissue show when the residue has dropped below the MRL. That time, with an added margin, becomes the **withdrawal period** (also called withholding period).

At international level, expert committees such as JECFA evaluate veterinary drugs and the Codex Alimentarius Commission adopts MRLs that countries can use as a reference. Individual countries and trading blocs may set their own values, so an MRL for a drug in one market can differ from another. For India, always check the current notification of the food regulator for the value that applies.

A common confusion: an MRL is a legal and analytical limit, not a toxic threshold. A level just above it is not automatically harmful, but it is a violation. The ADI is the health-based figure and the MRL is the enforcement figure derived from it.

Withdrawal-period logic

The withdrawal period is the minimum time between the last dose and the collection of milk, eggs, honey or slaughter for meat. It applies to a product, a species, a formulation and a route, because each of these changes the elimination curve. A withdrawal period set for an injectable in one species cannot be copied to another species or to a long-acting form.

Factors that lengthen real residue persistence include:

- Liver or kidney disease, which slows metabolism and excretion.
- Depot or long-acting formulations and large intramuscular volumes at one site.
- Higher doses or longer courses than the label, and repeated treatments.
- Poor feed intake, dehydration and heavy milk yield changes in mastitis.
- Combining drugs that compete for elimination.

Extra-label use is the key trap. When a drug is used outside its label, the labelled withdrawal no longer protects anyone, because it was never measured for that use. The veterinarian must then take responsibility for a conservative, justified withdrawal, ideally supported by published data or by advice from a residue authority. If no reliable figure exists, the safe choice is not to use the drug in food animals.

Also note that milk and meat withdrawals are different numbers for the same drug, and the longer one applies to a cull animal whose milk has already been discarded. Treating a cow does not stop at the end of the milk discard time if she is going to the abattoir.

The Indian food-safety system

In India, food safety is governed by the Food Safety and Standards Act, 2006, under which the Food Safety and Standards Authority of India (FSSAI) frames standards and regulations for food, including contaminants and residues. Veterinary drug and antibiotic limits in foods of animal origin are set through FSSAI regulations and amendments, and some uses of antimicrobials in food animals have been restricted or banned by the drug and veterinary authorities. These rules change from time to time. Students should **check the current notification** for any particular drug, limit or ban rather than relying on a textbook list.

Other parts of the system also matter. State animal husbandry and dairy departments, dairy cooperatives and large processors run milk-quality programmes, and export-oriented products such as shrimp, meat and honey are tested for residues under separate export-residue monitoring arrangements to meet importing-country limits. Antimicrobial stewardship policies, such as national action plans against resistance, link residue control to the wider resistance problem.

In practice, the weak points are often not the law but its enforcement: unrecorded treatment, sale of milk during treatment, over-the-counter drug supply and the use of banned or human-use drugs. The veterinarian can help by prescribing only appropriate products, keeping treatment records, and explaining the withdrawal in language the farmer will follow.

Testing and compliance on farms

Residue testing uses two tiers. **Screening tests** are quick and cheap and are meant to catch most positives. They include microbial inhibition tests, in which antibiotic stops bacterial growth or a colour change, and receptor-binding or lateral-flow strip tests, often designed for beta-lactams and tetracyclines. They tell you that an inhibitory substance may be present but usually not which one, and false positives and false negatives are possible. **Confirmatory tests**, mostly chromatography with mass spectrometry, identify the compound and measure its concentration against the MRL, and are used for legal action.

Compliance on the farm rests on simple habits:

- Identify every treated animal clearly and record drug, date, route and the date the product can be used.
- Keep treated animals' milk separate and discard it for the full period, including milk from all quarters, not only the treated one.
- Use the label dose and route, and avoid unneeded extra-label use.
- Keep feed and water free of medicated material meant for other animals, since carry-over also causes residues.
- Do not send treated animals to slaughter before the meat withdrawal has passed.
- Prevent discarded milk being fed to calves without thought, since this exposes them to antibiotic.

Good practice also protects the farmer: milk rejected at the dairy plant is a direct financial loss, and repeated violations can end supply contracts.

Concept cleared

ADI and MRL are different

ADI is a health-based intake figure derived from toxicology. MRL is an enforcement limit in a particular food, derived from the ADI and food consumption. The withdrawal period is the time needed for residue to fall below the MRL.

Withdrawal is product-specific

A drug can have different withdrawal times for milk, meat, eggs and honey, and for different species, doses, routes and formulations. A single number cannot be borrowed across these.

Extra-label use removes the safety margin

Labelled withdrawal was measured only for the labelled use. Outside the label the veterinarian must justify a conservative period or avoid the drug in food animals.

Residues carry three risks

They can cause hypersensitivity, favour resistance, and disrupt dairy processing. Some substances are banned in food animals regardless of any limit.

Memory aid: ADI then MRL then WP

A Dose Is safe (ADI), More Residue Lost (MRL) gives the legal limit, Wait Patiently (WP) until residue falls below it. Order: safe intake, legal limit, waiting time.

Compare and contrast

Residue behaviour by product

Product	Main route into product	Why it persists	Practical point
Milk	Diffusion from blood; direct from intramammary route	Ion trapping and fat solubility; udder depot	Pooled milk; discard milk from all quarters
Meat and offal	Tissue distribution and binding	Liver, kidney and injection-site depots	Meat withdrawal applies even after milk discard ends
Eggs	Deposition during yolk and albumen formation	Drug present until treated follicles are laid	Many drugs not approved for table-egg layers
Honey	Direct addition to hives	Not metabolised in honey	Major trade problem; avoid antibiotics in honey flow

ADI, MRL and withdrawal period

Term	Meaning	Set by	Used for
ADI	Daily lifetime intake without appreciable risk	Toxicology and a safety factor	Starting point for the MRL
MRL	Maximum legal residue concentration in a food	Regulators, with Codex or national bodies as reference	Enforcement and trade
Withdrawal period	Time from last dose to collection or slaughter	Residue-depletion studies on the product	Farm and veterinary decisions
Extra-label withdrawal	Veterinarian's justified conservative period	Prescribing veterinarian	Use outside the label

Species notes

Dairy cattle and buffalo

Milk and meat withdrawals are separate. Milk from every quarter is discarded after systemic or intramammary treatment. Pooling in village collection makes a single

Sheep and goats

Few products are licensed for these species, so extra-label use is common and withdrawal times must be chosen with care. Goat milk is often used for human consumption.

treated animal a risk to many suppliers.

Poultry
Eggs and meat have separate considerations. Medication through drinking water or feed reaches the whole flock, so withdrawal must cover every bird and line. Many antimicrobials are not suitable for laying hens.

Pigs
In-feed medication is common, so carry-over in feed mills and shared feeders can produce residues. Observe the full meat withdrawal before slaughter.

Honey bees
Antibiotics for brood disease can persist in honey. Treat only outside honey flow and prefer management and hygiene over drug use.

Clinical pearls

Self-test: 10 questions

1. The maximum residue limit (MRL) is best defined as:

MRL is an enforcement limit for a particular food. The time is the withdrawal period, and the toxicity figure is not what an MRL represents.

2. The acceptable daily intake (ADI) is derived mainly from:

ADI is a health-based figure from toxicology, which regulators then use to set MRLs.

3. Why can ion trapping increase drug concentration in milk?

Weak bases ionise in the slightly acidic milk and cannot easily diffuse back to plasma.

4. A drug is used outside its label in a dairy cow. The labelled withdrawal:

Labelled withdrawals were generated only for the labelled use.

5. Which statement about honey is correct?

Honey does not metabolise antibiotics, so residues can persist and affect trade.

6. A rapid strip test in milk is positive for beta-lactam. This should be interpreted as:

Screening tests are presumptive. Confirmation with chromatography and mass spectrometry is the legal standard.

7. Which factor is most likely to lengthen actual residue persistence?

Depots release drug slowly and keep tissue levels above the limit for longer.

8. A cow treated for mastitis has finished her milk discard time but is sold for slaughter. What must be checked?

Milk and meat withdrawals are separate and the tissue withdrawal may be longer.

9. The international body that adopts reference MRLs for veterinary drugs in food is:

Codex adopts MRLs after expert evaluation, for example by JECFA, as international reference values.

10. Which statement about Indian rules on veterinary drug limits is most appropriate?

Limits and bans are revised over time, so the current notification is the authority.

Key points to revise

1. A residue is the drug or its metabolites remaining in food after treatment.
2. Residues can cause allergy, favour resistance and spoil dairy fermentation.
3. ADI is health-based; MRL is the enforcement limit for a food.
4. Withdrawal period is the time needed for residue to fall below the MRL.
5. Milk, meat, eggs and honey each need their own withdrawal consideration.
6. Extra-label use removes the protection of the labelled withdrawal.
7. Indian limits and bans are set through FSSAI and other authorities; check the current notification.
8. Good records, animal identification and separation of treated milk prevent most violations.

Go deeper on this site

- Ch 11. Mastitis and intramammary therapy (in this book)
- Ch 9. Antimicrobial resistance and stewardship (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Concepts
- Veterinary Drug Concepts Clearly Explained

Sources

- Codex Alimentarius, FAO and WHO
- Food Safety and Standards Authority of India
- WHO, Antimicrobial resistance fact sheet

CHAPTER 11 OF 19

Mastitis and intramammary therapy

How the udder environment and the causal organism decide whether antibiotic therapy will work, and how lactating-cow therapy, dry-cow therapy, teat sealants and dips are used. The chapter links treatment choice to culture, residue control and the reduction of antibiotic use on dairy farms.

After this chapter you can

- Explain why pathogen type and udder physiology determine treatment success
- Distinguish contagious from environmental mastitis and the therapeutic consequence of each
- Compare lactating-cow and dry-cow therapy, including blanket and selective approaches
- Describe how teat sealants and teat dips prevent new infection
- Outline residue management and strategies to reduce antibiotic use in mastitis control

Why mastitis therapy is different

Mastitis is inflammation of the mammary gland, usually caused by bacteria that enter through the teat canal. It is the commonest reason for antimicrobial use in dairy herds, and it is also the commonest cause of antibiotic residues in milk. Therapy is not as simple as choosing a drug that kills the organism in a test tube.

Three features of the udder complicate treatment. First, the alveoli and ducts are a closed tree, so drug placed in the teat may not reach infected deep tissue, especially when ducts are blocked by swelling and debris. Second, milk is a poor environment for many drugs: its pH, fat and protein content change activity. Third, some bacteria live inside host cells or in microabscesses, where drug concentrations are low.

For this reason, treatment decisions should consider the organism, the stage of lactation, the duration of infection and the likelihood of cure, not only the clinical signs.

Contagious and environmental pathogens

The grouping of pathogens guides both therapy and control.

- **Contagious pathogens** spread from cow to cow, mainly at milking. Examples are *Streptococcus agalactiae*, *Staphylococcus aureus* and *Mycoplasma* species. Control relies on milking hygiene, post-milking teat dips, milking order and culling of chronic carriers.
- **Environmental pathogens** come from bedding, manure and wet surroundings. Examples are *Escherichia coli* and other coliforms, and *Streptococcus uberis*. Control relies on clean, dry bedding, stall hygiene, teat preparation and dry-period management.

The therapeutic meaning is important. *S. agalactiae* is usually very sensitive to penicillins and responds well. *S. aureus* often responds poorly in established infections, because it can sit inside cells, form scar tissue, and in some strains produce beta-lactamase. Coliform mastitis is often acute with endotoxin shock; the udder frequently clears the bacteria itself, so supportive care (fluids, anti-inflammatory drugs) is the priority and the role of antibiotics depends on the severity and on the veterinarian's judgement. *Mycoplasma* lacks a cell wall, so beta-lactam antibiotics cannot work, and infected cows are usually segregated or culled. Yeasts, algae such as *Prototheca*, and some fungi do not respond to antibacterial treatment, and antibiotics may even worsen yeast infections.

Culture and antibiotic choice in lactation

Culture is the most useful tool for rational use. A properly collected, aseptic quarter sample cultured on suitable media identifies the organism. On-farm culture systems let the herd team separate quarters that need antibiotic from those that do not: for example, a gram-negative result in a mild case, or no growth at all, may mean that no antibacterial treatment is required.

Choice of drug follows three principles.

1. **Narrowest effective spectrum.** For gram-positive pathogens such as streptococci, a narrow-spectrum penicillin is usually preferred. Broad-spectrum and critically important agents, such as later-generation cephalosporins and fluoroquinolones, should be kept for cases where culture or sensitivity testing justify them.

2. **Route.** Mild clinical cases of gram-positive infection are generally treated by the intramammary route, which gives high local concentration. Severe cases with systemic signs may need parenteral therapy in addition, since the udder may not take up intramammary drug when it is badly swollen, and bacteraemia may be present.
3. **Duration.** Treatment should continue for the labelled or evidence-supported duration; stopping early encourages relapse and selection of resistant survivors.

Remember that susceptibility on a laboratory plate does not guarantee cure in the udder. Breakpoints are often derived from blood concentrations, while milk and tissue conditions differ. Cure also depends on the cow: older cows with a long infection, high somatic cell counts and multiple quarters infected cure less often.

Dry-cow therapy and teat sealants

The dry period is a key moment in the udder's cycle. New infections are most common early in involution and just before calving, when the protective keratin plug is not yet formed or is weak. Dry-cow therapy has two aims: to cure infections present at drying off, and to prevent new infections during the dry period.

Dry-cow intramammary products are formulated for a slow release and a long duration of action, because the drug is not removed by milking. Two strategies are used.

- **Blanket dry-cow therapy** treats all quarters of all cows at drying off. It is simple and effective but leads to the most antibiotic use and treats many healthy quarters.
- **Selective dry-cow therapy** treats only cows or quarters considered infected, based on records such as somatic cell counts, clinical history, culture or tests. It reduces antibiotic use but needs good records and a low-prevalence herd to avoid more new infections.

Internal teat sealants are non-antibiotic pastes, often based on bismuth subnitrate, infused into the teat canal to act as an artificial keratin plug. They prevent bacteria from entering and can be used alone in cows known to be uninfected, or together with antibiotic in cows that need treatment. A key point is that a sealant does not cure existing infection and that infusion must be hygienic. Infusing contaminated material into the teat does more harm than good.

Teat dips and the mechanism of prevention

Most mastitis control is non-therapeutic. **Post-milking teat dips** disinfect the teat skin and canal while the sphincter is still open after milking, killing bacteria that would otherwise enter. Common active agents include iodophors, chlorhexidine and other antiseptics, and emollients prevent chapping. Post-dipping mainly reduces contagious infections because it removes organisms left on the teat from milking. **Pre-milking dips** or wipes reduce environmental pathogens, and teats must be dried so that residual dip does not enter milk.

Complementary practices give the full picture: well-maintained milking machines, correct liner function, clean hands or gloves, milking infected cows last, fresh water and bedding, and good nutrition including vitamin E and selenium in the dry period to support immunity. Somatic cell counts, California Mastitis Test results and bulk-tank cultures give early warning. The value of this approach is that every infection prevented is a treatment, a discard and a residue risk avoided.

A common confusion is to treat dips as therapy. They do not cure established intramammary infection, and they are not substitutes for antibiotics in clinical cases, but they remain the best long-term way to lower antibiotic use.

Residue management and reducing antibiotic use

Every intramammary product has its own milk discard time and a separate meat withdrawal time. Because the udder tubes act locally and milk is the product, **discard times are for milk from all quarters** after systemic therapy, and from the treated cow's milk supply as a whole according to the label. Dry-cow products bring a different issue: if a cow calves early, before the minimum interval after dry treatment, her early milk may contain drug. The label gives the required interval between treatment and calving. Check the current label and rules for the specific product, since they differ between products and countries.

Practical residue steps include clear marking of treated cows, milking them last, keeping their milk out of the tank, using a screening test before a treated cow's milk returns to the vat, and keeping treatment records. Do not feed waste milk containing antibiotic to calves without recognising that it can select resistant gut bacteria.

To reduce antibiotic use:

- Prevent infection with hygiene, dips, sealants and dry-period management.
- Use culture to treat only quarters likely to benefit, and consider no antibiotic in mild gram-negative or no-growth cases.
- Use selective dry-cow therapy where herd conditions allow it.
- Cull chronic, non-responsive cows, particularly those with *Staph. aureus* or mycoplasma infection.
- Choose narrow-spectrum agents first and keep critically important antibiotics for justified cases.
- Review results regularly, since stewardship is a cycle of measuring, adjusting and measuring again.

Indian dairy practice is often smallholder-based with hand milking, and the principles are unchanged: clean milking, teat dipping, early detection, and treatment guided by culture where it is available. Check the current regulations and notifications on antimicrobial use in food animals.

Concept cleared

Treat the pathogen, not the signs
Streptococci respond to narrow-spectrum penicillin, Staph. aureus often does not, coliform mastitis needs supportive care, and Mycoplasma and yeasts do not respond to standard antibacterials.

Dry period is a prevention window
Dry-cow products cure existing infection and protect against new ones in involution, when the keratin plug is not yet fully formed.

Sealant is a barrier, not a drug
Internal teat sealants block the teat canal physically. They do not cure infection and must be infused hygienically.

Prevention is the best stewardship

Dips, milking hygiene and dry-period management reduce infections and so reduce treatments, discards and residue risk.

Memory aid: SAS for contagious

Contagious mastitis: Strep agalactiae, Staph aureus, Mycoplasma spread at milking. Environmental: E. coli and Strep uberis come from bedding. Remember: 'milking machine spreads, bedding breeds'.

Compare and contrast

Contagious and environmental mastitis

Feature	Contagious	Environmental
Examples	S. agalactiae, S. aureus, Mycoplasma	E. coli, other coliforms, S. uberis
Source	Infected udders, spread at milking	Bedding, manure, wet surroundings
Main control	Milking hygiene, post-milking dip, culling	Clean dry housing, teat preparation, dry-period care
Therapy note	Variable: streptococci respond well, S. aureus and Mycoplasma poorly	Coliform cases often need supportive care; self-cure is common

Blanket and selective dry-cow therapy

Feature	Blanket	Selective
Cows treated	All cows, all quarters	Only cows or quarters judged infected
Antibiotic use	Highest	Lower
Requirements	Few records needed	Good records, culture or cell counts, low infection prevalence
Companion measure	Sealant optional	Sealant commonly used in uninfected cows

Species notes

Cattle

Most intramammary products are licensed for cows. Follow the label discard times, and use culture and cell-count records for selective therapy.

Buffalo

Mastitis is a major problem, with narrow, long teats and hand milking in many herds. Data specific to buffalo are fewer, so use the cattle principles and check the label for buffalo use.

Goats and sheep

Mastitis often shows as subclinical infection with coagulase-negative staphylococci. Few products are licensed for them, so extra-label use requires a careful, conservative withdrawal.

Sows and mares

Sows may develop mastitis as part of the postpartum syndrome, treated mainly by systemic therapy, as intramammary infusion is not practical. Mares are rarely affected.

Dogs and cats

Mastitis occurs in lactating or pseudopregnant animals. Choose a drug that is safe for nursing young and use systemic therapy guided by culture.

Clinical pearls

Self-test: 10 questions

1. Which pathogen is least likely to respond to beta-lactam intramammary therapy?

Mycoplasma has no cell wall, so cell-wall inhibitors cannot act on it.

2. Environmental mastitis is mainly controlled by:

Environmental organisms come from bedding and manure, so hygiene is the main control.

3. The main purpose of an internal teat sealant is to:

It mimics the keratin plug and does not treat infection.

4. Selective dry-cow therapy differs from blanket therapy because it:

Selection relies on records, cell counts or culture and reduces antibiotic use.

5. Post-milking teat dipping chiefly reduces which type of infection?

It removes organisms left on the teat skin during milking while the canal is open.

6. In a mild clinical case, culture shows no growth. The most reasonable action is:

No growth often means self-cure or non-bacterial cause, so antibiotic may add nothing.

7. Why can in-vitro sensitivity fail to predict cure in the udder?

Breakpoints may not reflect udder conditions, and some organisms hide from drug.

8. Which statement about coliform mastitis is most appropriate?

Coliforms cause endotoxin-mediated illness, so fluids and anti-inflammatory drugs matter most.

9. After a treated cow completes milk discard time, what else must be checked before she is sold for slaughter?

Milk and meat withdrawals are separate figures.

10. Which approach best reduces total antibiotic use in a herd?

Preventing infection and treating only quarters likely to benefit lowers use and residues.

Key points to revise

1. Mastitis causes the largest share of antibiotic use and residue risk on dairy farms.
2. Contagious pathogens spread at milking; environmental pathogens come from bedding and manure.
3. Streptococci usually respond to penicillins; S. aureus often responds poorly.
4. Coliform mastitis often needs supportive care, with antibiotic use depending on severity.
5. Culture identifies the organism and helps avoid unnecessary treatment.
6. Dry-cow therapy cures existing infection and prevents new ones; selective therapy lowers use.
7. Teat sealants form a physical barrier; teat dips disinfect the teat skin.
8. Reduce use by prevention, culture-guided treatment, narrow-spectrum choice and culling chronic cases.

Go deeper on this site

- Ch 12. Antifungal drugs (in this book)
- Ch 10. Drug residues, MRLs and food safety (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Concepts
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual
- National Mastitis Council
- WHO, Antimicrobial resistance

CHAPTER 12 OF 19

Antifungal drugs

Fungal cells are eukaryotes, so selective toxicity depends on a few unique targets, mainly ergosterol and the cell wall. This chapter explains how azoles, polyenes, griseofulvin, terbinafine and related drugs work, how they are matched to dermatophytosis and systemic mycoses, and why toxicity, interactions and slow therapy shape clinical use.

After this chapter you can

- Explain why fungi are harder to target than bacteria and name the main antifungal targets
- Describe the mechanisms and key adverse effects of azoles, polyenes, griseofulvin and terbinafine
- Outline the principles of treating ringworm in animals, including environmental control and zoonotic risk
- Match drug classes to major systemic mycoses in veterinary practice
- Explain resistance, drug interactions and limits on antifungal use in food animals

Why antifungal selectivity is difficult

Bacteria are prokaryotes, and many antibiotics exploit structures that mammals do not have. Fungi are **eukaryotes**. Their ribosomes, DNA replication and protein synthesis are close to those of the host, so a drug that damages these processes in fungi usually damages host cells too. Useful antifungal drugs therefore target the few features that differ.

The main differences are the following.

- **Ergosterol** is the main sterol of the fungal cell membrane, while mammalian membranes use cholesterol. Both the polyenes and the azoles act through ergosterol, in different ways.

- The **cell wall**, built from glucans and chitin, is absent in mammals. Echinocandins block glucan synthesis.
- Special pathways, such as the squalene epoxidase step of ergosterol synthesis, are targeted by terbinafine.

Fungal infections are also slow, often deep and granulomatous, and affect animals with weakened defences. As a result, treatment is usually measured in weeks or months, the drugs are expensive, and relapse after stopping early is common. Cheap in-vitro testing is limited, so clinical experience and species knowledge guide the choice.

Azoles: blocking ergosterol synthesis

The azoles inhibit the fungal cytochrome P450 enzyme **lanosterol 14-alpha-demethylase**. This blocks the conversion of lanosterol to ergosterol. The membrane becomes depleted of ergosterol and accumulates abnormal sterols, so it is leaky and its enzymes work badly. The effect is mostly fungistatic.

The family has two groups: the older *imidazoles* (ketoconazole, clotrimazole, miconazole, enilconazole, many used topically) and the *triazoles* (itraconazole, fluconazole, voriconazole, posaconazole), which are more selective for fungal enzyme and are preferred for systemic use.

Features worth remembering:

- **Itraconazole** has a broad spectrum, and is lipophilic, so absorption depends on formulation and feeding. It is widely used for dermatophytes, *Malassezia*, and several systemic mycoses.
- **Fluconazole** is water-soluble, reaches the central nervous system and urine well, and is therefore useful in cryptococcal meningitis and fungal urinary infections. It is less active against moulds such as *Aspergillus*.
- **Ketoconazole** inhibits mammalian steroid synthesis, an effect used in medical treatment of some endocrine diseases but a drawback in antifungal use. Newer agents have replaced it in many settings.

Because azoles also inhibit **mammalian cytochrome P450** enzymes, they raise the levels of other drugs metabolised by the same enzymes, and they can inhibit P-glycoprotein. Hepatotoxicity is the main class adverse effect, with anorexia and

vomiting often the first signs, so liver monitoring is part of long courses. Azoles can also be teratogenic, and use in pregnancy needs caution.

Polyenes and flucytosine

Amphotericin B and **nystatin** are polyenes. They bind ergosterol in the fungal membrane and form pores, so ions and small molecules leak out and the cell dies. This is a fungicidal action. The selectivity is incomplete, because the drug also binds cholesterol to a lesser extent.

That explains the main toxicity of conventional amphotericin B, which is **nephrotoxicity**: renal tubular cells are damaged and renal vasoconstriction occurs. Careful hydration, with saline loading, and monitoring of kidney values are the usual precautions. **Lipid-based formulations** carry the drug to fungal tissue with less renal exposure, but are costly. The drug is poorly absorbed from the gut and is given by slow intravenous infusion for systemic disease. Nystatin is too toxic for systemic use and is used topically or orally for surface or gut candidiasis.

Flucytosine is a pyrimidine analogue that enters fungal cells and is converted into a fraudulent nucleotide, interfering with RNA and DNA synthesis. Resistance appears quickly when it is used alone, so it is given in combination with amphotericin B, for example in cryptococcosis. Bone marrow suppression and skin reactions are among its adverse effects.

Echinocandins such as caspofungin inhibit glucan synthase and are intravenous drugs used mostly for invasive candidiasis and aspergillosis in specialised settings. Their veterinary use is limited.

Griseofulvin and terbinafine for dermatophytes

Griseofulvin is active only against dermatophytes, and works by disrupting microtubules and mitosis in fungal cells. After oral dosing it is deposited in keratin precursor cells, so new keratin that grows is resistant to infection and the infected keratin is shed as the hair or skin renews. This explains two clinical points. Treatment takes weeks, because it must outlast the turnover of infected keratin, and the drug has no effect on non-dermatophyte fungi. Absorption improves with a fatty meal.

Griseofulvin is **teratogenic** and must not be given to pregnant animals. It can cause bone marrow suppression, with cats infected with feline immunodeficiency virus being at particular risk, and it may cause gastrointestinal upset and hepatic effects. Many clinicians now prefer other drugs, where available.

Terbinafine is an allylamine that inhibits **squalene epoxidase**, early in the ergosterol pathway. Ergosterol falls and toxic squalene accumulates inside the cell, which gives a fungicidal effect against dermatophytes. It is keratophilic, concentrating in skin, hair and nails, and has a high activity against dermatophytes but less against yeasts and many moulds. It is used to treat dermatophytosis, and is generally well tolerated, with gastrointestinal upset and occasional liver enzyme rises reported.

The topical agents, such as miconazole, clotrimazole and enilconazole, may be used as washes, creams or rinses to reduce spore load on the hair, and lime sulphur dips are an older, inexpensive topical choice.

Ringworm: treatment and control

Ringworm (dermatophytosis) is caused by keratin-loving fungi such as *Microsporum canis* in cats and dogs, *Trichophyton verrucosum* in cattle, *Trichophyton equinum* in horses and *Microsporum gypseum* from soil. In healthy animals it is usually self-limiting over weeks to months, but treatment is still given to shorten the course, to stop spread and, importantly, to protect people, because the infection is **zoonotic**.

The principles are:

1. **Confirm the diagnosis** with Wood's lamp (which detects only some strains of *M. canis*), direct microscopy of hairs and fungal culture. Do not treat on appearance alone, since other skin disease can look similar.
2. **Combine topical and systemic therapy** in companion animals: topical treatment reduces spores on the coat, while a systemic drug eliminates infection in hair follicles.
3. **Decontaminate the environment.** Spores persist for a long time on bedding, grooming tools and surfaces. Cleaning, vacuuming, and disinfection with a suitable agent are necessary, or treated animals are reinfected.

4. **Continue until cure is proven**, usually by negative cultures, not just until the lesions appear to heal.
5. **Protect people**: use gloves, wash hands, and tell owners about the risk, with particular concern for children and immunosuppressed persons.

In cattle, ringworm is common in housed young stock and tends to resolve itself. Management of crowding, hygiene, and nutrition matter more than drug use, and topical treatment of lesions is the usual approach. Check which drugs are permitted in food animals before treating them.

Systemic mycoses, resistance and cautions

Systemic mycoses are caused by fungi that invade deep tissue, often after inhalation of spores from soil or bird droppings, or when immunity is weak. Examples include **aspergillosis** (nasal and disseminated disease in dogs, and mycotic infections in birds and in bovine abortion), **cryptococcosis** (nasal, skin and nervous system disease, especially in cats), **candidiasis** (a mucosal and opportunistic yeast infection), **sporotrichosis** (a subcutaneous infection that may spread to people and cats), and the geographically restricted blastomycosis, histoplasmosis and coccidioidomycosis, which are more important in certain regions than in India. Check the local disease pattern.

Drug choice follows the organism and the site. Triazoles, particularly itraconazole and fluconazole, form the base of treatment for many infections, and amphotericin B, with or without flucytosine, is reserved for severe or life-threatening disease. Fluconazole is chosen when the drug must reach the brain or urine. Treatment commonly lasts for months and continues beyond clinical recovery.

Resistance develops by several mechanisms: mutation or over-expression of the target enzyme, efflux pumps, and biofilm formation. Under-dosing and repeated short courses promote it. Some yeasts, such as certain *Candida* species, are intrinsically less susceptible to fluconazole, so identification matters.

Finally, **food animals**. Many antifungal drugs are not authorised for animals that produce milk, meat or eggs, and withdrawal data are generally lacking, so their use is restricted. Rules differ between countries, and for India you should check the current notification before using any antifungal in a food animal.

Concept cleared

Eukaryote problem

Fungi resemble host cells, so antifungals rely on unique targets: ergosterol, the glucan cell wall and squalene epoxidase.

Two ways to attack ergosterol

Azoles stop its synthesis by inhibiting 14-alpha-demethylase, while polyenes bind the finished sterol and punch holes in the membrane.

Keratin is the target for ringworm drugs

Griseofulvin and terbinafine concentrate in keratinised tissue, so therapy lasts until infected hair or skin is replaced.

Treat the environment too

Spores persist on bedding and tools, so ringworm control needs cleaning and disinfection as well as drugs.

Memory aid: Azoles stop, polyenes pop

Azoles stop ergosterol being made. Polyenes pop holes in the membrane. Terbinafine stops squalene epoxidase, and griseofulvin sits in keratin.

Compare and contrast

Main antifungal classes

Class	Target	Effect	Key adverse effect or caution
Azoles (itraconazole, fluconazole, ketoconazole)	14-alpha-demethylase, ergosterol synthesis	Mostly fungistatic	Hepatotoxicity, P450 interactions, teratogenicity
Polyenes (amphotericin B, nystatin)	Bind ergosterol and form pores	Fungicidal	Nephrotoxicity (amphotericin B); nystatin topical only
Allylamines (terbinafine)	Squalene epoxidase	Fungicidal for dermatophytes	Gastrointestinal upset, occasional liver enzyme rise
Griseofulvin	Microtubules in dermatophytes	Fungistatic	Teratogenic, marrow suppression, dermatophytes only
Echinocandins (caspofungin)	Glucan synthase in the cell wall	Fungicidal for Candida	Intravenous only, limited veterinary use

Itraconazole and fluconazole

Feature	Itraconazole	Fluconazole
Solubility	Lipophilic	Water-soluble
Absorption	Depends on formulation and feeding	Good
Tissue reach	Skin and many tissues	Reaches brain and urine well
Spectrum	Broad, includes Aspergillus and dermatophytes	Narrower, little mould activity
Typical use	Dermatophytes, Malassezia, some systemic mycoses	Cryptococcosis, fungal urinary infection

Species notes

Dogs

Malassezia dermatitis and dermatophytosis are common. Aspergillosis affects the nasal cavity.

Cats

Microsporum canis ringworm is the typical problem and is zoonotic. Cryptococcosis and sporotrichosis

Azoles and terbinafine are used with attention to liver values and drug interactions.

occur. Griseofulvin carries a marrow risk, particularly with FIV infection.

Cattle

Trichophyton verrucosum ringworm is common in housed young animals and is mostly self-limiting. Rely on hygiene and topical care, and check drug rules for food animals.

Horses

Dermatophytosis is spread by tack and grooming gear, so equipment must be cleaned. Guttural pouch mycosis is an important mycotic disease, which is treated with specific therapy.

Birds

Aspergillosis is an important respiratory disease, especially in stressed or captive birds. Treatment is prolonged and combines antifungal drugs with improved husbandry.

Clinical pearls

Self-test: 10 questions

1. Azole antifungals act by inhibiting:

Azoles block this P450 enzyme, preventing ergosterol synthesis. Squalene epoxidase is the terbinafine target and glucan synthase is the echinocandin target.

2. The main dose-limiting toxicity of conventional amphotericin B is:

Amphotericin B damages renal tubules and causes renal vasoconstriction, so hydration and monitoring are needed.

3. Which drug is active only against dermatophytes?

Griseofulvin has no useful activity against yeasts or moulds.

4. Terbinafine is fungicidal for dermatophytes because it:

Inhibition of squalene epoxidase reduces ergosterol and squalene accumulates.

5. Which drug would you choose to reach the brain and urine in cryptococcosis?

Fluconazole is water-soluble and penetrates cerebrospinal fluid and urine well.

6. Why must griseofulvin not be given in pregnancy?

Griseofulvin can cause fetal malformations.

7. A key reason azoles cause drug interactions is that they:

Inhibition of P450 raises levels of co-administered drugs metabolised by those enzymes.

8. Which statement about ringworm control is correct?

Spores persist and cause reinfection; the disease can spread to people and Wood's lamp detects only some strains.

9. Why is flucytosine used with amphotericin B and not alone?

Rapid emergence of resistance limits its use as a single agent.

10. Polyene antifungals kill fungi by:

They bind ergosterol and make the membrane leaky.

Key points to revise

1. Fungi are eukaryotes, so antifungal drugs target ergosterol, the cell wall or squalene epoxidase.
2. Azoles inhibit lanosterol 14-alpha-demethylase and block ergosterol synthesis.
3. Polyenes bind ergosterol and form membrane pores; amphotericin B is nephrotoxic.
4. Terbinafine inhibits squalene epoxidase and is keratophilic.
5. Griseofulvin is active only against dermatophytes and is teratogenic.
6. Ringworm control needs diagnosis, topical and systemic therapy, environmental cleaning and zoonotic precautions.
7. Systemic mycoses need months of therapy, usually with a triazole, and amphotericin B for severe disease.
8. Check current rules before using antifungals in food animals.

Go deeper on this site

- Ch 13. Antiviral drugs and interferons (in this book)
- Ch 11. Mastitis and intramammary therapy (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual
- CDC, About Fungal Diseases
- WOAH, World Organisation for Animal Health

CHAPTER 13 OF 19

Antiviral drugs and interferons

Why antiviral chemotherapy is limited in veterinary practice, how the few available agents work, what interferons and other immunomodulators can and cannot do, and why supportive care and vaccination remain the backbone of managing viral disease.

After this chapter you can

- Explain why selective toxicity is hard to achieve against viruses and why few antivirals are used in animals
- Describe the mechanism of nucleoside analogues and name examples used in cats and in human medicine
- Explain what interferons are and the evidence-based place of feline interferon omega
- Distinguish true antivirals from immunomodulators and from unproven supplements
- Outline a supportive approach to viral disease, including the role of antibiotics and vaccination

Why antivirals are the weak link in chemotherapy

Bacteria are separate cells with their own ribosomes, cell walls and enzymes, so an antibiotic can strike a bacterial target that the host lacks. A virus is different. It is an obligate intracellular parasite and uses the host cell's ribosomes, energy and many enzymes to copy itself. A drug that blocks a viral step can easily harm the host cell too.

This is the problem of **selective toxicity**. Useful antivirals therefore aim at steps that are specific to the virus, such as a viral polymerase, protease, neuraminidase or an enzyme that only the virus uses to activate a drug.

Two more problems limit use in animals. First, by the time clinical signs appear, viral replication has often peaked, so a drug that only stops replication comes late. Second, most antivirals are developed and licensed for human disease. Cost, toxicity data in animal species, and the need to treat large numbers of food animals make routine use impractical.

For this reason, veterinary virology relies on prevention (vaccination, biosecurity, quarantine) far more than on treatment.

How antivirals work: the main mechanisms

Most antivirals act at one stage of the viral life cycle. Learning the stage tells you the drug class.

- **Nucleoside analogues.** These resemble the building blocks of DNA or RNA. Inside the cell they are converted to a triphosphate form and are taken up by the viral polymerase in place of the normal base. This stops chain growth or introduces errors. Aciclovir and famciclovir (a prodrug of penciclovir) work against herpesviruses. Ribavirin and the nucleoside analogue GS-441524 are used against RNA viruses.
- **Viral selectivity through activation.** Aciclovir is first phosphorylated by a viral thymidine kinase. Uninfected cells do this poorly, so the active drug builds up mainly in infected cells. This is a good example of how selectivity is achieved.
- **Neuraminidase inhibitors** such as oseltamivir block release of new influenza virus particles.
- **Protease and entry inhibitors** are used in human HIV and hepatitis medicine and have little place in veterinary work.

A common confusion: antivirals are mostly *virostatic*. They hold replication down while the immune system does the clearing. They do not remove latent virus, so herpesviruses can return after treatment is stopped.

Antivirals used in companion animals

Use in animals is narrow and mostly in cats.

Feline herpesvirus 1. Famciclovir is the systemic agent discussed in feline guidelines such as those of the ABCD (European Advisory Board on Cat Diseases). Evidence comes from experimental studies, a shelter study and field reports, and it is considered to reduce signs and shedding. Topical antivirals applied to the eye, such as ganciclovir, are used for herpetic keratitis. Treatment reduces disease but cannot cure the latent infection in the trigeminal ganglion.

Feline infectious peritonitis (FIP). This was once almost always fatal. Nucleoside analogues, notably GS-441524 and related compounds, have changed this: the

ABCD guideline describes them as curative in most cases when given with supportive care, and notes that they are not available in all countries. Legal status, licensed products and the use of unlicensed products differ between countries, so check the current position in India and the guidance of the regulator before recommending any product.

Other viruses. There is no proven specific antiviral for canine parvovirus, canine distemper, feline panleukopenia or rabies. Rabies in particular must never be approached as a treatable disease in animals. Prevention by vaccination is the only dependable approach.

Zidovudine has been used in cats with FIV, but it can cause anaemia and its use is limited to selected cases under specialist advice.

Interferons and immunomodulators

Interferons are cytokines released by infected cells. They do not attack the virus directly. They bind receptors on neighbouring cells and switch on genes that make those cells resistant to infection, and they also help natural killer cells and T cells. This is the body's first antiviral line, which is why interferon is described as an *immunomodulator* and not a classic antiviral.

Feline interferon omega is licensed in some countries for cats and also for dogs with parvovirus in some regions. Feline guidelines call it safe, but the evidence for benefit in herpesvirus and calicivirus disease is limited. Human recombinant interferon alpha given by mouth is an old practice with weak evidence, and antibodies may develop against foreign interferon on repeated injection.

Other immunomodulators. Products such as inactivated bacterial or *Propionibacterium* preparations, acemannan and similar compounds are marketed to stimulate immunity. Evidence is mostly weak or anecdotal. Treat claims with caution and prefer products with controlled studies.

L-lysine is often given to cats with herpesvirus. The ABCD guideline states that there is no evidence of efficacy, and that it may even carry a risk of arginine deficiency in kittens. Students should know this as a well-known myth.

Supportive care: the real treatment

Since most viral diseases have no specific cure, good supportive care often decides the outcome.

- **Fluids and electrolytes.** Correct dehydration and acid-base disturbance, especially in vomiting and diarrhoea such as parvovirus enteritis.
- **Nutrition.** Early feeding, warmed palatable food, appetite stimulants and a feeding tube if the animal has not eaten for several days are all supported in feline guidelines.
- **Symptomatic relief.** Antiemetics, analgesia, nebulisation and cleaning of discharges. NSAIDs should be used only after hydration is restored.
- **Secondary bacterial infection.** Antibiotics do nothing to the virus. They are given only when a bacterial complication is suspected. This matters for stewardship: giving antibiotics for every viral fever adds to resistance without benefit.
- **Isolation and hygiene.** Separate infected animals, disinfect with agents effective against the virus and notify where a disease is reportable.

Corticosteroids can suppress the immune response and may worsen viral disease, so their use must be a deliberate decision.

Livestock, poultry and prevention

In food animals, antiviral drugs are not used as routine therapy. Foot and mouth disease, peste des petits ruminants, lumpy skin disease, Newcastle disease and bird flu are controlled by vaccination, movement control, culling or stamping out where policy requires, and biosecurity. Antibiotics may be needed for secondary infections in these outbreaks, which brings the usual residue and withdrawal responsibilities.

Antiviral drugs used in human medicine, such as oseltamivir, are a stewardship concern in animals because resistance in animal viruses could affect human treatment. Official bodies in many countries restrict this use. Check the current notifications of the Indian regulator before any such use.

For the clinician, the correct order of thought is: prevent by vaccine, confirm the diagnosis, give supportive care, and use a specific antiviral only when evidence and the law allow. Vaccination failures are mostly due to maternal antibody interference,

broken cold chain or exposure before immunity develops, and the veterinarian should look for these before blaming the vaccine.

Concept cleared

Selective toxicity is the central problem
Viruses use host machinery, so antivirals must target virus-specific enzymes or virus-specific activation steps to spare the host.

Nucleoside analogues
They are phosphorylated to a triphosphate and incorporated by viral polymerase, causing chain termination or errors. Aciclovir relies on viral thymidine kinase for selectivity.

Virostatic, not virucidal
Most antivirals suppress replication while immunity clears the virus. They do not eliminate latent herpesvirus.

Interferon is an immunomodulator
Interferons induce an antiviral state in neighbouring cells and boost immune cells. They do not act on the virus directly.

Memory aid: SIVA for viral disease management
Support, Isolate, Vaccinate, Antiviral only if proven. The order tells you where most of the effort should go.

Compare and contrast

True antivirals versus immunomodulators

Feature	Antiviral drug	Immunomodulator
Target	Viral enzyme or replication step	Host immune response
Examples	Famciclovir, aciclovir, GS-441524	Interferon omega, acemannan
Evidence in animals	Good for a few diseases (FHV-1, FIP)	Mostly limited or variable
Main limit	Narrow spectrum, availability, legal status	Weak evidence, antibody formation

Antibiotic versus antiviral logic

Feature	Antibiotic	Antiviral
Pathogen biology	Own cell structures	Uses host cell machinery
Selectivity	High	Difficult
Effect on virus	None	Usually virostatic
Role in viral illness	Only for secondary bacterial infection	Specific agents only for a few viruses

Species notes

Cat
The main species for antiviral use: famciclovir for herpesvirus, nucleoside analogues for FIP where legally available. Avoid lysine as an antiviral. Be careful with any human drug in cats because of species-specific toxicity.

Dog
No proven specific antiviral for parvovirus or distemper. Supportive fluid and nutrition care and vaccination are the basis of management.

Cattle, buffalo, sheep and goat
Antivirals are not used. Control relies on vaccination programmes and movement control. Antibiotics only

Poultry
No antiviral therapy. Vaccination and biosecurity prevent outbreaks. Antibiotic use for secondary

treat secondary infections, with withdrawal periods respected.

infection should follow stewardship and residue rules.

Horse

Antivirals such as aciclovir or valaciclovir are sometimes discussed for equine herpesvirus, but evidence is limited. Isolation and supportive care remain essential.

Clinical pearls

Self-test: 10 questions

1. Why is selective toxicity difficult for antiviral drugs?

Because viruses replicate inside host cells using host machinery, drugs that block replication can harm host cells.

2. Aciclovir is selectively activated in infected cells by:

Viral thymidine kinase phosphorylates aciclovir far better than host enzymes.

3. Famciclovir is mainly used in cats against:

Famciclovir is a penciclovir prodrug used for herpesvirus infection.

4. Interferons are best described as:

They act on host cells, not directly on the virus.

5. The status of L-lysine for feline herpesvirus according to feline guidelines is:

The ABCD guideline states there is no evidence of efficacy.

6. Antibiotics in a cat with viral upper respiratory disease are justified when:

Antibiotics do not act on viruses; they are for bacterial complications.

7. Most antivirals are best described as:

They suppress replication while immunity clears the virus.

8. Which statement about FIP treatment is most accurate?

Feline guidelines describe nucleoside analogues as curative and note they are not available in all countries.

9. Which is the foundation of controlling viral disease in livestock?

Antivirals are not routinely used in food animals; prevention is key.

10. Oseltamivir blocks which step in influenza virus replication?

It is a neuraminidase inhibitor.

Key points to revise

1. Viruses depend on host cells, so selective toxicity is hard to achieve.
2. Few antivirals are licensed or proven in animals.
3. Nucleoside analogues act on viral polymerase after phosphorylation.
4. Aciclovir selectivity depends on viral thymidine kinase.
5. Antivirals are mostly virostatic and do not remove latent virus.
6. Interferons are cytokines that induce an antiviral state and are immunomodulators.
7. Supportive care and vaccination are the foundation of managing viral disease.

8. Check current Indian notifications before using or recommending antivirals in animals.

Go deeper on this site

- Ch 14. Anthelmintics (in this book)
- Ch 12. Antifungal drugs (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- ABCD Cats Vets: Feline herpesvirus guideline
- ABCD Cats Vets: Feline infectious peritonitis guideline
- Merck Veterinary Manual: Pharmacology

CHAPTER 14 OF 19

Anthelmintics

The main anthelmintic classes, their molecular targets and spectrum, how resistance develops, and how targeted selective treatment such as the FAMACHA system slows it. Residue and withdrawal logic and stewardship are emphasised.

> **After this chapter you can**
>
> - State the mechanism and spectrum of benzimidazoles, imidazothiazoles, macrocyclic lactones, salicylanilides and praziquantel
> - Explain why each class is selective for the parasite
> - Describe how anthelmintic resistance arises and the concept of refugia
> - Explain FAMACHA and targeted selective treatment in small ruminants
> - Apply residue, withdrawal and stewardship principles to anthelmintic use

Principles of anthelmintic therapy

Helminths are multicellular parasites, so some of their biochemistry resembles ours. Anthelmintics are useful because they exploit small differences: a parasite protein

that binds the drug more tightly than the host protein, a receptor present only in worms, or a metabolic pathway worms rely on and the host does not.

Three questions help in choosing a drug: which worm (nematode, cestode or trematode), which life stage (adult, larval, inhibited larvae), and which species and product type (food animal, pet, lactating animal). No single class covers every worm, so the **spectrum** of each class must be known.

Modern use is also shaped by resistance. Because nearly all drug classes have lost effect in some parasite populations, the goal is no longer to kill every worm but to keep animals productive while preserving drug efficacy.

Benzimidazoles and imidazothiazoles

Benzimidazoles (for example albendazole, fenbendazole, oxfendazole) bind parasite beta-tubulin and prevent microtubule formation. Cell division, nutrient absorption and transport inside the worm fail. They are selective because they dissociate much more slowly from parasite tubulin than from mammalian tubulin. They have a broad spectrum against nematodes, and some also act on cestodes and the fluke Fasciola (albendazole). Many have action against eggs and larvae. Albendazole has caused concern in early pregnancy because of teratogenic potential, so label cautions must be read.

Resistance to benzimidazoles is mostly due to changes in the beta-tubulin gene, so the drug binds less well. Because the change is class-wide, resistance to one benzimidazole usually means resistance to all. This is **side resistance**.

Imidazothiazoles (levamisole and the tetrahydropyrimidines such as pyrantel and morantel) are agonists at the nematode nicotinic acetylcholine receptor. The worm muscle first contracts and then undergoes depolarising block, giving spastic paralysis, and the worm is expelled. Levamisole is active against nematodes only. It has a narrower safety margin than many other classes and signs of overdose resemble cholinergic stimulation.

Macrocyclic lactones

The macrocyclic lactones include the avermectins (ivermectin, doramectin, abamectin, eprinomectin) and the milbemycins (moxidectin, milbemycin oxime). They bind **glutamate-gated chloride channels** in nematode and arthropod nerve

and muscle cells. Chloride enters, the cell hyperpolarises and the worm is paralysed, including its pharyngeal pumping.

The spectrum is wide for nematodes and for arthropods such as mites, lice and some ticks, which is why these drugs are called *endectocides*. They have no useful action against cestodes and trematodes, which appear to lack the target. They are very potent and are active at tiny concentrations.

Safety rests on two facts: mammals have these channels only in the central nervous system, and the blood-brain barrier normally keeps the drug out through the P-glycoprotein pump. Some dogs, such as collie breeds with an MDR1 (ABCB1) mutation, have a defective pump and may develop neurotoxicity. Young animals and some species may also have a less complete barrier.

Macrocyclic lactones are highly lipid soluble, remain in fat and persist in the body. This has two consequences: long protection in some products, and long meat and milk withdrawal times. Persistence also means that low concentrations remain for weeks, exposing worms to sub-lethal drug and favouring resistance. Dung from treated animals can also harm dung beetles.

Salicylanilides, flukicides and praziquantel

Salicylanilides (closantel, rafoxanide, niclosamide) and the related nitrophenols uncouple oxidative phosphorylation in the worm's mitochondria. ATP generation collapses and the parasite dies. Closantel and rafoxanide are strongly bound to plasma protein, so blood-feeding parasites such as Haemonchus and the adult liver fluke ingest high drug levels. They are therefore useful for haemonchosis and for fascioliasis in older stages. Niclosamide acts on tapeworms in the gut. Closantel has a narrow safety margin and a long persistence, so correct dosing, species rules and the label are essential.

Other flukicides such as triclabendazole are valued because they act on both immature and adult flukes, while many other drugs kill only adults. The stage of the fluke at treatment therefore decides the choice.

Praziquantel is the main cestocide and also acts on many trematodes. It disrupts calcium homeostasis in the parasite. Muscle contracts, the tegument becomes vacuolated and the worm is damaged and exposed to host immunity. It is not active against nematodes, so combination products pair it with a nematode drug.

Praziquantel will treat *Dipylidium* and *Taenia* species in dogs and cats. Control of *Echinococcus* in dogs matters for human health because of hydatid disease.

Resistance, refugia and FAMACHA

Resistance genes are usually present at low frequency before a drug is ever used. Each treatment kills susceptible worms and lets resistant ones survive and breed, so over time the resistant fraction rises. The mechanisms include changes in the drug target (beta-tubulin, receptor subunits), reduced drug uptake and increased efflux or metabolism. Resistance within a class is typically shared.

Refugia are the worms not exposed to the drug, such as larvae on pasture or worms in untreated animals. They carry susceptible genes and dilute the resistant ones. Treating every animal at every dose-day leaves little refugia and speeds resistance.

Targeted selective treatment (TST) keeps refugia by treating only animals that need it. In small ruminants, the **FAMACHA** chart compares the colour of the lower eyelid mucous membrane with a printed scale, which estimates anaemia caused by the blood-sucking nematode *Haemonchus contortus*. Only animals with scores indicating clinical anaemia are treated. Other tools include body condition score, the dag score and faecal egg counts.

FAMACHA is useful only where Haemonchus is the main problem. It will not detect other worms that do not cause anaemia, and staff need training. Good practice also includes checking efficacy after treatment, for example with a faecal egg count reduction test, quarantine dosing of new animals, and avoiding underdosing by weighing animals or dosing for the heaviest in the group only when label allows.

Residues, withdrawal and stewardship

Anthelmintic residues in meat and milk are a food safety matter. Withholding periods depend on the drug, species, route and formulation and are set by regulators, so the product label and the current Indian notifications must be checked and followed. Meat and milk are separate: a drug may need a long meat withdrawal and be barred altogether in milk-producing animals. Examples in international guidance include closantel being prohibited for dairy animals and some drugs not being authorised for lactating animals. In India, the allowed

products and limits for residues should be checked in the current notification of the regulators.

Stewardship in practice means these points:

- Use a drug only when the animal or herd needs it, based on signs, FAMACHA or egg counts.
- Choose the class by the target parasite and its known local resistance.
- Avoid frequent rotation without monitoring and avoid routine whole-herd dosing.
- Do not use extralabel products in food animals without official guidance.
- Combine drug use with pasture management, rotational grazing and good nutrition.

Remember that a good clinical response does not prove susceptibility. Confirm with a faecal egg count reduction test when resistance is suspected.

Concept cleared

Class decides spectrum
Benzimidazoles and levamisole mostly kill nematodes, macrocyclic lactones cover nematodes and arthropods, salicylanilides target blood feeders and flukes, and praziquantel targets cestodes and trematodes.

Selectivity comes from target differences
Benzimidazoles bind parasite tubulin more tightly, macrocyclic lactones need invertebrate glutamate-gated channels, and mammalian CNS channels are protected by the blood-brain barrier.

Refugia slow resistance
Untreated worms keep susceptible genes in the population. Treating only animals that need it preserves them.

Side resistance

Resistance to one drug in a class usually extends to other members because they share the target.

Memory aid: Targets: TNG-CP

Tubulin (benzimidazoles), Nicotinic receptor (levamisole), Glutamate chloride channel (macrocyclic lactones), Calcium (praziquantel); Proton uncouplers (salicylanilides) as the remaining one.

Compare and contrast

Anthelmintic classes at a glance

Class	Target	Main spectrum
Benzimidazoles	Beta-tubulin	Nematodes, some cestodes and flukes
Imidazothiazoles	Nicotinic ACh receptor agonist	Nematodes
Macrocyclic lactones	Glutamate-gated chloride channels	Nematodes and arthropods
Salicylanilides	Uncoupling of oxidative phosphorylation	Haemonchus, flukes, tapeworms (niclosamide)
Praziquantel	Calcium homeostasis	Cestodes and trematodes

Blanket treatment versus targeted selective treatment

Feature	Blanket treatment	Targeted selective treatment
Animals treated	All	Only those needing it
Refugia	Small	Large
Resistance selection	Strong	Slower
Requirement	None	Monitoring tools and trained staff

Species notes

Sheep and goat

Haemonchus contortus is the major problem in hot humid regions and resistance is widespread. FAMACHA and faecal egg counts guide treatment. Goats often need different handling of dose and metabolism than sheep, so follow label and expert advice.

Cattle and buffalo

Calves are most affected by roundworms. Fluke control depends on local snail habitat. Milk and meat withdrawal rules must be checked before using any product.

Dog and cat

Praziquantel is used for tapeworms. Macrocyclic lactones carry a risk in dogs with the MDR1 mutation. Roundworm control in puppies and kittens has a zoonotic importance.

Horse

Resistance of small strongyles to benzimidazoles is common and cyathostomin resistance to other classes is being reported. Egg counts help select animals to treat.

Poultry and pig

Roundworm control relies on benzimidazoles, levamisole or piperazine in some countries. Withdrawal rules apply to meat and eggs.

Clinical pearls

Self-test: 10 questions

1. Benzimidazoles act by binding:

They prevent microtubule formation in the parasite.

2. Levamisole produces:

It acts as a nicotinic agonist on worm muscle.

3. Macrocyclic lactones are NOT effective against:

Cestodes and trematodes appear to lack the target channel.

4. The main target of praziquantel is:

It disrupts calcium and damages the tegument.

5. Closantel and rafoxanide act by:

They are salicylanilide uncouplers.

6. Refugia refers to:

Refugia dilute resistance genes.

7. FAMACHA is used to assess:

It scores eyelid mucous membrane colour.

8. Dogs with MDR1 mutation are at special risk with:

A defective P-glycoprotein pump lets the drug into the brain.

9. Resistance across drugs of the same class is called:

Shared targets give shared resistance.

10. Which statement on withdrawal is most correct?

Withholding periods depend on drug, route, species and local regulation.

Key points to revise

1. Benzimidazoles bind beta-tubulin.
2. Levamisole is a nicotinic agonist causing spastic paralysis.
3. Macrocyclic lactones open glutamate-gated chloride channels causing flaccid paralysis.
4. Salicylanilides uncouple oxidative phosphorylation.
5. Praziquantel disturbs calcium and acts on cestodes and trematodes.
6. Resistance is selected by repeated treatment and refugia delay it.
7. FAMACHA targets treatment in small ruminants infected with Haemonchus.
8. Withdrawal rules differ for meat and milk; check the current Indian notification.

Go deeper on this site

- Ch 15. Ectoparasiticides, insecticides and acaricides (in this book)
- Ch 13. Antiviral drugs and interferons (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Anthelmintics
- Merck Veterinary Manual: Mechanisms of Anthelmintic Action
- Merck Veterinary Manual: Withholding Periods After Anthelmintic Treatment

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Ectoparasiticides, insecticides and acaricides

Mechanisms, uses and toxicity of organophosphates, pyrethroids, amitraz, macrocyclic lactones and isoxazolines; how dips and pour-ons deliver drug; and why tick resistance and residues demand integrated control and stewardship in India.

After this chapter you can

- Explain the mechanism of organophosphates, pyrethroids, amitraz, macrocyclic lactones and isoxazolines
- Describe key toxicities, including organophosphate poisoning with its antidote and permethrin toxicity in cats
- Compare dips, sprays, pour-ons and spot-ons as delivery systems
- Explain how acaricide resistance develops in ticks and why it is a concern in India
- Apply residue, withdrawal and integrated tick control principles

Why ectoparasite control matters

Ticks, mites, lice, fleas and flies cause direct harm through blood loss, skin damage, worry and reduced production. They are also vectors of serious diseases such as babesiosis, theileriosis and anaplasmosis in cattle, and tick-borne disease in dogs. In India, tick-borne disease is a major cause of loss in cattle and in crossbred and exotic breeds in particular.

Ectoparasiticides are drugs applied to, or absorbed by, the animal so that the parasite is killed when it feeds or contacts the drug. The terms are used loosely: an **insecticide** kills insects, an **acaricide** kills ticks and mites, and a drug active against both is often called an ectoparasiticide.

Most agents are neurotoxins for the parasite. Selectivity is partly based on receptor differences, partly on the fact that the parasite receives a high dose relative to its body size, and partly on how the drug is delivered. Because the margin of safety is limited, toxicity in the host and in the environment must always be considered.

Organophosphates and amitraz

Organophosphates (OP; for example coumaphos, diazinon, chlorpyrifos) inhibit acetylcholinesterase. Acetylcholine builds up at synapses and the parasite suffers continuous stimulation and then paralysis. The binding is persistent, in contrast to the reversible binding of carbamates. The same mechanism harms mammals, so the safety margin is narrow.

Poisoning produces the muscarinic signs often remembered as SLUDGE or the DUMBELS group (salivation, lacrimation, urination, defecation, miosis, bradycardia, bronchoconstriction), nicotinic signs (muscle fasciculations, weakness) and central signs. **Atropine** blocks the muscarinic effects, and oximes such as pralidoxime may reactivate the enzyme if given early, before the enzyme-drug complex ages. Do not treat OP poisoning with atropine alone and expect nicotinic signs to resolve. Avoid using two cholinesterase inhibitors together, since effects add.

Amitraz is a formamidine that acts on octopamine receptors of mites and ticks, causing over-excitation and detachment. In mammals it can act on alpha2-adrenergic receptors and cause sedation, bradycardia and hyperglycaemia, and signs are reversed by an alpha2 antagonist such as atipamezole or yohimbine. Amitraz is toxic in horses and must not be used on them, and it should not be used on cats. Amitraz is widely used in cattle dips and sprays and in tick collars for dogs.

Pyrethroids and macrocyclic lactones

Pyrethrins are natural extracts from chrysanthemum flowers, and **pyrethroids** (permethrin, cypermethrin, deltamethrin, flumethrin) are synthetic, more stable analogues. They hold the voltage-gated sodium channels of parasite axons open, so nerve membranes depolarise repeatedly and the parasite is paralysed. The effect is quick, which gives a *knock-down* effect, and some compounds also repel parasites. Synergists such as piperonyl butoxide block parasite detoxifying enzymes and raise the effect.

Mammals are relatively safe because their sodium channels are less sensitive and they metabolise pyrethroids rapidly. **Cats** are a major exception. They are poor at glucuronidation, and spot-on products made for dogs that contain permethrin can cause tremor and seizures in cats. Cats may also be poisoned by contact with a treated dog. Pyrethroids are very toxic to fish and bees, so disposal of dip wash must be controlled.

Macrocyclic lactones such as ivermectin and doramectin act on glutamate-gated chloride channels of nematodes and arthropods, causing flaccid paralysis. They are effective against mites, lice and some ticks, and are used by injection or pour-on in livestock. Because they persist in fat, withdrawal periods in meat and milk can be long, and some products are not suitable for lactating animals.

Isoxazolines and other newer agents

Isoxazolines (afoxolaner, fluralaner, sarolaner, lotilaner) are antagonists of arthropod GABA-gated chloride channels, and of glutamate-gated channels. They block chloride entry and cause hyperexcitation and death of fleas and ticks that feed on the treated animal. Selectivity is good because affinity for mammalian GABA receptors is much lower. They give weeks of protection after a single oral or topical dose, and a parasite dies after it bites, so disease transmission may still occur in the short interval before death.

Neurological signs such as tremor, ataxia and seizures have been reported in some dogs and cats, and regulators in some countries advise caution in animals with a history of seizures. Read the current label before use in such animals.

Other agents include **neonicotinoids** (imidacloprid, nitenpyram), which act on insect nicotinic receptors, **fipronil**, a phenylpyrazole that blocks GABA channels, **spinosyns**, and **insect growth regulators** such as methoprene and lufenuron, which interrupt development of eggs and larvae. Insect growth regulators do not kill adult fleas, so they work best along with an adulticide and treatment of the environment. Fipronil is not appropriate for rabbits.

Dips, sprays, pour-ons and spot-ons

The delivery system decides how the drug is distributed, how long it acts and what risks arise.

- **Dips and sprays** wet the whole animal. In a dip, the concentration of the bath falls as animals carry out the liquid and as dirt accumulates, so the dip must be maintained and replenished as recommended, or it will under-dose parasites and select for resistance. Dip wash and spray waste are environmental pollutants and must be disposed of safely.
- **Pour-ons and spot-ons** are applied to the skin and spread by the oily layer or are absorbed. They are simple, but underdosing from estimating weight is common. Some pour-ons of macrocyclic lactones work better against lice than equivalent injections.
- **Systemic oral and injectable products** kill parasites that feed on the animal.
- **Collars and ear tags** release drug slowly. Persistent low levels expose parasites to sub-lethal concentrations over time, which favours resistance in the biting fly

and tick populations.

Operators must wear protection, particularly with organophosphates, and animals must not lick treated areas. Do not treat young, sick or debilitated animals without label advice.

Tick resistance in India, residues and integrated control

Resistance has been recorded in ticks, flies and lice to almost every class of ectoparasiticide. The tick *Rhipicephalus (Boophilus) microplus* is the best known example and has developed resistance to organophosphates, pyrethroids and amitraz in several regions. Indian studies have reported resistance in cattle ticks to some of these classes. The picture varies by region and by farm, so local susceptibility testing is the sound basis for choosing a drug. Check the current literature and state veterinary advice for your area.

Resistance mechanisms include target-site mutations (for example in sodium channels for pyrethroids and in acetylcholinesterase for organophosphates), increased detoxification enzymes and reduced penetration. Resistance is promoted by underdosing, diluted dips, frequent treatment and use of one class only. A tick has a short generation time and one host is used for all stages in the one-host tick, so selection is strong.

Integrated control reduces dependence on chemicals. It includes pasture rotation, rest of paddocks, breeding for tick resistance, good nutrition, hygiene and shed management, strategic rather than constant treatment, monitoring of efficacy, and where available, anti-tick vaccines as supplements. Rotation between classes must follow resistance results, not habit.

Residues. Ectoparasiticides given to dairy and meat animals can leave residues in milk and tissues. Withdrawal periods and permitted residue limits are set by regulators. Always read the label and check the current notifications of the Indian regulators before use, especially in lactating animals. Also note that organophosphate and pyrethroid dips pose risks to farm workers and to aquatic life.

Concept cleared

Most agents are parasite neurotoxins

Organophosphates inhibit cholinesterase, pyrethroids hold sodium channels open, amitraz stimulates octopamine receptors and isoxazolines block GABA-gated chloride channels.

Selectivity is relative

It depends on receptor differences, dose per body size and metabolism. Cats with permethrin and horses with amitraz show where it fails.

Underdosing breeds resistance

Diluted dips, weak pour-ons and constant low drug levels select resistant ticks.

Chemicals are only one part of control

Integrated control uses pasture management, breeding, hygiene, monitoring and vaccines to reduce acaricide pressure.

Memory aid: OP poisoning: DUMBELS

Defecation, Urination, Miosis, Bradycardia, Emesis, Lacrimation, Salivation. Treat with atropine for these muscarinic signs, plus an oxime if early.

Compare and contrast

Main ectoparasiticide classes

Class	Mechanism	Key caution
Organophosphates	Inhibit acetylcholinesterase	Narrow safety margin; atropine and oximes for poisoning
Pyrethroids	Keep sodium channels open	Toxic to cats (permethrin), fish and bees
Amitraz	Octopamine receptor agonist	Avoid in horses and cats; sedation in mammals
Macrocyclic lactones	Glutamate-gated chloride channels	Long withdrawal; MDR1 dogs; milk restrictions
Isoxazolines	Block arthropod GABA-gated chloride channels	Caution with seizure history per label

Dip versus pour-on

Feature	Dip or spray	Pour-on or spot-on
Coverage	Whole body wetted	Spread from application site
Main risk	Bath dilution, waste disposal	Underdosing from weight guess
Operator exposure	Higher	Lower but still present
Resistance risk	High if bath weak	High if dose is low

Species notes

Cattle and buffalo

Rhipicephalus microplus is the key tick. Dips, sprays and pour-ons are used. Resistance testing, withdrawal in milk and meat and integrated control are needed. Crossbred cattle are more susceptible than indigenous Bos indicus.

Dog

Isoxazolines, pyrethroids and amitraz collars are common. Watch for seizure history with isoxazolines and MDR1 sensitivity with macrocyclic lactones. Keep treated dogs away from cats if permethrin is used.

Cat

Horse

Very sensitive to permethrin and other insecticides. Use only products labelled for cats. Do not use amitraz.

Amitraz is contraindicated. Pyrethroid and macrocyclic lactone products must follow the label.

Sheep, goat and poultry

Dips and sprays control lice, keds and mites in sheep and goats. In poultry, mites and lice need treatment of both birds and shed. Check egg and meat withdrawal rules.

Clinical pearls

Self-test: 10 questions

1. Organophosphates act by:

They cause acetylcholine accumulation.

2. Which drug is used to treat the muscarinic signs of OP poisoning?

Atropine blocks muscarinic receptors.

3. Pyrethroids act on:

They delay channel closure in parasite nerves.

4. Which species is especially sensitive to permethrin?

Cats have poor glucuronidation and develop tremor and seizures.

5. Amitraz acts on:

It is a formamidine octopamine agonist.

6. Sedation from amitraz in mammals is reversed by:

It acts at alpha2 receptors, so an alpha2 antagonist reverses it.

7. Isoxazolines are antagonists of:

They block chloride entry in arthropod neurons.

8. Which practice most promotes tick resistance?

Sub-lethal exposure selects resistant ticks.

9. Insect growth regulators such as methoprene:

They are not adulticides.

10. Before using an acaricide in a lactating dairy animal, the vet should:

Residue limits and withdrawal periods are regulated and vary by product.

Key points to revise

1. Organophosphates inhibit acetylcholinesterase irreversibly in practice.
2. Pyrethroids prolong sodium channel opening in parasite nerves.
3. Amitraz acts on octopamine receptors and can sedate mammals.
4. Isoxazolines block arthropod GABA-gated chloride channels.
5. Cats are highly sensitive to permethrin.

6. Dips need correct concentration and replenishment.
7. Tick resistance in India varies by region; test locally and avoid underdosing.
8. Residue limits and withdrawal periods must be checked in current Indian notifications.

Go deeper on this site

- Ch 16. Antiprotozoal drugs (in this book)
- Ch 14. Anthelmintics (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Ectoparasiticides
- Merck Veterinary Manual: Ectoparasiticides Used in Large Animals
- Merck Veterinary Manual: Ectoparasiticides Used in Small Animals

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Antiprotozoal drugs

How drugs act against the protozoa that matter in Indian veterinary practice: coccidia, Babesia, trypanosomes, Theileria and Histomonas. The chapter stresses mechanism, spectrum, resistance, residue logic and stewardship rather than doses.

After this chapter you can

- Distinguish ionophores from chemical coccidiostats by mechanism and by their main safety problems
- Explain why coccidiostats are given as prophylaxis and how resistance, rotation and vaccination fit together
- Name the main babesicides and trypanocides and explain curative versus prophylactic use
- Describe the place of buparvaquone in theileriosis and why early treatment matters

- Explain why drug choices for histomoniasis are limited and why prevention dominates

Why protozoa need special drugs

Protozoa are single-celled eukaryotes. Their cells resemble host cells more than bacteria do, so antibacterials such as penicillin are useless against them. Antiprotozoal drugs must therefore find a pathway that the parasite needs and the host lacks or uses differently. Examples are thiamine uptake, folate synthesis, mitochondrial electron transport and the unusual kinetoplast DNA of trypanosomes.

Coccidiostats: ionophores and chemical agents

Coccidiosis is caused by *Eimeria* in poultry and ruminants and by *Cystoisospora* in pups and piglets. The parasite multiplies in gut epithelium. Most damage is done by the time signs appear, so control relies on **prophylaxis**: the drug is placed in feed or water before disease develops. A drug that only suppresses development while immunity builds is called a **coccidiostat**; one that kills the parasite is a coccidiocide. Many agents behave as either depending on exposure.

Ionophores (monensin, salinomycin, lasalocid, narasin, maduramicin) form complexes with sodium, potassium and calcium and carry them across the parasite membrane. Ion balance and water content are lost and the parasite swells and dies. They act on extracellular stages, especially sporozoites and early merozoites, and allow some low-level infection that helps natural immunity. Horses are highly sensitive to ionophores, and accidental feeding of poultry or cattle feed to horses, or overdosed mixing, is a classic cause of cardiac and skeletal muscle damage. Ionophore-treated feed must never be given to horses or to species not named on the label.

Chemical coccidiostats work on specific steps:

- **Amprolium** is a thiamine (vitamin B1) analogue. It blocks parasite thiamine uptake. It is widely used in water during outbreaks, but its spectrum covers some Eimeria species poorly.
- **Sulfonamides** (sulfaquinoxaline, sulfadimidine and others), often with a folate partner, block folate-dependent nucleic acid synthesis. They are used for outbreaks, and resistance is widespread.

- **Diclazuril and toltrazuril** (triazine-type agents) act on intracellular development stages and are used in poultry, calves, lambs and piglets according to species and label.

A common confusion is that sulfonamides or amprolium are the best choice for everything. They are mainly outbreak drugs. Routine prevention in intensive flocks uses ionophores or other feed agents.

Resistance, rotation, vaccines and residues in coccidiosis

Continuous use of one anticoccidial selects resistant Eimeria strains. Two main strategies are used to slow this. In a **rotation** programme the drug is changed between flocks or at set intervals. In a **shuttle** programme one drug is used in starter feed and another in grower feed within the same flock. Sensitivity testing in a laboratory can show which products still work on a particular farm.

Live oocyst vaccines are an alternative. Low doses of sporulated oocysts give controlled infection, and immunity is largely T-cell mediated and species-specific. Vaccination is common for breeders and layers, which need long-lasting immunity.

Residue logic. Feed additives pass into tissues, so most carry a **withdrawal period** before slaughter, and several are banned in laying birds whose eggs are for human consumption. Withdrawal feed must be truly free of the drug. Residue limits and approved uses differ between countries; the current Indian rules, including any restrictions on use in layers, should be checked in the current notification of the regulator.

Babesicides

Babesia and *Theileria* are both tick-borne, but Babesia multiplies in red cells, causing haemolysis, fever, haemoglobinuria and anaemia. Two babesicides remain in common use for cattle and other animals.

- **Diminazene aceturate** is an aromatic diamidine. It is believed to interfere with parasite DNA and is also active against trypanosomes. It is given as a single injection. Dogs and camels are particularly sensitive and nervous signs from overdose can occur, so the label dose must be followed exactly.
- **Imidocarb dipropionate** works through a mechanism that is not fully understood and is active against Babesia. At higher labelled use it can give protection for

some weeks and may help clear carrier states. It has anticholinesterase effects, and salivation, tremors or colic may appear.

Important clinical points: some species do not respond well. *Babesia gibsoni* in dogs and *Babesia felis* in cats are poorly handled by ordinary babesicides. Supportive care, such as fluids, transfusion for severe anaemia and anti-inflammatory drugs, can save life while the parasite is being treated.

Trypanocides: curative and prophylactic use

In India the important trypanosome is *Trypanosoma evansi*, which causes **surra** in horses, camels, cattle, buffalo and dogs. It is mechanically transmitted by biting flies, so tsetse is not involved. African trypanosomiasis (tsetse-borne) uses the same drug classes.

- **Diminazene aceturate** is mainly curative. It leaves the body fairly rapidly and gives little long protection.
- **Isometamidium chloride** is curative and also gives prophylaxis for weeks to months because it persists in tissues. This long depot effect is its advantage and its danger: residual sub-therapeutic levels select for resistance.
- **Quinapyramine** salts are used in horses, camels, pigs and dogs. The sulfate form is curative and the less soluble form is used for prophylaxis.
- **Suramin** is given by the intravenous route in horses, camels and dogs. It is a polyanion that blocks trypanosome enzymes. It does not enter the brain well, so it cannot cure late central nervous system infection.

Most trypanocides have a **narrow therapeutic index**, so correct dosing, deep injection and correct weight estimation matter. **Resistance** develops and cross-resistance occurs, for example between diminazene and isometamidium in some parasite populations. The sanitised-treatment idea, in which a curative drug that has no long persistence is used to clear parasites before a prophylactic drug is given, is intended to reduce resistance selection.

Anti-theilerials and histomonostats

Theileriosis. *Theileria annulata* (tropical theileriosis) is a major cause of loss in crossbred cattle in India, and *T. parva* causes East Coast fever in Africa. The parasite invades lymphocytes and macrophages and transforms them so that

infected cells multiply with the host cell. Destroyed lymphoid tissue and anaemia follow.

Buparvaquone, a hydroxynaphthoquinone, is the key drug. It is believed to inhibit the parasite mitochondrial electron transport chain (cytochrome b). It is most effective when started **early**, before extensive lymphoid and haematopoietic damage. In advanced disease it works poorly and more than one dose may be needed. Supportive treatment, including fluids, anti-inflammatory agents, and drugs for pulmonary oedema, is added. Resistance in *T. annulata* has been reported, and a cytochrome b mutation is the proposed basis, so stewardship matters. For *T. parva*, oxytetracycline has been used for prevention alongside a sporozoite immunisation, but it has little curative effect once disease is established.

Histomoniasis (blackhead). *Histomonas meleagridis* affects turkeys most severely and chickens less so. The organism is carried inside eggs of the caecal worm *Heterakis gallinarum*, which protects it in soil. Historically, **nitroimidazoles** (such as dimetridazole and ronidazole) and some arsenicals were used. Many countries have withdrawn or banned nitroimidazoles and arsenical growth or treatment products for food-producing animals because of residue and public health concerns. Hence few or no legal drugs remain in many regions. Whether any such products are permitted in India should be checked in the current notification. Control therefore depends on **prevention**: separating turkeys from chickens, rotating or cleaning ranges, and routine control of Heterakis with an anthelmintic, which breaks the cycle.

Concept cleared

Prophylaxis because damage comes early
In coccidiosis most intestinal damage happens before clinical signs, so anticoccidials work best when given in feed before disease, not after.

Ionophore mechanism and danger
Ionophores carry ions across the parasite membrane and collapse its ion balance. The same effect on a sensitive host such as the horse damages heart and skeletal muscle.

Curative versus prophylactic trypanocides

A trypanocide that persists in tissue protects for weeks but leaves sub-therapeutic levels that select for resistance. A short-lived curative drug does not protect but is less likely to select.

Early buparvaquone

Buparvaquone kills the parasite but cannot rebuild damaged lymphoid tissue, so its benefit falls sharply as disease advances.

Memory aid: Amprolium blocks thiamine

Think AMP-ro-LIUM = 'A Mimic of the vitamin Pro-B1': amprolium copies thiamine and starves the coccidian.

Compare and contrast

Ionophores versus chemical coccidiostats

Feature	Ionophores	Chemical agents
Examples	Monensin, salinomycin, lasalocid, narasin	Amprolium, sulfonamides, diclazuril, toltrazuril, nicarbazin
Mechanism	Carry ions across parasite membrane	Specific steps such as thiamine uptake or folate synthesis
Main use	Continuous feed prophylaxis	Outbreaks or specific prophylaxis by label
Main hazard	Toxic to horses and some species; narrow margin	Species effects such as nicarbazin in layers; resistance
Resistance	Slow to develop but widespread tolerance	Often develops faster

Common trypanocides

Drug	Mainly	Key point
Diminazene	Curative	Also babesicide; sensitive species such as dogs and camels
Isometamidium	Curative and prophylactic	Long persistence, resistance risk
Homidium	Curative	Intercalating agent; injection site reactions
Quinapyramine	Curative or prophylactic by salt	Used in horses, camels, pigs, dogs
Suramin	Curative	Intravenous; poor brain entry

Species notes

Poultry

Feed anticoccidials, rotation or shuttle programmes and live vaccines are central. Observe withdrawal. Nicarbazin is unsuitable for layers. Blackhead control rests on management and worm control.

Cattle and buffalo

Babesiosis, tropical theileriosis and surra all occur. Use babesicides or buparvaquone early, add supportive care, and base control on tick management.

Horses and camels

Horses are highly sensitive to ionophores. Surra occurs in both and quinapyramine and suramin are used. Camels are sensitive to some drugs, so follow labels.

Dogs and cats

Diminazene can cause nervous signs in dogs. Babesia gibsoni and Babesia felis respond poorly to ordinary babesicides. Pups and kittens may have Cystoisospora needing species-appropriate treatment.

Turkeys

Most susceptible to histomoniasis. Keep apart from chickens and control Heterakis.

Clinical pearls

Self-test: 10 questions

1. Why is coccidiosis in poultry controlled mainly by prophylaxis?

By the time signs appear, much epithelial damage has already occurred, so drugs are placed in feed beforehand.

2. Which statement about ionophores is correct?

Ionophores disturb ion gradients; horses are especially sensitive.

3. Amprolium acts by:

Amprolium is a thiamine analogue.

4. A shuttle programme in poultry means:

Two drugs are used within the same flock cycle to slow resistance.

5. Which drug is a nitroimidazole historically used for blackhead but now restricted in many countries?

Nitroimidazoles have been withdrawn in many countries for food animals; check current Indian rules.

6. Which is the main anti-theilerial drug?

Buparvaquone is the principal treatment for Theileria infections.

7. Why is buparvaquone less effective late in disease?

The drug kills parasites but cannot restore destroyed tissue.

8. Which trypanocide gives prolonged prophylaxis but may select resistance?

Persistence in tissues gives protection and leaves sub-therapeutic levels.

9. Which Babesia infections respond poorly to ordinary babesicides?

These species are not readily treated with normal babesicides.

10. Which measure best reduces blackhead risk in turkeys?

Heterakis eggs carry Histomonas, so worm control and separation break the cycle.

Key points to revise

1. Protozoal drugs target pathways absent or different in the host.
2. Coccidiosis is controlled mainly by prophylaxis, since damage precedes signs.
3. Ionophores disturb ion balance; horses are highly sensitive.
4. Amprolium blocks thiamine uptake and is used mainly in outbreaks.
5. Diminazene and imidocarb are the main babesicides; B. gibsoni and B. felis respond poorly.
6. Isometamidium gives prophylaxis but carries a resistance risk.
7. Buparvaquone must be given early in theileriosis; resistance has been reported.
8. Histomoniasis control depends on prevention because few legal drugs remain.

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- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index

- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Overview of Coccidiosis in Poultry
- Merck Veterinary Manual: Trypanosomiasis in Animals
- Merck Veterinary Manual: Theileriosis in Animals

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Antiseptics, disinfectants and farm biosecurity

The main classes of antiseptics and disinfectants, why contact time and organic matter decide success, and how teat dips and footbaths fit into farm biosecurity. The chapter also covers choosing a product and its toxicity to animals, people and the environment.

> **After this chapter you can**
>
> - Distinguish antiseptics from disinfectants and explain why the same chemical may be both
> - Describe the main chemical classes with their strengths, limits and toxicity
> - Explain contact time, concentration, organic matter and cleaning before disinfection
> - Explain the purpose and common faults of teat dips and footbaths
> - Apply a simple approach to choosing a disinfectant for a given farm problem

Antiseptic, disinfectant and the idea of biosecurity

An **antiseptic** is applied to living tissue to prevent or suppress infection. A **disinfectant** is a germicide applied to inanimate surfaces such as floors, instruments and milking equipment. The same compound can be either, depending on concentration, contact conditions and number of organisms. For example, a dilute iodine solution can go on skin, but a stronger one is meant for equipment. Both are non-selective, which means they damage microbes and, if misused, host tissue too.

Most act by **denaturing proteins, damaging cell membranes or inhibiting enzymes**. Using more product than needed does not improve results and may

cause toxicity, while too little can leave survivors.

Biosecurity means all procedures that reduce the risk and consequence of infection. Disinfection is only one part. Others include controlling movement of animals, people, vehicles and equipment, quarantine, safe disposal of waste and carcasses, and pest control. A disinfectant works only when it forms part of such a system.

Main classes and what each does well

No single agent is best for everything. Learn each class by its spectrum, its weak points and its toxicity.

- **Alcohols** (ethanol, isopropanol) denature protein. They act quickly, evaporate and are useful for skin and small items. They are poor against bacterial spores and some non-enveloped viruses, and they are inactivated by organic matter. Used alone they leave no residual action.
- **Biguanides: chlorhexidine.** It damages the cell membrane and has good activity against many bacteria, with some residual activity on skin. It is less active against some viruses and spores, and is reduced by organic matter and soap. It can injure the eye and ear, so it should not be put in the middle ear or in the eye.
- **Iodine and iodophors.** Iodine is a broad-spectrum oxidant. Iodophors carry iodine bound to a carrier, so they irritate less. They are useful in surgery preparation and teat dips. They are inactivated by organic matter and can stain.
- **Chlorine compounds** (hypochlorite). These are cheap and effective against many bacteria and viruses. They are strongly inactivated by organic matter and corrode metals. Chlorine gas can be released if bleach is mixed with acids, and a toxic gas can also form if mixed with ammonia.
- **Quaternary ammonium compounds** (QACs). Surfactants that disrupt membranes. They are good cleaners and low in odour, but are weaker against non-enveloped viruses and some Gram-negative bacteria, and are inactivated by soap residues and hard water.
- **Phenols and cresols.** Active in the presence of some organic matter. They are toxic to cats and also to pigs and young animals if misused, and can be absorbed through skin. Avoid in cat housing.

- **Alkalis and acids** (sodium hydroxide, lime, washing soda, citric acid). Used for specific viruses, for example in foot and mouth disease control, and for housing. They are caustic and need protective equipment.

Contact time, concentration and organic matter

Three factors decide whether a disinfectant works: **concentration, contact time and cleanliness of the surface**. Contact time is the period the surface must stay wet with the product at the stated dilution. A product sprayed and wiped off in seconds has not been given the chance to act. The label states the time for each target organism, and the value for spores or non-enveloped viruses is much longer than for ordinary bacteria.

Organic matter (manure, blood, milk, pus, soil) is the commonest cause of failure. It physically shields microbes and chemically reacts with the active agent. Chlorine, iodine and QACs are especially affected. Therefore the sequence is: remove gross dirt, wash with detergent, rinse, then disinfect, then allow to dry. A disinfectant is not a substitute for cleaning.

Other factors are temperature (warmer is generally faster, within limits), pH, water hardness, and mixing of incompatible products. **Never mix disinfectants**. Mixing can neutralise them or produce toxic gas.

Teat dips

Teat dipping is a mastitis control step. Contagious pathogens such as *Staphylococcus aureus* and *Streptococcus agalactiae* spread at milking, and the teat canal stays open for a period after milking. A **post-milking dip** kills organisms on the teat skin and reduces new infections. A **pre-milking dip** targets environmental bacteria and must be wiped off before the cluster is attached, giving a suitable contact time, to avoid residues in milk.

Common active ingredients include iodophors, chlorhexidine, chlorine-releasing products and organic acids, often with emollients to protect skin. Points to remember:

- Cover the whole teat, not just the tip. Dipping or spraying must wet all the skin.
- Use a fresh dip. Dip cups and sprayers get contaminated, and organic matter reduces activity. Do not return used dip to the stock bottle.

- Observe contact time and wipe pre-dip off thoroughly.
- Product choice must follow the label, and the dip should be a product licensed for use on teats.

Teat dips do not cure existing infection. They reduce new infection. They are part of a programme that includes milking hygiene, machine maintenance, dry cow therapy as advised by a veterinarian, and culling of chronically infected animals.

Footbaths

Footbaths are used to control infectious foot lesions in cattle and sheep, such as digital dermatitis, and also as a biosecurity step at the entrance to a unit. They are only useful if used properly. Common agents are copper sulfate, formalin, zinc sulfate and peracetic acid-based products.

Common faults: the bath is too short, so the animal's feet are not fully submerged for adequate time; the bath is overloaded with manure so that the active ingredient is inactivated; the solution is not renewed after the set number of animals; and the animals walk in with dirty feet. Boots must be scrubbed clean first and then dipped.

A footbath is a **supporting measure**. It cannot fix poor floors, wet standing, poor hoof trimming or untreated lame animals. The Merck Veterinary Manual notes that foot baths may be considered in an outbreak as part of tackling indirect transmission.

Safety and environment. Formalin is irritant and hazardous to people. Copper and zinc can build up in slurry and soil and harm crops, microbes and sheep (sheep are sensitive to copper). Spent footbath solution should be disposed of according to local environmental guidance, not poured into watercourses.

Choosing a disinfectant and toxicity

An ideal disinfectant is broad-spectrum, fast, stable, active despite some organic matter, not corrosive, not toxic and affordable. No product meets all these, so a choice is made by asking four questions.

1. **What is the target?** Bacteria, enveloped virus, non-enveloped virus, spores, oocysts or fungi. Oocysts of coccidia resist many common disinfectants, and heat or specific products are needed.

2. **What is the surface and how dirty?** Porous concrete and wood hold organic matter. Metal can corrode.
3. **Who and what is exposed?** Animals present, staff, milk or food contact, and drainage into the environment.
4. **Is it licensed and legal?** Use products licensed for animal use and follow local regulations. For notifiable disease outbreaks, officials may specify the disinfectant and its concentration. Check the current guidance rather than relying on memory.

Toxicity must be considered each time. Phenols are dangerous to cats. Iodine can cause thyroid effects if absorbed in quantity, particularly in neonates. Chlorhexidine harms the middle ear and eye. QACs and aldehydes irritate skin and airways. Alkalis burn. Fumes from chlorine mixtures injure the lungs of animals and staff.

Concept cleared

Clean first, then disinfect
Organic matter shields microbes and inactivates chlorine, iodine and QACs, so washing with detergent comes before disinfection.

Contact time
A disinfectant needs time wet on the surface at the right dilution. Spraying and wiping immediately gives little kill.

More is not better
Over-strong solutions add toxicity without extra kill, and under-strength solutions leave tolerant survivors.

Teat dips prevent, not cure
A teat dip reduces new intramammary infection after milking. It does not treat an established infection.

Memory aid: CCC before disinfecting

Clean, Contact time, Concentration: remove dirt first, give the product time, and mix at the label strength.

Compare and contrast

Main disinfectant classes

Class	Strength	Main limit or hazard
Alcohols	Fast skin and small item action	No spore kill, evaporate, no residual
Chlorhexidine	Good bacterial action, residual on skin	Ear and eye injury; reduced by organic matter
Iodophors	Broad, used for surgery and teats	Inactivated by organic matter; stains; absorption
Hypochlorite	Cheap, broad	Inactivated by organic matter; corrosive; toxic gas with acid or ammonia
Peroxygens	Broad, includes many viruses	Corrosive and irritant at strength
QACs	Good cleaning action	Weak on non-enveloped viruses; inactivated by soap
Phenols	Tolerate some organic matter	Toxic to cats and young animals

Antiseptic versus disinfectant

Feature	Antiseptic	Disinfectant
Applied to	Living tissue	Inanimate surfaces
Tolerance needed	Must not damage tissue	May be harsher
Examples	Chlorhexidine, dilute iodophor	Hypochlorite, peroxygens, QACs
Same chemical?	Yes, at lower concentration	Yes, at higher concentration

Species notes

Dairy cattle

Poultry and pigs

Teat dips after milking, clean udders before milking, and footbaths for digital dermatitis. Mind residues in milk and copper in slurry.

All-in all-out, clean-out and drying before disinfection. Oocysts need special products or heat. Keep a footbath or boot change at each house.

Cats
Very sensitive to phenols and cresols. Avoid these in cat housing, clinics and on surfaces cats lick.

Sheep
Sensitive to copper, so take care with copper sulfate footbaths and spent solution.

Dogs and small animal clinics
Chlorhexidine and alcohol for skin, and suitable surface products for wards. Keep chlorhexidine out of the ear and eye.

Clinical pearls

Self-test: 10 questions

1. An antiseptic is applied to:

Antiseptics are used on body tissues; disinfectants are for surfaces.

2. Which is the commonest cause of disinfectant failure?

Organic matter shields microbes and inactivates many agents.

3. Which class is particularly dangerous to cats?

Cats are sensitive to phenols and cresols.

4. What should never be done with household bleach?

Mixing releases toxic gases.

5. Alcohols are poor against:

Alcohols do not reliably kill spores.

6. A post-milking teat dip mainly:

It lowers the spread of organisms at and after milking.

7. A common reason footbaths fail is:

Manure inactivates the active ingredient.

8. Contact time refers to:

The disinfectant needs time wet on the surface at the correct dilution.

9. Which is true of QACs?

Anionic soap residues reduce QAC activity, and non-enveloped viruses are less susceptible.

10. Which is a concern with copper sulfate footbaths?

Copper accumulates in the environment and sheep are sensitive to it.

Key points to revise

1. Antiseptics are for tissues and disinfectants for surfaces; many chemicals serve as both.
2. Most agents denature protein, damage membranes or inhibit enzymes.
3. Alcohols are fast but do not kill spores.
4. Chlorine, iodine and QACs are inactivated by organic matter.
5. Contact time, concentration and prior cleaning determine success.
6. Teat dips lower new infections but do not cure existing ones.
7. Footbaths need renewal, cleaning of boots first and proper disposal of spent solution.
8. Choose by target, surface, exposure and legal status, and check toxicity.

Go deeper on this site

- Ch 18. Anticancer drugs (in this book)
- Ch 16. Antiprotozoal drugs (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Overview of Antiseptics and Disinfectants
- Merck Veterinary Manual: Antiseptics and Disinfectants
- Merck Veterinary Manual: Principles of Biosecurity

CHAPTER 18 OF 19

Anticancer drugs

Why conventional cytotoxic drugs kill fast-dividing cells, how the main drug classes work, and why bone marrow, gut and other tissues suffer. Also covers resistance, combination protocols, species-specific toxicities and the safe handling of hazardous drugs.

> **After this chapter you can**

- Explain the cytotoxic principle and why normal rapidly dividing tissues are also injured
- Distinguish cell-cycle-specific from cell-cycle-nonspecific agents and link each to a drug class
- Describe the mechanism of the main classes of anticancer agents with one example each
- Predict the common adverse effects and the species-specific toxicities to remember
- State the principles of safe handling and disposal of cytotoxic drugs

The cytotoxic principle

Conventional anticancer drugs are **cytotoxic**. They damage DNA, block DNA or RNA synthesis, or disturb the machinery of cell division. Cells that divide often are hit hardest. Tumour cells divide often, so they are injured, but so are normal tissues that renew quickly: bone marrow, intestinal lining, hair follicles and germ cells.

This is the root of the narrow therapeutic index. The drug has no real way to tell a tumour cell from a healthy dividing cell. The more drug given, the more tumour cells are killed, so treatment usually aims for the highest dose the patient can tolerate. The limit is set by damage to normal tissue, mostly the marrow.

Chemotherapy may be given before surgery or radiation (neoadjuvant), after it (adjuvant), or alone. The aim ranges from complete remission in sensitive tumours such as lymphoma, to palliation and better quality of life in others. In veterinary practice the aim is usually a good quality of life, not cure at any cost.

Cell cycle and drug classes

A cell passes through G1, S (DNA synthesis), G2 and M (mitosis). Some cells rest in G0 and are largely spared by drugs that need active division.

- **Cell-cycle-nonspecific agents** act in any phase, including resting cells. Kill increases with concentration. Alkylating agents are the main example.
- **Cell-cycle-specific agents** act in one phase. Antimetabolites work mostly in S phase. Vinca alkaloids and taxanes work in M phase. These drugs work best on tumours with many dividing cells and are often given repeatedly.

This idea explains why protocols give drugs in cycles. Each cycle kills a fixed fraction of cells, not a fixed number. A drug that cycle-nonspecifically reduces the tumour may push surviving cells into division, where a phase-specific drug can then reach them. Rest periods between cycles let the marrow and gut recover.

Common confusion: students think chemotherapy kills a fixed number of cells per dose. It kills a fraction, so repeated cycles are needed, and a few surviving resistant cells can regrow the tumour.

Main agents and their mechanisms

Learn each class by its target.

- **Alkylating agents** (cyclophosphamide, chlorambucil, lomustine) add alkyl groups to DNA and cause cross-links and strand breaks. **Platinum compounds** (cisplatin, carboplatin) act in a similar way by cross-linking DNA.
- **Antimetabolites** (methotrexate, cytarabine, 5-fluorouracil, gemcitabine) resemble normal building blocks. Methotrexate blocks dihydrofolate reductase and so reduces the thymidine and purines needed for DNA. Cytarabine is a false nucleoside that blocks DNA synthesis.
- **Anticancer antibiotics** (doxorubicin, mitoxantrone, bleomycin) bind or break DNA. Doxorubicin intercalates into DNA and inhibits topoisomerase II.
- **Mitotic inhibitors**. Vinca alkaloids (vincristine, vinblastine) block microtubule assembly, so the spindle cannot form. Taxanes (paclitaxel) stabilise microtubules so they cannot disassemble. Either way mitosis fails.
- **Hormonal and lympholytic agents**. Glucocorticoids such as prednisolone kill lymphoid cells and are part of lymphoma protocols.
- **Miscellaneous**. L-asparaginase removes asparagine, which some lymphoid tumour cells cannot make for themselves. Hydroxyurea blocks ribonucleotide reductase.
- **Targeted agents** act on specific molecular markers or abnormal signalling pathways, for example tyrosine kinase inhibitors used in some canine tumours. They are generally more selective, though not free of toxicity.

Combination protocols and resistance

Tumours are seldom treated with one drug. Combination protocols use drugs with **different mechanisms and different dose-limiting toxicities**. This increases tumour kill without adding up the same toxicity, and it lowers the chance that one resistant clone survives.

Resistance arises because tumours are genetically unstable. Some cells carry changes that allow survival, and these are selected by treatment. Common mechanisms:

- Increased efflux of drug by P-glycoprotein (the MDR1 or ABCB1 pump), which lowers intracellular drug.
- Reduced drug uptake or reduced activation of a prodrug.
- Increased DNA repair.
- Altered drug target, for example more dihydrofolate reductase.
- Cells resting in G0 that escape phase-specific drugs.

Resistance to one drug can give **cross-resistance** to others that are pumped out by the same transporter. Large tumours have more cells and so more chance of a resistant clone, which is one reason early treatment of small tumour burden works better.

Adverse effects and species-specific toxicities

Predict toxicity from tissue turnover.

- **Myelosuppression** is the commonest dose-limiting effect. Neutropenia typically appears about a week after treatment and is the main danger because of sepsis. Blood counts are therefore checked around the expected nadir, and a febrile neutropenic patient is an emergency.
- **Gastrointestinal**: nausea, vomiting, diarrhoea, mucosal damage. Antiemetics are used for prevention or treatment.
- **Sterile haemorrhagic cystitis** from cyclophosphamide, because its metabolite acrolein irritates the bladder. It is reduced by encouraging urination and by protective agents.
- **Cardiotoxicity** from doxorubicin is cumulative and dose-related in dogs, so total exposure is tracked. In cats the same drug is more of a kidney concern.

- **Extravasation** of vesicant drugs such as doxorubicin and vincristine causes severe tissue necrosis, so intravenous access must be secure.
- **Others**: hair loss (especially in breeds with continuously growing coat), reduced fertility, and harm to the foetus.

Remember the species traps: **cisplatin is contraindicated in cats**, and **5-fluorouracil is dangerous for cats** because of neurotoxicity. Collies and related breeds with the MDR1 mutation may show more toxicity from drugs that are P-glycoprotein substrates, such as vincristine and doxorubicin. Dosing is often by body surface area, though very small animals may need adjusting; follow a current protocol and specialist advice.

Safe handling and disposal

Cytotoxic drugs can harm the people who handle them as well as the patient. Many are carcinogenic, mutagenic or toxic to reproduction. Exposure occurs through skin contact, inhalation of aerosols or dust, accidental needle injury, and contact with patient urine, faeces or vomit, since drug and metabolites are excreted for a period after dosing.

Basic principles, in line with occupational health guidance such as that from NIOSH:

- Prepare drugs in a designated area, ideally in a ventilated safety cabinet, and avoid creating aerosols.
- Wear appropriate protective equipment: suitable chemotherapy-rated gloves (often double), a closed gown and eye protection. Do not use tablets in a way that crushes or splits them in open air.
- Use closed or luer-lock systems to reduce spills and leaks.
- Label drugs and waste clearly. Place used items in separate, sealed cytotoxic waste containers for proper disposal, not ordinary rubbish or sinks.
- Have a spill kit and know the spill procedure.
- Pregnant, breastfeeding or trying-to-conceive staff should avoid handling these drugs.
- Advise owners to wear gloves when handling the patient's excreta for the period advised by the clinician and to wash hands afterwards.

For disposal rules, biomedical waste requirements in India, and any limits on use of particular drugs in animals, check the current notification and institutional policy.

Concept cleared

Fractional cell kill

Each cycle of chemotherapy kills a fraction of tumour cells, not a fixed number. Repeated cycles and combination drugs are needed, and any surviving resistant cells can regrow.

Narrow therapeutic index

Cytotoxic drugs cannot distinguish tumour from healthy dividing cells. Doses are pushed to the edge of marrow and gut tolerance, so toxicity is expected and must be monitored.

Cell-cycle specificity

Phase-specific drugs (antimetabolites in S, vinca alkaloids in M) need dividing cells. Nonspecific drugs (alkylating agents) also act on resting cells. This shapes scheduling and drug sequencing.

Multidrug resistance

Efflux pumps such as P-glycoprotein can remove several unrelated drugs from tumour cells, giving cross-resistance. The same pump is involved in the canine MDR1 mutation.

Memory aid: Mitotic poisons

VINCA = Vincristine Inhibits Nascent Cytoskeleton Assembly (stops spindle building), while taxanes do the opposite and freeze microtubules. Either way: M phase stops.

Compare and contrast

Major classes of cytotoxic drugs

Class	Example	Main mechanism	Cell-cycle effect
Alkylating agents	Cyclophosphamide, lomustine	Cross-link and break DNA	Mostly nonspecific
Platinum compounds	Carboplatin, cisplatin	DNA cross-links	Mostly nonspecific
Antimetabolites	Methotrexate, cytarabine	Block DNA synthesis	S phase
Anticancer antibiotics	Doxorubicin	Intercalate DNA, inhibit topoisomerase II	Mostly nonspecific
Vinca alkaloids	Vincristine	Prevent microtubule assembly	M phase
Taxanes	Paclitaxel	Stabilise microtubules	M phase

Toxicity to remember by drug

Drug	Characteristic toxicity	Note
Cyclophosphamide	Sterile haemorrhagic cystitis	Caused by acrolein
Doxorubicin	Cardiotoxicity in dogs, extravasation injury	Cumulative exposure tracked
Vincristine	Extravasation, neuropathy, marrow effects	Vesicant
Cisplatin	Kidney injury, vomiting	Contraindicated in cats
5-Fluorouracil	Neurotoxicity	Dangerous in cats

Species notes

Dog

Lymphoma is the most common tumour treated with multi-drug protocols. Doxorubicin cardiotoxicity is cumulative. MDR1-mutant breeds

Cat

Cisplatin and 5-fluorouracil are unsafe. Doxorubicin tends to affect the kidney. Cats rarely lose body hair but may lose whiskers.

may have more toxicity from some drugs.

Horse
Cytotoxic drugs are used rarely. Local treatments such as intralesional cisplatin or carboplatin implants for skin tumours are an example.

Cattle and food animals
Systemic chemotherapy is rarely used because of cost and the problem of drug residues in food. Check current regulations before any use in food-producing animals.

Small pets and owners
Excreta of treated pets contain drug for some days, so owners need clear handling advice.

Clinical pearls

Self-test: 10 questions

1. Why do conventional anticancer drugs commonly cause marrow suppression and vomiting?

Marrow and gut epithelium renew quickly, so they are damaged along with tumour cells.

2. Which statement about cell-cycle-nonspecific drugs is correct?

Alkylating agents are the typical example.

3. Which drug class mainly acts in S phase by mimicking normal building blocks?

Antimetabolites such as methotrexate and cytarabine interfere with DNA synthesis.

4. Vincristine acts by:

Without microtubules no mitotic spindle forms, so M phase is blocked.

5. Sterile haemorrhagic cystitis is characteristic of:

Its metabolite acrolein irritates the bladder wall.

6. Which drug is contraindicated in cats?

Cisplatin is unsafe in cats, and 5-fluorouracil is also dangerous for them.

7. A common mechanism of multidrug resistance in tumour cells is:

Efflux pumps lower intracellular drug and can cause cross-resistance.

8. Why are combination protocols used?

Drugs with different targets and different dose-limiting effects are combined.

9. Which is the safest practice when handling cytotoxic tablets or injections?

Reduce skin, aerosol and needle exposure, and dispose of waste properly.

10. Doxorubicin in dogs is particularly associated with:

Cumulative dose is tracked to limit cardiac damage.

Key points to revise

1. Cytotoxic drugs kill rapidly dividing cells, normal and tumour.

2. The therapeutic index is narrow and the marrow is usually dose limiting.
3. Cells in G0 are relatively resistant to phase-specific drugs.
4. Alkylating agents and platinum compounds damage DNA by cross-linking.
5. Antimetabolites act in S phase; vinca alkaloids and taxanes in M phase.
6. Combination protocols use drugs with different mechanisms and different toxicities.
7. P-glycoprotein efflux is a major route of multidrug resistance.
8. Cytotoxic drugs are hazardous to handlers and need strict handling and waste rules.

Go deeper on this site

- Ch 19. Immunopharmacology (in this book)
- Ch 17. Antiseptics, disinfectants and farm biosecurity (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Overview of Antineoplastic Agents
- NIOSH: Preventing Occupational Exposure to Antineoplastic and Other Hazardous Drugs in Health Care Settings
- Merck Veterinary Manual: Cancer Treatment in Animals

CHAPTER 19 OF 19

Immunopharmacology

How drugs and biological products are used to build, suppress, boost or borrow immunity: vaccine types, immunosuppressants, immunostimulants, antisera and antitoxins, and monoclonal antibodies. The focus is on mechanism, why products succeed or fail, and the safety and residue logic that follows.

After this chapter you can

- Distinguish active from passive immunity and give a product example of each

- Compare killed, modified live, subunit, toxoid and recombinant vaccines with their advantages and risks
- Explain how common immunosuppressants work and what their main risks are
- Describe the logic of antisera, antitoxins and immunostimulants
- Explain how monoclonal antibodies act and why they differ from small-molecule drugs

Active and passive immunity

Immunopharmacology deals with products that change the immune system for benefit. The first idea to fix is the difference between two kinds of protection.

Active immunity means the animal's own immune system makes antibodies and memory cells after infection or vaccination. It takes days to develop but is long-lasting and rapidly recalled on re-exposure. **Passive immunity** means ready-made antibodies are supplied from outside, such as colostrum from the dam or antiserum given by injection. Protection is immediate but temporary, because the antibodies are gradually broken down and no memory is created.

A vaccine therefore builds protection for the future, while an antiserum or antitoxin treats or prevents an immediate threat. Mixing up these two is a common examination error.

Vaccines: types and what they mean

A vaccine presents antigen without causing the disease. How the antigen is prepared decides its strength, safety and need for boosters.

- **Killed (inactivated)** vaccines use organisms killed by chemicals. They cannot revert to virulence and are stable, but they usually give a weaker, antibody-dominated response and need adjuvants and repeated doses.
- **Modified live (attenuated)** vaccines use weakened organisms that multiply in the host. They usually give a stronger and longer response, including cell-mediated immunity, but can in principle revert to virulence, can be shed to other animals, are damaged by heat and poor cold chain, and may be unsafe in pregnant or immunosuppressed animals.

- **Subunit** vaccines contain purified protective antigens, avoiding unneeded or toxic parts.
- **Toxoid** vaccines are inactivated toxins, for example tetanus toxoid. They protect by producing antibodies against the toxin.
- **Recombinant and vector vaccines** use cloned antigens or insert protective genes into a harmless carrier. Gene-deleted and vectored vaccines can allow infected animals to be told apart from vaccinated ones (DIVA).

Adjuvants boost the response by increasing local inflammation. They are mostly needed for killed and purified vaccines, and they can cause local reactions or hypersensitivity.

Why vaccines fail or cause problems

Vaccine failure is usually not the product alone. Think through the causes:

- **Maternal antibody interference.** Antibodies from colostrum neutralise vaccine antigen in young animals, especially with live vaccines, so early doses may not take. This is why young animals need repeated doses until maternal antibody has faded.
- **Cold chain and handling errors.** Heat, light or freezing can destroy live vaccines.
- **Immunosuppression, stress, malnutrition and heavy parasite burden** weaken the response.
- **Wrong antigen.** A vaccine works only against the strains and pathogens it contains. A disease with several causes, such as bovine respiratory disease, is not controlled by one organism's vaccine.
- **Giving a modified live vaccine and antiserum together**, since the antibody will neutralise the vaccine organism.

Adverse effects include local swelling, fever, allergic reactions, and rarely injection-site problems. For some diseases, such as feline infectious peritonitis and equine infectious anaemia, antibody may contribute to disease, so a vaccine cannot be assumed to help. Vaccine use should follow the current national schedule and manufacturer instructions; check the current notification for regulations on licensed products in India.

Immunosuppressants

Immunosuppressants are used in immune-mediated disease, such as immune-mediated haemolytic anaemia and thrombocytopenia, atopic skin disease, and to prevent graft rejection. They reduce immune activity in a broad, not antigen-specific, way.

- **Glucocorticoids** (prednisolone, dexamethasone) bind nuclear receptors, reduce cytokine production, kill lymphocytes and reduce antibody-coated cell clearance. They are the first-line choice but have many side effects with long use.
- **Azathioprine** is a purine antimetabolite that lowers lymphocyte proliferation. It is used with steroids to spare dose. Cats are highly sensitive to its marrow toxicity and it is generally avoided in them.
- **Cyclosporine** inhibits calcineurin and so reduces activation of T cells and IL-2 production. It is used in atopic dermatitis and some immune-mediated conditions.
- **Cytotoxic drugs** such as cyclophosphamide or mycophenolate, used for severe disease in some cases.

The main risks are infection, delayed wound healing, marrow suppression for some drugs, and drug-specific toxicity. A response is slow to appear for the non-steroid drugs, so patience and monitoring matter. Never stop long-term steroids suddenly, because the adrenal axis is suppressed.

Immunostimulants, antisera and antitoxins

Immunostimulants aim to raise immune activity, for example by acting on macrophages or inducing cytokines. Examples include bacterial-derived products, levamisole in some uses, and interferons. Evidence for many products used in practice is limited, so claims should be treated with caution. Vitamin and mineral deficiencies and parasitism, if present, should be corrected first.

Antisera and antitoxins are passive immunity products. They contain antibodies, often from hyperimmunised animals (frequently horses), against a microbe or toxin.

- **Antitoxin** neutralises a toxin that is free in the body, for example tetanus antitoxin and snake antivenom. It must be given early, because it cannot reverse toxin already bound to tissue.

- **Antiserum** provides antibody against an organism, used to give quick cover in a high-risk situation.

Because these products are foreign protein, they can cause **serum sickness or anaphylaxis**, especially on repeat use, so facilities for emergency treatment should be ready. Protection lasts weeks at most. Animals given tetanus antitoxin still need toxoid for lasting immunity, given at a separate site.

Monoclonal antibodies

A **monoclonal antibody** (mAb) is a single, identical antibody engineered to bind one target very precisely. In veterinary medicine they are now used for specific signals, not for a whole organism.

Examples:

- **Lokivetmab** is a caninised antibody that neutralises IL-31, a cytokine linked to itch in canine atopic dermatitis.
- **Bedinvetmab** (dogs) and **frunevetmab** (cats) bind nerve growth factor, which blocks an osteoarthritis pain pathway.

Concepts to understand:

- **Speciation.** The antibody is caninised or felinised so the patient's body does not see it as foreign. A well-matched antibody is less likely to trigger anti-drug antibodies, though they can still occur and may reduce effect.
- **No liver or kidney metabolism.** Antibodies are broken down as proteins, so drug interactions are fewer, and the half-life is long, allowing injections at long intervals.
- **Target biology predicts side effects.** Blocking a normal signal may have consequences that match what that signal does.
- **Cost and specificity.** They are targeted and expensive, and do not replace general diagnosis and management.

The suffix **-mab** identifies monoclonal antibodies, and a species stem such as *-vet-* marks them for veterinary use. Check the current regulatory status of these products for India.

Concept cleared

Active versus passive immunity

Active immunity is made by the host and has memory but is slow. Passive immunity is borrowed antibody that works at once but fades and leaves no memory.

Live versus killed vaccine trade-off

Live vaccines give stronger and longer immunity but carry reversion, shedding and cold-chain risks. Killed vaccines are safer and stable but weaker and need adjuvant and boosters.

Maternal antibody interference

Colostral antibody protects the newborn but also neutralises vaccine antigen, so early vaccination may fail and repeated doses are scheduled.

Specificity of monoclonal antibodies

A mAb blocks one chosen molecule. This gives precision and few metabolic interactions, but effects follow the target's biology and anti-drug antibodies can develop.

Memory aid: Passive products

PASSIVE = Prompt, Antibody supplied, Short-lived, Substitute for memory, Immediate cover, Very temporary, Ends soon. Active products are slow but remembered.

Compare and contrast

Vaccine types

Type	Strength of response	Main advantage	Main concern
Killed	Weaker, antibody	Cannot revert, stable	Needs adjuvant and boosters
Modified live	Stronger, includes cell-mediated	Long immunity	Reversion, shedding, cold chain, pregnancy
Subunit or toxoid	Antibody to selected antigen	No unneeded components	Needs adjuvant, boosters
Recombinant or vectored	Varies by design	Safe, can allow DIVA	Product specific

Active versus passive products

Feature	Vaccine or toxoid	Antiserum or antitoxin
Type of immunity	Active	Passive
Onset	Days to weeks	Immediate
Duration	Long, with memory	Short, no memory
Typical use	Prevention	Emergency treatment or short-term cover
Key risk	Local or allergic reaction, failure	Serum sickness or anaphylaxis

Species notes

Dog and cat

Core vaccines follow a schedule that accounts for maternal antibody. Lokivetmab and bedinvetmab are used in dogs, frunevetmab in cats. Cats are especially sensitive to azathioprine.

Cattle and buffalo

Mass vaccination against diseases like foot-and-mouth disease and haemorrhagic septicaemia depends on cold chain and correct schedules. Check the current national programme.

Horse

Poultry

Tetanus toxoid is routine, and tetanus antitoxin gives temporary cover after a wound in an unvaccinated horse. Horse-derived antisera are a major source of antitoxins.

Flock vaccination uses live and killed products by different routes. Maternal antibody in chicks can interfere with early vaccination.

Sheep and goat

Clostridial toxoid vaccines are widely used. Check the current manufacturer schedule for dams, because colostral transfer protects lambs and kids.

Clinical pearls

Self-test: 10 questions

1. Which is an example of passive immunity?

Colostrum supplies ready-made antibody. The others produce active immunity.

2. A main disadvantage of modified live vaccines is:

Live organisms multiply and may revert or spread to other animals.

3. Tetanus toxoid is an example of:

It is a formalin-inactivated toxin that produces antitoxin antibodies.

4. Why might a puppy fail to respond to an early live vaccine?

Maternal antibodies bind vaccine antigen, so repeated doses are scheduled.

5. Cyclosporine suppresses immunity mainly by:

Calcineurin inhibition reduces IL-2 production and T-cell activation.

6. Which drug is particularly risky for marrow suppression in cats?

Cats are deficient in the enzyme that detoxifies it, so azathioprine is generally avoided.

7. An antitoxin is most useful when:

It neutralises circulating toxin and cannot reverse bound toxin.

8. A major risk of repeated horse-derived antiserum in other species is:

Foreign protein can trigger hypersensitivity, especially on repeat exposure.

9. Lokivetmab acts by:

It is a caninised antibody that binds the itch-related cytokine IL-31.

10. Why do monoclonal antibodies have few metabolic drug interactions?

Antibodies are catabolised to amino acids, so CYP-based interactions are not a concern.

Key points to revise

1. Active immunity is host-made and has memory; passive immunity is supplied antibody and is temporary.
2. Modified live vaccines are strong but carry reversion, shedding and cold-chain risks.
3. Killed and subunit vaccines are safer but usually need adjuvant and boosters.

4. Maternal antibody can block vaccine response in the young.
5. Glucocorticoids, azathioprine and cyclosporine suppress immunity by different mechanisms.
6. Cats are sensitive to azathioprine marrow toxicity.
7. Antisera and antitoxins can cause serum sickness or anaphylaxis.
8. Monoclonal antibodies bind one target, are speciated to lower immunogenicity, and have long half-lives.

Go deeper on this site

- Ch 18. Anticancer drugs (in this book)
- Ch 17. Antiseptics, disinfectants and farm biosecurity (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Types of Vaccines for Animals
- Merck Veterinary Manual: Active Immunity in Animals
- Current Review of Monoclonal Antibody Therapeutics in Small Animal Medicine (PMC)

How to use Book 3: a short discussion

Chemotherapy means treating disease with drugs that harm the invader while sparing the host. In veterinary practice that covers bacteria, fungi, viruses, worms, ticks, protozoa and cancer cells, and it also covers the quieter work of disinfection and immune modulation. This book gathers those topics into nineteen chapters. Unlike the systemic drugs in Book 2, these medicines are chosen by the organism more than by the organ, so the questions change: what is the target, how will it become resistant, and what will remain in milk, meat or eggs?

Start with the principles

Chapter 1 explains how to choose an antibacterial drug: spectrum, killing versus inhibiting, how concentration and time shape the effect, and why a culture and sensitivity test is worth the wait. Chapter 9 explains resistance and stewardship, the habits that keep drugs working. Read these two first. Every class chapter in between is easier once you can see why a drug is chosen, not only what it does.

Class by class

Chapters 2 to 8 walk through the antibacterial classes in a consistent pattern: how the drug works, where it reaches, what it is good for, what can go wrong, and how bacteria escape it. The same pattern is used for antifungal, antiviral and antiparasitic drugs. Comparison tables set related drugs side by side, which is how most examination questions are framed.

Food safety is part of pharmacology

In food animals a drug is not finished when the animal recovers. Residues of antimicrobials can pass into milk, meat, eggs and honey, and they contribute to resistance in the wider community. Chapters 10 and 11 explain withdrawal periods, maximum residue limits and mastitis therapy in plain terms. Because Indian rules and limits are revised from time to time, the book points you to the current notification rather than printing numbers that may be out of date.

No dose tables, and why

As in the earlier books, there are no dose tables. A dose depends on the product, the species, the route and the country, and it should come from the label or a current formulary. What the book gives you is the reasoning that makes a dose sensible, so that you can recognise a poor choice even when a number looks plausible.

Making the most of the self-tests

Each chapter ends with ten questions and an explanation for every answer. Attempt them before reading the Revise points, and repeat a chapter after a week. Use the search box to find a drug or a term and then read the surrounding chapter so the fact stays connected to its mechanism.

Parasites, cancer and the immune system

The later chapters widen the idea of chemotherapy. Anthelmintics, ectoparasiticides and antiprotozoal drugs are the daily tools of livestock practice in India, where worms, ticks and blood parasites cause steady losses. The same resistance logic applies to them as to antibiotics: under-dosing, treating every animal at every visit and rotating drugs without thought all push resistant parasites to the front. The chapter on anticancer drugs explains how cytotoxic agents work, why they harm fast-dividing healthy tissues, and how staff are protected when handling them. The final chapter on immunopharmacology links vaccines, antisera and immunosuppressive drugs, showing how drugs can also be used to switch an immune response on or off.

A note on evidence

Therapy keeps changing as new resistance patterns appear and new products are approved. Treat this book as the stable framework, and check current guidelines, product labels and local regulations before acting on any specific detail.

Continue with the related guides on this site, including the veterinary drugs list and the Drug Index, to link each class to real products and cases. This material is written for education and does not replace the judgement of a registered veterinarian.

BVSC & AH STUDY BOOK 4 OF 7

Applied and Supportive Therapeutics

Seven chapters on the drugs and supportive care used every day in practice: skin, eye and ear products, vitamins and minerals, fluids, herbal medicines, feed additives, and medicines for poultry and fish. Each chapter ends with a 10-question self-test.

7 chapters | **70** practice questions | **No** dose tables

By Dr. Rameez Bloch, BVSc & AH, MVSc

Start here

Pick a chapter from the list on the left (or the top bar on a phone). The chapters are practical: they turn the science of Books 1 to 3 into everyday decisions about skin, eye and ear products, nutrition, fluids, herbal and ethnoveterinary remedies, feed additives and flock or pond medication. Each chapter has six parts: Learn, Concepts, Compare, Species, Quiz and Revise. Your quiz progress is saved on this device only.

CHAPTER 1 OF 7

Dermatological drugs

How skin drugs are chosen and used: vehicles and topical principles, medicated shampoos, antiseptic and antifungal products, antipruritics and the drugs used in atopic dermatitis. The emphasis is on safety, species cautions and what to tell the owner.

After this chapter you can

- Explain how the vehicle and contact time influence the result of a topical skin product

- Describe the action and main cautions of common shampoo and antiseptic ingredients
- Compare the antipruritic drug groups by mechanism, speed of action and safety concerns
- Outline a multimodal approach to canine atopic dermatitis and why pruritus control alone is not enough
- Counsel an owner or farmer on safe use of skin products, including species cautions and residue concerns

Principles of topical skin therapy

Skin is both a barrier and a route. A topical product must reach the layer where the problem lives: surface, hair follicle, stratum corneum or deeper dermis. Most topical drugs act on the surface and follicle only, so they suit superficial disease and do little for deep infection.

The **vehicle** matters as much as the drug. Solutions, lotions and sprays spread easily over haired skin. Creams are water-based and good for moist or inflamed areas. Ointments are greasy, occlusive and soften crusts, but they trap heat and are poorly suited to wet skin. Gels and spot-on products are convenient for dogs and cats.

Three practical points follow. First, **contact time** decides how much drug works, so the label instructions for how long a shampoo stays on the coat should be followed. Second, animals **lick**, so every topical drug is also an oral exposure, which is serious in cats because of grooming. Third, **the person applying the product** needs gloves, since many ingredients irritate human skin.

Medicated shampoos

Shampoo therapy treats the whole body, removes scale, crust and allergens, and delivers an active ingredient in one step. The ingredient is chosen by the skin problem.

- **Chlorhexidine**: a broad antibacterial and some antifungal action, with good residual effect on the skin. Mostly well tolerated, but it can dry the skin and should be kept out of the eyes and ears.

- **Benzoyl peroxide**: antibacterial and follicular flushing, useful in greasy skin and deep follicular disease. It can dry and irritate, and it bleaches fabric and coloured coats.
- **Sulfur and salicylic acid**: keratolytic and keratoplastic, so they loosen scale and normalise keratinisation in seborrhoeic conditions. They can dry the skin.
- **Coal tar**: slows cell turnover in seborrhoea but is smelly, staining and irritant. Many references advise avoiding it in cats.
- **Colloidal oatmeal, lipids and ceramide products**: soothe and support the barrier, so they suit dry or allergic skin and frequent bathing.

A common confusion is that stronger means better. Frequent use of drying shampoos damages the barrier and worsens itch, so a moisturiser or conditioner is often added.

Antiseptic and antifungal skin products

Antiseptics kill or inhibit microbes on living tissue without being absorbed in large amounts. Because they act through several mechanisms, resistance is less of a problem than with antibiotics, which is why topical antiseptic therapy is encouraged for **superficial pyoderma** in line with antimicrobial stewardship.

Chlorhexidine is the standard skin antiseptic. **Povidone-iodine** is broad and cheap, but it stains and can irritate, and iodine absorption is a theoretical concern with large-area or repeated use. Alcohol-based products sting on broken skin.

For dermatophytosis (ringworm), topical **azoles** such as miconazole or enilconazole where available, and lime sulphur dips, reduce spore load on the coat. Lime sulphur smells strongly, stains jewellery and can be licked off by cats, so a collar is advised. Topical therapy alone seldom cures ringworm, as the infection sits in the hair shaft, so systemic therapy and environmental decontamination are usually combined. Infected hairs and contaminated bedding keep reinfecting the animal.

Topical antibiotics that are important in human medicine should be reserved; *check the current guidance and notifications on antimicrobial use* before choosing them for animals.

Antipruritics

Itch is a symptom, not a diagnosis. The first step is to find and treat the cause: fleas, scabies, infection, yeast, food reaction or atopy. Antipruritic drugs then reduce suffering while the cause is managed.

- **Glucocorticoids** are fast and effective. They suppress inflammation broadly, but with long systemic use they cause polyuria, polydipsia, appetite change, infection risk and suppression of the adrenal axis. Topical steroids can thin the skin. Newer topical forms were designed to act locally with less systemic effect.
- **Oclacitinib** blocks Janus kinase enzymes (mainly JAK1) and so reduces signalling by itch-related cytokines such as IL-31. It acts within a day, but it can mask or worsen infection and demodicosis, and the label restricts use in young dogs. Check the product label and availability in India.
- **Lokivetmab** is a monoclonal antibody that neutralises IL-31. It is not immunosuppressive and is eliminated without liver or kidney metabolism, but it is given by injection at a clinic and the effect is dog-specific.
- **Ciclosporin** inhibits T-cell activation through calcineurin. It is slow, taking weeks, and the main side effect is vomiting.
- **Antihistamines** help few dogs with atopic itch and are mostly useful in combination, with sedation as a side effect.
- **Essential fatty acids** are supportive and slow.

Atopic dermatitis: a multimodal plan

Canine atopic dermatitis is a genetically predisposed, chronic inflammatory and itchy skin disease linked to a defective barrier and an exaggerated immune response to environmental allergens. It is a **diagnosis of exclusion**, since parasites, infection and cutaneous adverse food reaction must be ruled out. A strict, properly conducted food trial is the only reliable test for food allergy.

Treatment stands on several legs, because no single drug controls everything.

1. Control fleas and other parasites strictly.
2. Treat secondary bacterial and *Malassezia* infections, ideally with topical products.
3. Repair and protect the barrier with bathing, moisturisers and fatty acids.
4. Control itch with one of the antipruritics above, chosen for speed, safety and cost.

5. Consider **allergen-specific immunotherapy** after allergy testing, which is the only treatment that changes the immune response. It works slowly and not in every dog.

Two common confusions: starting steroids before the work-up masks the diagnosis, and stopping the drug as soon as the itch settles invites a flare. Owners need to understand that atopy is managed, not cured.

Safety, species cautions and the owner or farmer

Cats are the main species at risk. They groom, they have limited glucuronidation, and many products safe in dogs are toxic to them. Avoid tea tree and other essential oils, and avoid high-concentration phenolic and salicylate products. Do not use a dog product in a cat unless the label says it is allowed.

Always check that the product is for the correct species, and warn owners not to mix products. Keep treated animals from licking each other. Use an Elizabethan collar or let the coat dry before contact with children.

For **food animals**, skin products can be absorbed, especially across inflamed skin or when used as dips and pour-ons. Residues may reach milk, meat or eggs. The farmer should observe the label **withdrawal period** and keep treatment records, and the vet should check the current notification on residue limits for India rather than relying on memory. Do not use products intended for pets on dairy animals.

Finally, tell the owner what success looks like, how long treatment will last, and which signs, such as spreading redness, pus or sudden worsening, mean they must return.

Concept cleared

Vehicle decides delivery
The same drug in a shampoo, cream or ointment behaves differently. Choose the vehicle for the lesion, the haircoat and the animal's grooming habits.

Antiseptics first for superficial infection

Topical antiseptics reduce the need for systemic antibiotics in superficial pyoderma, supporting stewardship and lowering resistance pressure.

Itch is a symptom

Antipruritics treat suffering, not the cause. Parasites, infection and food reactions must be investigated, or the itch returns.

Drug classes differ in speed and safety

Steroids and oclacitinib act quickly, ciclosporin needs weeks, lokivetmab avoids immunosuppression. Match the drug to the patient's needs and risks.

Memory aid: VICE for a topical plan

Vehicle, Infection control, Contact time, Ensure species safety. Check each before dispensing any skin product.

Compare and contrast

Common medicated shampoo ingredients

Ingredient	Main action	Best use	Key caution
Chlorhexidine	Antibacterial, some antifungal	Superficial pyoderma, yeast	Drying, avoid eyes and ears
Benzoyl peroxide	Antibacterial, degreasing, follicular flushing	Greasy skin, follicular disease	Drying, bleaches fabric
Sulfur and salicylic acid	Keratolytic, keratoplastic	Scaling, seborrhoea	Drying
Coal tar	Slows cell turnover	Seborrhoea in dogs	Odour, staining, avoid in cats
Colloidal oatmeal and lipids	Soothing, barrier support	Dry or allergic skin	Few; may not control infection

Antipruritic drug groups in the dog

Drug	Mechanism	Onset	Main caution
Glucocorticoid	Broad anti-inflammatory	Fast	Systemic and skin side effects with long use
Oclacitinib	JAK inhibitor, blocks IL-31 signal	Within a day	Infection, demodicosis, age limits on label
Lokivetmab	Anti-IL-31 antibody	Fast	Injection, species specific, cost
Ciclosporin	Calcineurin inhibitor, T cells	Weeks	Vomiting, slow onset
Antihistamine	H1 blockade	Fast	Limited benefit, sedation

Species notes

Dog

Most skin products are designed for dogs. Frequent bathing with drying shampoos needs a moisturiser, and atopic dogs need a long-term multimodal plan.

Cat

Grooming makes ingestion likely. Avoid essential oils, tar shampoos and any non-feline product, and use a collar after lime sulphur or similar products.

Horse

Topical antifungals and shampoos are widely used for rain scald, ringworm and sweet itch. Wear gloves, as ringworm spreads to people, and disinfect tack and brushes.

Cattle and small ruminants

Ringworm and ectoparasite treatments may be sprays or dips. Residues in milk and meat matter, so check the label withdrawal period and local notifications.

Rabbits and small mammals

Skin is thin and grooming is constant. Use only products labelled or advised for the species, and avoid wetting the animal heavily.

Clinical pearls

Self-test: 10 questions

1. Which statement about the vehicle of a topical drug is correct?

The vehicle influences how the drug spreads and is retained. Ointments are occlusive and unsuited to wet skin.

2. Why is licking a particular concern after applying a topical product to a cat?

Cats groom extensively and have limited glucuronidation, so oral exposure can cause toxicity.

3. Which shampoo ingredient is keratolytic and keratoplastic?

Sulfur and salicylic acid loosen scale and normalise keratinisation.

4. A tar shampoo is generally avoided in which species?

Cats groom and are sensitive to tar products, so most references advise avoiding them.

5. Which approach best fits the principle of antimicrobial stewardship in superficial pyoderma?

Topical antiseptics treat superficial infection locally and reduce systemic antibiotic use.

6. Why does topical therapy alone often fail in ringworm?

The infection lies in the hair and spores contaminate surroundings, so systemic and environmental measures are added.

7. Which drug neutralises IL-31 without being immunosuppressive?

Lokivetmab is a monoclonal antibody against IL-31. Oclacitinib blocks JAK signalling and does suppress some immune pathways.

8. Which antipruritic usually needs weeks to show full effect?

Ciclosporin acts on T-cell activation and has a slow onset.

9. What is the only reliable test for cutaneous adverse food reaction?

Serum and skin tests are unreliable for food allergy, so a controlled diet trial is used.

10. What should a farmer observe when a skin product is used on a dairy animal?

Skin products can be absorbed, so residues may reach milk or meat. Check the label and current notification.

Key points to revise

1. Vehicle, contact time and licking decide the real exposure from a topical product.
2. Shampoo ingredients are chosen by the skin problem and can dry the skin if overused.
3. Chlorhexidine is the standard antiseptic and supports stewardship in superficial pyoderma.
4. Ringworm needs topical, systemic and environmental measures together.
5. Itch must be investigated before antipruritics are started.
6. Glucocorticoids, oclacitinib, lokivetmab and ciclosporin differ in speed, safety and cost.
7. Atopic dermatitis is controlled, not cured, and needs a multimodal plan including parasite control.

8. Cats and food animals need special caution: toxicity in cats, residues and withdrawal in food animals.

Go deeper on this site

- Ch 2. Ophthalmic and otic drugs (in this book)
- Ch 3. Vitamins and minerals in therapy (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual, Integumentary System
- Merck Veterinary Manual, Pharmacology
- WSAVA Global Guidelines

CHAPTER 2 OF 7

Ophthalmic and otic drugs

How eye and ear drugs are delivered and why the route is limiting, with the main groups: ocular antimicrobials and anti-inflammatories, mydriatics, glaucoma drugs, ear cleaners and otic antimicrobials. The focus is on cautions that prevent blindness, deafness and treatment failure.

> ### After this chapter you can
>
> - Explain why topical ocular drug delivery is inefficient and how ointments, drops and the order of application affect it
> - Describe the actions and cautions of mydriatics and cycloplegics, including atropine and tropicamide
> - Explain the main glaucoma drug groups by how they lower intraocular pressure
> - Describe the role of ear cleaners and the reasons otic drugs can be ototoxic
> - Counsel owners and farmers on safe eye and ear treatment and species cautions

Eye drops and ointments: delivery

The eye is a poor place for drugs to stay. Tears wash away drops quickly, blinking drains fluid through the nasolacrimal duct, and the cornea is a barrier with both fat-loving and water-loving layers. Only a small part of a drop enters the eye. The rest drains into the nose and throat and is absorbed there, which is how topical eye drugs can have **systemic effects**.

Drops are clear, easy to see through and do not blur vision, but they must be given often. **Ointments** stay longer and can be given less often, but they blur vision, can delay the effect of other drops, and should be avoided where the globe may be perforated. **Suspensions** must be shaken so the drug is evenly mixed.

When more than one drop is given, wait a few minutes between them so the second does not wash out the first, and give ointment last. Lesions should be examined with **fluorescein stain** before any steroid is considered. Preservatives such as benzalkonium chloride can themselves irritate the surface after long use.

Antimicrobial and anti-inflammatory eye drugs

Topical antibiotics are the commonest eye drugs and are used for conjunctivitis and corneal ulcers. They do not penetrate the eye well, so a deep infection needs a different approach. In a corneal ulcer the infection and the enzymes released by tissue and bacteria can dissolve the cornea quickly, so frequent re-examination matters more than the choice of brand. Antivirals are used mainly for feline herpesvirus keratitis. Antifungals are important in horses, where fungal keratitis is common after trauma.

Two anti-inflammatory groups are used. **Corticosteroids** are powerful, but they delay healing and weaken the cornea. They are **contraindicated in an ulcerated cornea**. This is the most important single rule in veterinary ophthalmology. **Topical NSAIDs** give less anti-inflammatory power with less risk, but they also slow healing and have been linked to corneal melting in some ulcers, so they too should be used with care.

Immunomodulators such as ciclosporin or tacrolimus drops are used in keratoconjunctivitis sicca, the dry eye of dogs caused by immune destruction of the tear gland. They stimulate tear production and reduce inflammation, work over weeks and usually need long-term use.

Mydriatics and cycloplegics

Mydriatics widen the pupil. **Cycloplegics** paralyse the ciliary muscle, which relieves the painful spasm of uveitis. Both groups are mainly muscarinic antagonists.

Atropine acts for days. It is used to relieve pain in uveitis and deep ulcers, and to stop the iris sticking to the lens (posterior synechiae). Because some drug drains through the nasolacrimal duct into the mouth, it tastes bitter and cats and dogs may salivate heavily. In horses, repeated use can reduce gut motility and has been associated with colic, so the animal needs observation. It also raises intraocular pressure, so it is **contraindicated in glaucoma** and should be used carefully in animals predisposed to it.

Tropicamide acts for hours and is mainly used to dilate the pupil to examine the lens and the back of the eye. It is a diagnostic drug, not a treatment for uveitis.

A common confusion is thinking a large pupil in a painful eye means improvement. The pupil that stays dilated after atropine is expected, and the animal will be sensitive to bright light for days, so keep it out of the sun.

Glaucoma drugs

Glaucoma is raised intraocular pressure that damages the optic nerve and retina. It is an **emergency**, because vision can be lost within hours in acute cases. Pressure depends on a balance between aqueous humour made by the ciliary body and aqueous humour leaving through the drainage angle. Drugs either reduce production or increase outflow.

- **Carbonic anhydrase inhibitors** such as dorzolamide, used as drops, reduce aqueous production. Oral forms exist but have more systemic effects, including acid-base disturbance and electrolyte changes.
- **Prostaglandin analogues** such as latanoprost increase outflow and constrict the pupil. They work well in dogs, but should not be used when uveitis or anterior lens luxation is present, since they can worsen both. They are less dependable in cats and horses.
- **Beta-blockers** such as timolol reduce aqueous production. Enough may be absorbed to slow the heart or affect the airways, so cats with respiratory or cardiac disease need care.

- **Osmotic agents** such as mannitol pull water from the eye. They are used in an emergency, require hydration and cardiac assessment, and give only short-term benefit.

Long-term control also needs a plan for the other eye, as primary glaucoma is often bilateral.

Ear cleaners and otic antimicrobials

Otitis externa is rarely a single disease. Think of **predisposing** factors (conformation, moisture), **primary** causes (allergy, parasites, foreign bodies), **secondary** infection and **perpetuating** changes such as swollen or narrowed canals. Drugs deal mostly with infection, so unless the primary cause is addressed the ear flares again.

Cleaners remove wax, pus and debris that block drug contact and feed microbes. **Ceruminolytics** soften wax. **Astringent and acidifying** cleaners dry the canal and make it less friendly to microbes. Cleaners with a high dose of detergent or alcohol irritate inflamed skin. A cotton bud pushes debris deeper and is not advised.

Otic medications are commonly combinations of an antibacterial, an antifungal and a corticosteroid. The steroid reduces swelling and pain, which opens the canal. Culture and cytology guide the choice, particularly where rods such as *Pseudomonas* are present and repeated treatments have failed.

The great caution is the **eardrum**. If the tympanic membrane is ruptured, some drugs reach the middle and inner ear and can cause deafness or vestibular signs. Aminoglycosides and chlorhexidine are examples of drugs considered ototoxic in this setting. Check the tympanum, and check the product label, before use.

Cautions and counselling

For both eye and ear drugs, owners fail most often at the stage of giving the drug. Show them how, using a clean hand, a bottle that does not touch the eye or ear, and a calm restraint. Tell them how many days to continue and not to stop when the eye looks better.

Warn against **human eye or ear drops** kept at home. Some contain steroids that would be harmful for an ulcerated cornea. A red, painful, squinting eye or a head-tilting animal needs examination, not repeated home drops.

Opened bottles can become contaminated and should be discarded after the period on the label. Do not share bottles between animals. A collar prevents rubbing.

In **food animals**, infectious bovine keratoconjunctivitis (pinkeye) is a common eye problem. Eye products applied or injected in cattle must still respect the label withdrawal times for milk and meat, so a farmer should keep treatment records. Check the current Indian notification on residues rather than guessing.

Concept cleared

The eye is hard to medicate
Tears, blinking and the corneal barrier limit how much of a drop enters the eye, and drained fluid is absorbed systemically. Frequency, order and contact time matter.

No steroids in an ulcer
A steroid delays corneal healing and may cause melting. Stain with fluorescein before choosing any anti-inflammatory.

Pressure is production minus outflow
Glaucoma drugs either reduce aqueous production or increase drainage. Atropine, which can raise pressure, is avoided.

Check the eardrum first
A ruptured tympanum lets otic drugs reach the inner ear, so ototoxic drugs and strong cleaners become dangerous.

Memory aid: STAIN before STEROID
Stain the cornea with fluorescein before any steroid is considered. If the stain is taken up, the steroid is not used.

Compare and contrast

Atropine and tropicamide

Feature	Atropine	Tropicamide
Duration	Days	Hours
Main use	Uveitis pain, deep ulcers, preventing synechiae	Diagnostic pupil dilation
Bitter taste and salivation	Common, especially in cats	Less common
Glaucoma	Contraindicated	Use with caution, check pressure
Horse concern	Reduced gut motility, colic risk	Less concern

Glaucoma drug groups

Group	Effect on pressure	Example	Key caution
Carbonic anhydrase inhibitor	Less aqueous produced	Dorzolamide	Oral forms disturb acid-base and electrolytes
Prostaglandin analogue	More outflow, miosis	Latanoprost	Avoid in uveitis and lens luxation
Beta-blocker	Less aqueous produced	Timolol	Slow heart, airway effects
Osmotic diuretic	Water drawn out of eye	Mannitol	Needs hydration and cardiac check, short effect

Species notes

Dog

Dry eye is common and usually immune-mediated. Primary glaucoma is often bilateral, and prostaglandin analogues work well.

Cat

Feline herpesvirus is a major cause of eye disease. Atropine causes marked drooling, and beta-blockers need care in cats with heart or airway disease.

Horse

Cattle

Ulcers can become fungal and melt quickly. Atropine can reduce gut motility, so watch for colic signs, and treat any painful eye as urgent.

Pinkeye is common and spreads in groups with flies and dust. Observe withdrawal for any eye or injected treatment.

Rabbits and small mammals
Many rabbits have atropine-splitting enzymes, so atropine may work poorly. Eye drugs for these species should follow species-specific advice.

Clinical pearls

Self-test: 10 questions

1. Why can topical eye drops cause systemic effects?

Excess fluid drains through the nasolacrimal duct to the nose and throat, where it is absorbed.

2. In which order should an eye drop and an eye ointment be given?

Ointment can block later drops, so drops go first with a short interval and the ointment last.

3. Which drug group is contraindicated in a corneal ulcer?

Steroids delay healing and may cause melting of the cornea.

4. Which test should precede the use of any topical steroid in the eye?

Fluorescein uptake reveals a corneal ulcer, which rules out steroids.

5. Which statement about atropine is correct?

Atropine is a long-acting muscarinic blocker; the bitter taste and gut effects are well known, and it is avoided in glaucoma.

6. Which drug is mainly used as a short-acting diagnostic mydriatic?

Tropicamide acts for hours and is used for examination.

7. Latanoprost lowers intraocular pressure mainly by:

Prostaglandin analogues increase outflow and constrict the pupil.

8. When should a prostaglandin analogue be avoided?

These drugs can worsen inflammation and lens-related obstruction.

9. Why must the tympanic membrane be assessed before using otic drugs?

In perforation, drugs such as aminoglycosides and chlorhexidine can damage hearing and balance.

10. A farmer treats pinkeye in a dairy cow. What should the vet advise?

Residues in milk and meat matter even for eye treatments, so the label and current rules apply.

Key points to revise

1. Topical ocular drugs have poor contact time and may be absorbed systemically through the nasolacrimal duct.

2. Ointments last longer but blur vision, and should be given after drops.
3. Corticosteroids are contraindicated in a corneal ulcer.
4. Atropine acts for days and tropicamide for hours; atropine is avoided in glaucoma.
5. Glaucoma drugs reduce aqueous production or increase outflow.
6. Prostaglandin analogues are avoided in uveitis and anterior lens luxation.
7. Ear drugs need an intact tympanic membrane check because of ototoxicity.
8. Owners should avoid leftover human eye and ear drops and must be taught how to dose properly.

Go deeper on this site

- Ch 3. Vitamins and minerals in therapy (in this book)
- Ch 1. Dermatological drugs (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual, Eye Diseases and Disorders
- Merck Veterinary Manual, Ear Disorders
- Merck Veterinary Manual, Pharmacology

CHAPTER 3 OF 7

Vitamins and minerals in therapy

Vitamins and minerals are nutrients, but in practice they are used as drugs: given to correct deficiency, and capable of causing harm when overdone. This chapter explains fat- and water-soluble vitamins, key trace minerals, the narrow gap between deficiency and toxicity, and sensible supplementation in livestock.

After this chapter you can

- Contrast fat-soluble and water-soluble vitamins in storage, toxicity risk and dosing logic
- Explain how ruminants differ from dogs, cats and poultry in vitamin supply

- Describe the main deficiency and toxicity syndromes of copper, selenium, zinc, iron, iodine and cobalt at concept level
- Explain why a trace mineral can be deficient and toxic at nearby intake levels, and why species differ
- Give practical advice to a farmer on supplement use, labels, and avoiding duplication

Why nutrients are treated as drugs

Vitamins and minerals are needed in small amounts for enzymes, membranes, bone, blood and immunity. When intake is too low, a deficiency disease appears. When intake is too high, a toxicity appears. A feed-grade or injectable supplement is therefore a drug with a **narrow therapeutic window**, and it should be chosen with the same care as an antibiotic.

A useful habit is to ask three questions before supplementing. Is there a real deficiency, from the diet, soil or region? Is there an *interference* that blocks absorption or use, even when intake looks adequate? Is the animal already receiving the same nutrient from another product? Many field problems come from the third question, because mineral mixtures, injectables and feed premixes often overlap.

Fat-soluble vitamins: A, D, E and K

These vitamins dissolve in fat, are absorbed with dietary lipid, and are **stored** in liver and fat. Storage protects against short gaps in the diet, but it also means that repeated large doses can accumulate to toxic levels.

- **Vitamin A** supports vision, epithelial health, reproduction and immunity. Deficiency causes night blindness, poor growth and rough epithelium. Excess is harmful, and in pregnancy it can damage the developing foetus. Cats cannot convert plant carotene into vitamin A, so they need it preformed in the diet.
- **Vitamin D** raises calcium and phosphorus absorption and supports bone. Deficiency gives rickets in young animals and osteomalacia in adults. Excess causes high blood calcium and calcification of soft tissues, kidneys and vessels. Cholecalciferol rodenticides poison animals by this exact mechanism.

- **Vitamin E** is an antioxidant that protects cell membranes. It works closely with selenium, so deficiency of either gives overlapping muscle and reproductive disease.
- **Vitamin K** is needed to make clotting factors. Gut bacteria make some, so deficiency is uncommon, but it appears when anticoagulant rodenticides or spoiled sweet clover (dicoumarol) block its recycling. Treatment replaces vitamin K, which then restores clotting factors, but only after a lag while new factors are made.

Water-soluble vitamins: B complex and C

Water-soluble vitamins are not stored in large amounts; excess is mostly excreted in urine. They are therefore safer in overdose, but a diet that lacks them causes deficiency within days to weeks. A common confusion is to say they are "completely safe". Safer does not mean harmless, and repeated injections still carry cost, injection-site and product-quality issues.

Ruminants are a special case. Rumen microbes make B vitamins, and vitamin C is made in tissues by most domestic species, so routine deficiency is uncommon. Two exceptions matter in practice. **Thiamine (B1)** deficiency causes cerebrocortical necrosis (polioencephalomalacia) when the rumen is disturbed, for example by thiaminase-producing microbes, high-concentrate feeding or excess dietary sulphur. Early treatment with thiamine can be life-saving. **Vitamin B12** needs **cobalt** for its synthesis by rumen microbes, so cobalt-poor pastures produce a B12 deficiency with poor appetite and wasting.

In dogs and cats, deficiency usually follows an unbalanced home-made or restricted diet. Cats fed raw fish containing thiaminase can develop thiamine deficiency with neurological signs. In poultry, riboflavin deficiency gives curled-toe paralysis in chicks. Vitamin B supplements are often given alongside antibiotics or in anorexic patients, which is reasonable when the intake is truly low.

Trace minerals: what each does and how it fails

Trace minerals work as parts of enzymes or hormones. Link each to a function and the disease is easier to remember.

- **Selenium** is part of glutathione peroxidase and protects cells from oxidative damage. Deficiency causes nutritional muscular dystrophy (white muscle disease) in calves, lambs and foals, and retained placenta and weak neonates. Excess causes chronic and acute toxicity; the gap between adequate and toxic intake is small, and soil selenium varies widely by region.
- **Copper** is needed for pigment, connective tissue, iron handling and the immune system. Deficiency gives anaemia, poor growth, faded coat and bone problems. Sheep accumulate copper in the liver and are especially prone to toxicity, which ends in sudden haemolysis; cattle tolerate more, but are not immune.
- **Zinc** supports skin, hoof and immunity. Deficiency causes parakeratosis, particularly in pigs fed diets high in calcium. Large oral zinc intake can cause toxicity, for instance from swallowed metal objects.
- **Iron** carries oxygen. Suckling piglets are born with low stores and the sow's milk is poor in iron, so iron is given to prevent anaemia. Overdose of iron is toxic to the gut and liver.
- **Iodine** is needed for thyroid hormones; deficiency causes goitre and weak or stillborn young.
- **Cobalt** is needed by rumen microbes to make vitamin B12, as above.

Deficiency, toxicity and interference

The key idea is the **dose-response curve with two ends**. Below the requirement, performance falls; there is a comfortable plateau; above the tolerance limit, harm appears. For selenium and copper, the plateau is narrow, so "a little extra to be safe" is a bad habit.

Absorption is also controlled by **antagonists**. High molybdenum and sulphur in forage lock up copper in ruminants and produce a secondary copper deficiency, even when copper content looks normal. Excess calcium reduces zinc availability. Excess of one mineral can therefore cause deficiency of another, and the cure for deficiency is sometimes to remove the antagonist rather than to add more mineral.

Species matter. Sheep tolerate little copper. Cats need preformed vitamin A. Ruminants rely on rumen synthesis for most B vitamins. Dogs and cats are often poisoned by human multivitamins, where iron, vitamin D or other ingredients can reach harmful amounts relative to body weight, so owners should not share human supplements with pets without veterinary advice.

Diagnosis rests on history, ration review, signs and, where available, blood, liver or feed analysis. Treatment by guess often fails because the problem is an antagonist, a different mineral, or a non-nutritional cause.

Supplements in livestock: practical use

Supplements reach animals in three ways: **feed premixes and mineral mixtures**, **water-soluble powders** and **injectables**. Each has a logic. Mixtures suit herd-level, long-term correction. Injectables act faster and are used for an individual deficiency or a high-risk moment, such as selenium and vitamin E for newborns in deficient areas, or iron for piglets. Water-soluble products suit poultry flocks but are consumed unevenly when water intake falls in hot weather.

What to tell the farmer:

1. Use a product designed for the species. A mineral mixture made for cattle may be unsafe for sheep because of its copper content.
2. Read the label for what is in the mixture and avoid adding a second product that duplicates it.
3. Store vitamin products away from heat, light and moisture, since several vitamins break down and the label strength is lost.
4. Correct the cause, such as feed quality, water, parasites or antagonists, rather than depending on repeated injections.
5. Ask for a ration review when the same problem recurs.

Residues are a secondary concern for most vitamins and minerals, but injectable products and high-dose preparations still carry label instructions. Follow the label withdrawal period where given, and check the current regulatory notification for any specific limits. Do not assume that a nutrient has no waiting period only because it is a vitamin.

Concept cleared

Storage decides safety

Fat-soluble vitamins are stored, so excess builds up and can poison. Water-soluble vitamins are mostly excreted, so overdose is less dangerous but not harmless.

Two-sided dose-response

Every nutrient has a deficient range, an adequate range and a toxic range. For selenium and copper the adequate range is narrow.

Interference gives secondary deficiency

Molybdenum and sulphur reduce copper availability in ruminants, and excess calcium reduces zinc. Removing the antagonist can be the correct therapy.

Rumen changes the rules

Rumen microbes make B vitamins if cobalt is available, so deficiencies in ruminants are uncommon except for thiamine disturbance and cobalt-related B12 deficiency.

Memory aid: Fat-soluble vitamins: ADEK

ADEK vitamins are stored in fat, so they can build up. Think A for Accumulates in the liver, D for Deposits calcium in soft tissue, E for Eats free radicals with selenium, K for Kills bleeding by making clotting factors.

Compare and contrast

Fat-soluble versus water-soluble vitamins

Feature	Fat-soluble (A, D, E, K)	Water-soluble (B complex, C)
Absorption	With dietary fat	Mostly direct, often by carriers
Body storage	Liver and fat	Little storage
Toxicity risk	Higher, by accumulation	Lower, excess excreted
Deficiency onset	Slow, after stores empty	Faster when intake stops
Example problem	Vitamin A excess, vitamin D calcification	Thiamine deficiency in ruminants and cats

Selected trace minerals

Mineral	Main role	Deficiency picture	Toxicity concern
Selenium	Antioxidant enzyme	White muscle disease, weak neonates	Narrow safe margin
Copper	Enzymes, pigment, iron use	Anaemia, poor coat, poor growth	Sheep, sudden haemolysis
Zinc	Skin, hoof, immunity	Parakeratosis	Gut and organ damage with excess
Iron	Oxygen transport	Piglet anaemia	Gut and liver injury
Iodine	Thyroid hormones	Goitre, weak young	Disturbed thyroid function
Cobalt	Rumen B12 synthesis	Wasting, poor appetite	Rare

Species notes

Cattle and buffalo

Rumen makes B vitamins if cobalt is present. Watch for copper antagonism by molybdenum and sulphur, and for selenium-responsive disease in deficient regions.

Sheep and goats

Sheep are highly susceptible to copper toxicity, so mineral mixtures designed for cattle can be dangerous. Thiamine-responsive brain disease follows rumen disturbance in small ruminants.

Pigs

Piglets need iron early because of low stores and low milk iron. High dietary calcium raises the risk of zinc-responsive parakeratosis.

Poultry

Rapid growth makes birds sensitive to deficiency of vitamin E and selenium, and of riboflavin. Water-soluble supplements depend on water intake.

Dogs and cats

Cats need preformed vitamin A and are sensitive to thiamine loss from raw fish. Human multivitamins can poison pets, mainly through iron and vitamin D.

Clinical pearls

Self-test: 10 questions

1. Which statement about fat-soluble vitamins is correct?

Fat-soluble vitamins are absorbed with lipid and stored, which is why excess can accumulate.

2. A calf in a selenium-deficient area shows stiffness and weakness with muscle damage. The most likely condition is

Selenium and vitamin E deficiency produce nutritional muscular dystrophy.

3. Which species is most sensitive to copper toxicity?

Sheep accumulate copper in the liver and may undergo sudden haemolysis.

4. High molybdenum and sulphur in forage mainly cause

These antagonists bind copper in the rumen and reduce availability.

5. Cobalt is needed in ruminants because it

Without cobalt, rumen B12 synthesis falls and deficiency follows.

6. Cholecalciferol rodenticide poisoning acts mainly by

Excess vitamin D increases calcium and phosphorus and causes mineralisation of soft tissues.

7. Why do cats need preformed vitamin A?

Cats lack adequate conversion of carotene to vitamin A, so animal-source vitamin A is required.

8. Which problem is linked to thiaminase or excess sulphur in ruminants?

Thiamine deficiency or interference causes cerebrocortical necrosis.

9. A farmer wants to add a second mineral product on top of a mineral mixture already fed. The best first advice is

Duplicate intake of selenium or copper can push animals into the toxic range.

10. Why are water-soluble vitamins in drinking water less reliable in a hot spell?

Dose received depends on water consumption, which changes with weather and illness.

Key points to revise

1. Vitamins and minerals have narrow windows and should be used with drug-like care.
2. Fat-soluble vitamins are stored and can accumulate to toxic levels.
3. Water-soluble vitamins are mostly excreted but are not free of problems.
4. Vitamin D excess causes soft-tissue calcification.
5. Selenium and vitamin E work together against oxidative muscle damage.
6. Ruminants make B vitamins in the rumen if cobalt is available.
7. Sheep are very susceptible to copper toxicity.
8. Supplements should match the species and not duplicate other products.

Go deeper on this site

- Ch 4. Fluid, electrolyte and acid-base therapy (in this book)
- Ch 2. Ophthalmic and otic drugs (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Nutritional Requirements of Dairy Cattle
- Merck Veterinary Manual: Toxicoses in Animals From Human Multivitamins and Supplements
- Merck Veterinary Manual: Nutritional Requirements of Small Animals

CHAPTER 4 OF 7

Fluid, electrolyte and acid-base therapy

Fluid therapy is often the most life-saving treatment in a sick animal, but the wrong fluid or the wrong speed can do harm. This chapter covers how to judge dehydration, how crystalloids and colloids differ, how to correct potassium and calcium safely, and when oral rehydration is enough.

> ### After this chapter you can

- Distinguish dehydration from hypovolaemia and assess each at the bedside
- Compare crystalloids and colloids and match fluid type to the problem
- Explain the safety rules for correcting potassium and calcium
- Relate common clinical conditions to acid-base disturbances and the role of buffers in fluids
- Explain how oral rehydration works and what to tell a farmer or owner

Why fluids come first

Body water is divided into **intracellular** fluid and **extracellular** fluid; the extracellular part includes plasma (inside vessels) and interstitial fluid (between cells). Vomiting, diarrhoea, bleeding, heat, burns and poor intake remove fluid and electrolytes. When enough is lost, blood flow to organs falls, the kidneys are injured and drugs that depend on perfusion and renal clearance behave unpredictably.

Many drug problems begin with a dehydrated patient. A nephrotoxic antibiotic or an NSAID is much more dangerous in a dehydrated animal, so correcting hydration is part of drug safety, not only supportive care.

Two different problems must be separated. **Dehydration** is loss of water from the interstitial and cell compartments; it develops slowly and is corrected over hours. **Hypovolaemia** is a shortage of circulating blood volume; it is an emergency that needs rapid restoration. An animal can have one without the other.

Assessing dehydration and perfusion

Bedside assessment combines several signs, because no single sign is reliable. For **hydration** look at skin tent (skin returning slowly to place), dryness of the mucous membranes, and how deeply the eyes sit in the orbit. In calves, eye recession and loss of suckle reflex are practical signs. Elastic skin is less reliable in old, thin or obese animals, and in young animals the skin tent can mislead.

For **perfusion** check heart rate, pulse quality, capillary refill time, mucous membrane colour, limb temperature and mental state. Cold limbs, weak pulses and depression point to poor circulation. Laboratory help includes packed cell volume with total protein, which rise with water loss (unless there is anaemia or protein loss), plus urea, creatinine, electrolytes and blood gas where available.

The plan then has parts: replace the deficit, cover daily maintenance needs, and add replacement for continuing losses such as ongoing diarrhoea. Re-assess repeatedly, because the patient, not a formula, tells you when enough has been given. Signs of too much fluid include nasal discharge, increased respiratory effort, chemosis (swollen conjunctiva), and rising body weight; stop or slow the infusion if these appear.

Crystalloids and colloids

Crystalloids are solutions of small molecules that move freely across the vessel wall, so most of the volume leaves the blood within a short time. They are the main fluids for replacement and maintenance.

- **Replacement isotonic crystalloids** (for example Ringer's lactate, Hartmann's solution and other balanced solutions) have electrolyte content similar to extracellular fluid and contain a buffer, such as lactate or acetate, that is converted to bicarbonate. They are the usual first choice in diarrhoea and most dehydration.
- **0.9% saline** has sodium and chloride only. It suits some metabolic alkaloses with chloride loss and certain high-potassium states. Large volumes can cause a chloride-related acidosis.
- **Dextrose solutions** are mainly a source of free water and a little energy, since glucose is metabolised. They do not restore circulating volume well, and are not for shock.
- **Hypertonic saline** draws water into the vessels from other compartments and gives a short, quick rise in volume. It is used in selected emergencies, and its effect is brief, so isotonic fluid should follow.

Colloids contain large molecules that stay in the vessels and hold water there by oncotic pressure. They include plasma, albumin and synthetic products. They are used when low protein or ongoing leak is a problem, or to give a longer-lasting volume effect. Concerns about bleeding tendency and kidney injury with some synthetic colloids have led to restrictions in some countries, so check current guidance and product labelling before use.

A common confusion is that a litre of crystalloid is a litre of blood volume. It is not; only a fraction stays in the vessels, which is why larger volumes of crystalloid are

needed than of colloid.

Correcting potassium and calcium safely

Potassium and calcium are dangerous to correct fast, because both control heart rhythm.

Hypokalaemia follows anorexia, vomiting, diarrhoea, and increased urine loss; in cattle it occurs in downer cows and with some metabolic disease. Muscle weakness is the typical sign. Potassium is added to fluids at a controlled, limited rate, and it is **never given as a rapid intravenous push**, which can stop the heart. Follow the formula on a reliable reference, and monitor serum potassium and ECG where possible.

Hyperkalaemia occurs in urinary obstruction, kidney failure and Addisonian crisis. It causes bradycardia and characteristic ECG changes (tall T waves, flat P waves). Calcium gluconate protects the heart muscle quickly but does **not lower** the potassium level; its effect is brief. Insulin with glucose, and in some cases bicarbonate, move potassium into cells. The real cure is removing the cause, such as relieving the obstruction.

Hypocalcaemia, including milk fever in dairy cows, is treated with slow intravenous calcium. Auscultate the heart during the infusion, and stop at once if the heart rate slows, rhythm becomes irregular or the animal becomes distressed. Calcium injected outside the vein damages tissue, and calcium should not be mixed carelessly with other drugs or with certain fluids.

Acid-base disturbances in practice

Acid-base status reflects the balance between acids and bicarbonate, and the lungs control carbon dioxide. Four simple patterns cover most cases.

- **Metabolic acidosis**: bicarbonate loss or acid gain. Examples are diarrhoea in calves, shock with lactic acid build-up, kidney failure and ketoacidosis. Calves with diarrhoea may show depression and weak suckle largely because of acidosis, not only dehydration.
- **Metabolic alkalosis**: acid or chloride loss. Examples are vomiting of stomach contents in dogs and abomasal displacement or outflow obstruction in cattle, usually with low chloride and potassium.

- **Respiratory acidosis**: poor ventilation, for example under anaesthesia.
- **Respiratory alkalosis**: over-breathing from pain, fever or heat.

Most acid-base problems improve when the **underlying cause and perfusion** are corrected, since restored blood flow lets the liver and kidneys clear acid. Balanced fluids with a buffer help, and sodium bicarbonate is reserved for selected severe or persistent acidosis because over-treatment can cause alkalosis, low ionised calcium and fluid overload. Lactate-containing fluids can be less suited to animals with severe liver failure, as lactate is cleared by the liver.

Oral rehydration and advice to the owner or farmer

When the gut still works, the oral route is safe, cheap and often enough. Sodium and glucose are absorbed together by a shared carrier in the small intestine, and water follows. Because this carrier keeps working in infectious diarrhoea, a solution containing **sodium, glucose and an alkalinising agent** can rehydrate a calf, kid or lamb at home or in the shed. Good products also supply potassium and, in some, amino acids.

Practical points:

1. Use a commercial or recommended mix prepared exactly as the label states. Wrong dilution can worsen diarrhoea.
2. Continue to **offer milk** or milk replacer unless the veterinarian says otherwise; withholding food slows recovery and weakens the animal. Feed the electrolyte solution between milk feeds, not mixed in the same bottle unless the label allows.
3. Do not rely on plain water, salt-and-sugar guesses or home mixes without a tested recipe.
4. Call the veterinarian early if the calf cannot stand or suck, has cold limbs or a very sunken eye, is bloated, or has blood in stool. These animals need intravenous therapy.

For dogs and cats, mild dehydration with an animal that can still drink and keep fluid down may be managed with oral fluids under advice, but vomiting, collapse or a very young or old patient needs veterinary care. Fluid therapy should always be accompanied by finding the cause of the loss.

Concept cleared

Dehydration is not hypovolaemia

Dehydration is water loss from tissues and develops slowly; hypovolaemia is low circulating volume and needs rapid correction. Assess both.

Fluid type follows the problem

Balanced isotonic crystalloids for replacement, colloids for sustained plasma volume, dextrose for free water, hypertonic saline for brief emergency volume.

Cardiac safety governs electrolyte correction

Potassium and calcium both change heart rhythm, so they are given slowly, with monitoring, and never as a quick potassium push.

Oral route uses sodium-glucose coupling

Intestinal sodium-glucose co-transport still works in diarrhoea, so a correct oral electrolyte solution can rehydrate animals that can still suck and swallow.

Memory aid: Safe electrolyte rules: SLOW K and CA

Potassium and calcium both go SLOW and with a stethoscope or ECG. Remember K is never a push, and calcium is stopped if the heart slows.

Compare and contrast

Crystalloids versus colloids

Feature	Crystalloids	Colloids
Main particles	Small ions and glucose	Large molecules
Stay in vessels	Only a fraction	Longer retention
Main use	Replacement and maintenance	Low protein, sustained volume
Cost and availability	Cheaper, widely available	Costlier, may be restricted
Main concern	Fluid overload, oedema	Bleeding tendency, kidney concerns with some products

Common fluids at a glance

Fluid	Main feature	Typical use	Caution
Balanced isotonic solution	Electrolytes plus buffer	Most dehydration	Lactate in severe liver failure
0.9% saline	Sodium and chloride	Chloride-losing alkalosis, some hyperkalaemia	Large volumes may cause acidosis
Dextrose solution	Free water and energy	Water deficit, some energy needs	Poor volume expander
Hypertonic saline	Draws water into vessels	Selected emergencies	Brief effect; follow with isotonic fluid

Species notes

Cattle and buffalo

Calves with diarrhoea are mainly acidotic and need alkalinising oral solutions or intravenous therapy if they cannot suck. Milk fever needs slow intravenous calcium with heart monitoring.

Sheep and goats

Small body size makes fluid overload easy, so volumes and speed need extra care. Urinary obstruction in males can cause high potassium.

Horses

Pigs and poultry

Large fluid losses in colic or diarrhoea are corrected with large volumes of balanced crystalloid, usually through a catheter, with attention to electrolytes.

Group treatment is by drinking water, which depends on intake; sick animals drink less. Individual intravenous therapy is rarely practical.

Dogs and cats

Cats are prone to fluid overload and to potassium problems with kidney disease and urinary obstruction. Monitor respiration and weight during therapy.

Clinical pearls

Self-test: 10 questions

1. Dehydration differs from hypovolaemia because dehydration

Hypovolaemia is circulating volume shortage and needs rapid correction; dehydration is gradual tissue water loss.

2. Which finding most supports dehydration in a calf?

Eye recession and delayed skin return are practical hydration signs.

3. Why can large volumes of crystalloid be needed in shock?

Crystalloids redistribute quickly out of the vessels.

4. Which fluid is poor at restoring circulating volume?

Glucose is metabolised, leaving mostly free water that spreads through all compartments.

5. The safe rule for potassium supplementation is that it

Fast potassium can cause cardiac arrest.

6. In hyperkalaemia with bradycardia, calcium gluconate

Calcium stabilises cardiac membranes but potassium must be shifted or removed by other means.

7. During intravenous calcium for milk fever, the priority is to

Calcium affects cardiac rhythm and extravasation damages tissue.

8. Vomiting of stomach contents typically causes

Loss of hydrochloric acid and chloride raises bicarbonate relative to acid.

9. Why can oral rehydration work in infectious diarrhoea?

The co-transporter remains functional and draws water along with sodium.

10. A farmer's calf with diarrhoea cannot stand and has cold limbs. The best advice is to

Such calves are acidotic, hypovolaemic and unlikely to absorb oral fluid adequately.

Key points to revise

1. Separate dehydration from hypovolaemia.

2. Use several clinical signs together to assess hydration.
3. Balanced isotonic crystalloids are the usual first choice for replacement.
4. Colloids stay in vessels longer; check current guidance on synthetic products.
5. Potassium is never given as a rapid push.
6. Calcium is given slowly with heart auscultation.
7. Treat the cause of acid-base disturbance and restore perfusion.
8. Oral rehydration works through sodium-glucose co-transport and should be paired with continued milk feeding.

Go deeper on this site

- Ch 5. Nutraceuticals, herbal and ethnoveterinary medicine (in this book)
- Ch 3. Vitamins and minerals in therapy (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: The Fluid Resuscitation Plan in Animals
- Merck Veterinary Manual: Maintenance Fluid Plan in Animals
- Merck Veterinary Manual: Nutritional Requirements of Dairy Cattle

CHAPTER 5 OF 7

Nutraceuticals, herbal and ethnoveterinary medicine

How to think about herbal products, nutraceuticals and traditional farmer remedies with the same rigour used for any drug: what counts as evidence, where the real hazards lie, how they interact with licensed drugs and what to tell the owner or farmer.

After this chapter you can

- Distinguish a nutraceutical, a herbal product and an ethnoveterinary practice, and state what level of evidence each usually has
- Explain why 'natural' does not mean safe, using species-specific examples

- Describe how herbal and nutraceutical products can interact with conventional drugs
- Explain why residues and withdrawal remain a concern in food animals even for plant products
- Counsel a farmer or owner honestly about a traditional remedy without dismissing it

Why this topic needs a clear head

Farmers and pet owners in India use herbal and traditional remedies every day. Turmeric paste on a wound, neem leaves for skin disease, jaggery and ajwain for a bloated calf, and a long list of commercial herbal tonics are all common. A veterinarian will meet these practices at almost every clinic visit, so the aim is neither to ban them nor to accept them blindly.

The useful approach is to ask the same questions about a plant product that you ask about any drug. What is the active constituent? Is there evidence that it works in this species? What is the safe range? Does it interact with other drugs? What happens to its residues in milk, meat or eggs?

A **nutraceutical** is a food-derived or supplement-type product given for a health benefit beyond basic nutrition, such as omega-3 fatty acids, glucosamine, probiotics or silymarin. A **herbal product** is made from plant material and usually contains a mixture of many compounds. **Ethnoveterinary medicine** is the traditional knowledge that communities use to treat their own animals. These three overlap, but they differ in how well they have been tested.

What counts as evidence

Evidence comes in layers. At the top are well-designed controlled trials in the target species. Below them are small trials, trials in other species, laboratory studies and case reports. At the bottom is tradition alone. Many herbal remedies sit near the bottom for animals, and that is a statement about the evidence, not a proof that they do not work.

- **Laboratory activity is not clinical benefit.** A plant extract that kills bacteria in a dish may never reach that concentration in the animal, or may be destroyed in the rumen or gut.

- **Human data are not animal data.** Dogs, cats, ruminants and horses handle compounds differently, so a result in people cannot simply be carried across.

Another practical problem is **product variability**. The content of a plant depends on the variety, soil, season, part used and storage. Quality control of such products is uneven, and there have been reports in various countries of products found to contain undeclared conventional drugs. Be cautious with unlabelled mixtures.

Regulatory status of herbal and nutraceutical products for animals in India has been changing. Check the current notifications of the relevant authorities before you recommend, sell or label any such product.

Some commonly used agents and what is known

- **Turmeric (curcumin).** Widely used as an anti-inflammatory and wound remedy. Laboratory data are extensive, but curcumin is poorly absorbed, so the clinical benefit in animals is less clear than the laboratory data suggest. Topical use is generally low risk.
- **Neem.** Used on skin, as an insect repellent and as a general tonic. Neem products have shown activity against some parasites in laboratory work, but toxicity has been reported after excess or concentrated preparations, especially neem oil given by mouth. Treat 'a little is good so more is better' as a warning.
- **Garlic and onion (Allium species).** Sold as natural dewormers and immune boosters. These plants contain compounds that damage red cells and can cause Heinz body haemolytic anaemia, and dogs and cats are particularly vulnerable. Cats are especially sensitive.
- **Silymarin (milk thistle).** Used as a liver support. It has some supporting data, mostly from small studies, and is a reasonable low-risk adjunct beside proper treatment of the cause.
- **Glucosamine, chondroitin and omega-3 fatty acids.** Used for joint disease in dogs. Evidence is mixed in quality, with omega-3 fatty acids having comparatively better support. They support, and do not replace, analgesia and weight control.
- **Aloe vera.** The inner gel is used on wounds. The leaf latex contains anthraquinones that act as strong laxatives, so whole-leaf products given by mouth are not harmless.

Safety: natural is not the same as safe

A plant is a chemical factory, and many of its products evolved to deter animals from eating it. Several points matter in practice.

Species differences. Cats are deficient in some glucuronidation pathways, so many essential oils and phenolic compounds persist and accumulate. Tea tree oil and concentrated oils applied to the skin or diffused indoors have caused poisoning in cats and dogs. Dogs and cats react to Allium plants as described above.

Dose and concentration. A herbal extract is not a kitchen spice. Concentrated extracts and oils carry a different risk from the whole leaf.

Organ effects. Some plants carry hepatotoxic compounds such as pyrrolizidine alkaloids. A liver already damaged by disease is more vulnerable, so 'liver tonics' of unknown content in a jaundiced animal deserve care.

Delay in proper care. The commonest harm from herbal use is not poisoning but time lost. A calf with bacterial pneumonia or a cow with acute bloat can die while a home remedy is tried. Teach farmers the signs that mean 'call the veterinarian now'.

Interactions and residues

Herbal products are pharmacologically active, so they can interact with conventional drugs. The mechanisms are the same ones met earlier in the book.

- **Metabolism.** Some plant compounds induce or inhibit liver enzymes and drug transporters such as P-glycoprotein. Studies in people with St John's wort are a classical example, and similar concerns apply to veterinary patients, although species-specific data are limited.
- **Additive effects.** A sedative herb with a sedative drug, or a herb that affects blood clotting with an anticoagulant or an NSAID, may add up. Fish oil is sometimes discussed in this context; be careful before surgery or in bleeding disorders.

Residues. This is a point students often miss. A plant origin does not remove the need for a withdrawal period. For most herbal products no withdrawal period or maximum residue limit has been established, and that means *unknown*, not *zero*. In animals that produce milk, meat or eggs, ask what was given, when and how much, and take a cautious approach. Where a conventional drug is also in use, the

withdrawal period of that drug still applies. Check the current rules and notifications of the Indian authorities for residues and for any permitted herbal products in food animals.

Ethnoveterinary practice in India and talking to farmers

India has a deep tradition of ethnoveterinary knowledge, and national institutions and universities have documented many practices for conditions such as mastitis, wounds, diarrhoea, retained placenta and parasites. This documented knowledge is a valuable source of hypotheses and may be the only affordable option in some places, so treat it with respect while still checking it.

A good consultation follows a simple sequence.

1. **Ask without judgement.** Farmers hide what they have given if they expect a scolding. Ask 'what have you already tried?'
2. **Record it.** Note the product, amount, route and duration, particularly if the animal produces milk or goes for slaughter.
3. **Sort the remedies.** Harmless and possibly helpful (warm compresses, clean water, jaggery), uncertain, and harmful (oral oils in a distressed animal, force-drenching a recumbent animal, caustic wound applications).
4. **Never delay the effective treatment.** For a serious condition, proper care goes first, and a harmless traditional practice can sit beside it.
5. **Explain residues.** Say plainly that milk and meat can carry drug residues and that unknown mixtures have no tested safe waiting time.

The honest message is: some traditional remedies are harmless, a few may help, some are harmful, and most have not been tested well enough to say. Our job is to find out which is which for the animal in front of us.

Concept cleared

Evidence ladder

Controlled trials in the target species are strongest. Laboratory results, human data and tradition are weaker and cannot be taken as proof of benefit in the animal.

Natural is not safe

Plant products are active chemicals. Concentration, species and the state of the liver and kidney decide whether a plant product helps or harms.

Unknown is not zero

A herbal product with no established withdrawal period has an unknown residue risk, which must be treated cautiously in food animals.

Interactions follow normal pharmacology

Herbal compounds can induce or inhibit metabolism, add to the effects of drugs or reduce absorption, exactly as conventional drugs do.

Memory aid: Questions to ask about any plant product: WHAT-EVIDENCE

Ask: What is in it, How much, Any proof in this species, Toxicity, Interactions, Residues and withdrawal. Never skip the last two in food animals.

Compare and contrast

Nutraceutical, herbal product and ethnoveterinary practice

Feature	Nutraceutical	Herbal product	Ethnoveterinary practice
Typical source	Food-derived or supplement compounds	Plant material, often mixed	Community knowledge using local plants and methods
Standardisation	Often defined content	Variable, may be unstandardised	None, depends on the preparer
Evidence	Mixed, some trials	Mostly laboratory and tradition	Documented tradition, limited testing
Main concern	Quality and overstated claims	Variability, toxicity, hidden drugs	Delay in proper care, unknown residues

Reasons a remedy appears to work

Explanation	Meaning	How to check
True pharmacological effect	The compound acts on the disease	Controlled trial in the species
Natural recovery	The disease would have resolved anyway	Compare with an untreated control group
Co-treatment	A conventional drug was also given	Record every product used
Placebo and owner expectation	Perceived improvement	Blinded, objective outcomes

Species notes

Cats

Poor at conjugating many phenolic compounds, so essential oils, tea tree oil and some herbal oils are risky. Onion and garlic can damage red cells.

Dogs

Allium plants can cause Heinz body anaemia. Concentrated oils and extracts also carry risk, and xylitol-containing supplements are dangerous.

Cattle and buffalo

Milk is consumed daily, so any herbal or home remedy matters for residues. Large oral volumes in a weak animal risk aspiration.

Small ruminants

Plant dewormers and tonics are widely used by small farmers. Check parasite control with faecal egg counts rather than assuming a herbal drench works.

Poultry

Herbal feed and water additives are common. Eggs and meat are food, so unknown withdrawal remains a concern, and herbal products cannot replace biosecurity and vaccination.

Clinical pearls

Self-test: 10 questions

1. Which statement best describes an ethnoveterinary practice?

Ethnoveterinary medicine is traditional knowledge used by communities, which may or may not have been tested.

2. A plant extract kills bacteria in a laboratory dish. What is the correct conclusion?

Laboratory activity does not show that the compound reaches effective levels in the animal.

3. Garlic and onion are a particular concern in dogs and cats because they can cause

Allium compounds damage red cells and can cause Heinz body anaemia, with cats especially sensitive.

4. Why are essential oils and concentrated tea tree oil risky in cats?

Limited conjugation lets phenolic compounds accumulate to toxic levels.

5. A farmer gives a herbal mixture to a lactating cow. The label shows no withdrawal period. How should the veterinarian regard it?

No stated period means the residue risk is unknown, not absent.

6. Which is the commonest real harm from home remedies?

Time lost before proper care is the most frequent cause of harm.

7. A herbal product that induces hepatic enzymes may

Induction speeds metabolism, so drugs cleared by those enzymes can become less effective.

8. The best first step when a farmer mentions a traditional remedy is to

Open questions give the information needed and keep the farmer's trust.

9. Why can two bottles of the same herbal tonic act differently?

Lack of standardisation causes batch-to-batch variation.

10. Aloe vera leaf latex given orally is best described as

The latex contains anthraquinones with strong laxative action, unlike the inner gel used on wounds.

Key points to revise

1. Nutraceutical, herbal product and ethnoveterinary practice differ in standardisation and evidence.
2. Evidence from laboratory studies, other species or tradition is weaker than a controlled trial in the target species.
3. Natural does not mean safe; species, dose and concentration decide risk.
4. Cats are especially sensitive to essential oils and some plant phenolics.
5. Herbal products can interact with conventional drugs through metabolism, additive effects and absorption.
6. Most herbal products lack established withdrawal periods or residue limits, which means unknown risk in food animals.

7. Ask about, record and respect traditional practices, but never delay effective treatment.
8. Check the current Indian regulatory position before recommending or labelling herbal products for animals.

Go deeper on this site

- Ch 6. Feed additives, growth promoters and ionophores (in this book)
- Ch 4. Fluid, electrolyte and acid-base therapy (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- WHO: Antimicrobial resistance fact sheet
- WHO: One Health
- WOAH: Codes and Manuals

CHAPTER 6 OF 7

Feed additives, growth promoters and ionophores

What feed additives are, why antibiotic growth promoters are being phased out worldwide, how ionophores work and why they poison horses and dogs, and how residue and regulatory thinking applies to medicated feed.

After this chapter you can

- Classify feed additives and distinguish a nutritional additive from a drug
- Explain why antibiotic growth promoters were withdrawn and how that links to resistance
- Describe the mechanism and uses of ionophores in ruminants and poultry
- Explain why ionophores are toxic to horses, dogs and other species, and how accidents happen
- Explain residue and withdrawal logic for medicated feed and what to tell the farmer

What a feed additive is

A **feed additive** is a substance added to feed in small amounts to improve the feed, the animal's performance or the quality of the product. The line between a nutrient, an additive and a drug is thin and is decided by *purpose* and *law*. Vitamins and minerals correct a dietary need. Enzymes, probiotics, organic acids and toxin binders improve digestion or feed quality. Antimicrobials, coccidiostats and ionophores act on microbes and parasites, so they behave as drugs, and are treated by regulators with more care.

Regulation differs from country to country and is revised from time to time. In India, rules on feed quality, feed additives and the use of antimicrobials in animals sit with several authorities. Check the current notifications before advising a farmer or a feed manufacturer.

Remember one key idea: anything added to **feed** reaches every animal in the group, sick or healthy, at a dose that depends on how much each animal eats. That makes feed a poor route for precise dosing and a good route for accidents.

Antibiotic growth promoters and their phase-out

Decades ago it was found that giving very low levels of antibiotics in feed over a long time improved growth and feed efficiency in pigs and poultry. These are called **antibiotic growth promoters** (AGPs). The exact mechanism is not fully settled, but the effect is thought to come from changes in the gut microbiota and less sub-clinical infection.

The problem is that long, low-level exposure is the ideal condition for selecting resistant bacteria. Resistant organisms and resistance genes can reach people through food, direct contact and the environment. For this reason Sweden and later the European Union stopped AGP use, and the WHO has recommended that medically important antimicrobials should not be used in healthy animals to promote growth. Other countries, including the United States, have also restricted growth-promotion use of medically important antimicrobials.

India has also moved towards restricting antimicrobial use in animals, including action on colistin in animal production. The details change, so state them only as 'check the current notification'.

Common confusion: phase-out of AGPs does *not* mean that animals can never receive antibiotics. Treatment of sick animals under veterinary supervision remains allowed. What is being curtailed is routine use for growth. Good farm management, biosecurity, vaccination, clean water and balanced feed replace much of what AGPs did, and non-antibiotic alternatives such as probiotics, organic acids and enzymes are used. The evidence for these alternatives is variable.

Ionophores: what they are and how they work

Ionophores are antimicrobial compounds made by microbes. Examples include monensin, lasalocid, salinomycin, narasin and maduramicin. They are not used in human medicine, which is one reason they were long treated differently from antibiotics, although they are still managed carefully.

Mechanism. An ionophore is a fat-soluble molecule that binds cations such as sodium, potassium and calcium and carries them across cell membranes. This destroys the ion gradients the cell relies on, and the organism dies of energy and osmotic failure. Gram-positive bacteria and protozoa such as *Eimeria* are sensitive. Gram-negative bacteria are protected by their outer membrane.

Uses.

- **Poultry:** coccidiosis prevention in broilers and replacement pullets. Resistance can develop, and programmes are often rotated or combined with vaccines.
- **Cattle and small ruminants:** in the rumen, ionophores favour microbes that produce more propionate and less methane, improving feed efficiency and helping control coccidiosis. They can also reduce the risk of some forms of acidosis and bloat.

Safe use depends on correct mixing, a labelled species and a labelled dose. The margin of safety is narrow, which leads to the next section.

Ionophore toxicity

Ionophores damage **cardiac and skeletal muscle**, because the same disruption of ion balance occurs in muscle cells when the dose is too high or the animal is too sensitive. The species differ greatly in sensitivity.

- **Horses** are exceptionally sensitive, especially to monensin. Feed intended for cattle or poultry must never be fed to horses.
- **Dogs** are also sensitive, and cases follow access to poultry or cattle feed, or to litter and feed spill.
- **Other species**, including cats, sheep, goats, camelids, rabbits and turkeys, can also be affected. Some ionophores are tolerated by one species and are not by another, so use only products labelled for that species.

How accidents happen. Feed-mill cross-contamination, mixing errors, wrong feed bags, feeding the wrong ration to the wrong species, and use of poultry litter or feed residues as feed for other animals.

Signs. Anorexia, colic-like signs, weakness, a stiff or wobbly gait, sweating in horses, recumbency, dark urine from muscle breakdown, and signs of heart failure. Acute cases may die suddenly. Survivors can have lasting damage to the heart.

Management. There is no specific antidote. Remove the feed at once, call for urgent supportive care and monitor the heart and muscle enzymes. Binding agents may be used early after ingestion by veterinarians. Antioxidant treatment such as vitamin E has been discussed, but the evidence is limited. Prognosis depends on the amount eaten and on cardiac damage, so be guarded.

Drug interactions. Some drugs, notably tiamulin and certain macrolides, can slow hepatic metabolism of ionophores and cause toxicity at normally safe levels, particularly in poultry and pigs. Read the label for incompatible combinations before mixing.

Residues, withdrawal and medicated feed

A **residue** is the drug or its metabolites remaining in milk, meat, eggs or other products. A **maximum residue limit (MRL)** is the highest concentration regarded as acceptable in a food. A **withdrawal period** is the time after the last dose before the product can enter the food chain so that residues fall below the limit. Codex Alimentarius and national authorities set the standards. For India, check the current FSSAI and other notifications for MRLs and withdrawal times.

Medicated feed brings special problems.

- **Carry-over.** Traces of medicated feed left in mixers, conveyors and bins can contaminate the next batch, a cause of unintended residues and of toxicity in sensitive species.
- **Uneven intake.** Sick animals eat less, so they get less drug while healthy animals eat more.
- **Label discipline.** Use only for the labelled species, purpose and period. Some ionophores must not be given to laying hens producing eggs for human consumption, and some have a pre-slaughter withdrawal. Read the label.
- **Records.** Keep feed batch records, dates and the animals fed, so that a residue problem can be traced.

Residue violations carry economic, trade and public-health costs. Exports of meat and fish products may be rejected for residues.

What to tell the farmer or feed manufacturer

Give short, practical advice.

1. **Check the bag.** Is it labelled for your species? Never feed cattle or poultry feed to horses or dogs.
2. **Store separately** and keep animals and dogs away from feed stores.
3. **Do not use poultry litter or feed leftovers** as feed for other species unless a veterinarian has advised that it is safe and legal.
4. **Follow withdrawal times** and keep a written record.
5. **Do not use antibiotics as a routine growth booster.** Improve housing, hygiene, vaccination and nutrition, and use treatment only when needed and prescribed.
6. **If an animal becomes ill after a feed change** or a new batch, remove that feed, keep a sample, and call the veterinarian at once.

Keep a sample of the suspect feed. It lets the laboratory confirm the cause and protects the farmer if there is a dispute with the feed supplier.

Concept cleared

Purpose and law define an additive

A feed ingredient becomes a drug when its purpose is to affect microbes, parasites or disease, and it is then regulated more tightly.

Low-dose antibiotics select for resistance

Long sub-therapeutic exposure favours resistant bacteria, which is the reason for the global phase-out of growth promotion.

Ionophores carry ions across membranes

They collapse ion gradients in susceptible microbes and, at high exposure, in cardiac and skeletal muscle.

Feed reaches every animal

Medicated feed gives uneven dosing and carry-over risk, so label and mixing discipline matter.

Memory aid: Ionophore poisoning: HORSE-DOG-FEED

Horses and dogs are hit hardest. Think of feed errors first, and the heart and muscles as targets. Stop the feed, support the patient and keep the sample.

Compare and contrast

Ionophore sensitivity in different species

Species	Sensitivity	Typical route of exposure	Main target
Horse	Very high	Cattle or poultry feed	Heart and skeletal muscle
Dog	High	Poultry or cattle feed, spilled feed	Skeletal muscle, heart and nerves
Cattle	Tolerates labelled dose	Medicated ration	Overdose affects heart and muscle
Poultry	Tolerates labelled dose	Medicated feed	Interactions and overdose cause toxicity

Growth promotion versus treatment

Feature	Growth promotion	Therapeutic use
Animals	Healthy	Sick or in-contact at risk
Duration	Long, continuous	Defined short course
Supervision	Often none	Veterinary
Resistance risk	High, selective pressure	Lower if used correctly
Current trend	Being phased out or restricted	Allowed with prudent use

Species notes

Horses
Extremely sensitive to ionophores such as monensin. Cattle and poultry feed must be kept away from them.

Dogs
Poisoning follows eating poultry or cattle feed. Signs include weakness, muscle damage and heart problems.

Cattle and buffalo
Ionophores improve feed efficiency and control coccidiosis, but mixing errors can cause serious cardiac damage.

Sheep and goats
Use only products labelled for them, because sensitivity differs and some feeds designed for cattle may be unsafe.

Poultry
Ionophores control coccidiosis. Check withdrawal, avoid use in layers where the label forbids it and watch for interactions with tiamulin and some macrolides.

Clinical pearls

Self-test: 10 questions

1. The main public-health reason for phasing out antibiotic growth promoters is

Long, low-level exposure favours resistant organisms, which can reach people.

2. Which statement about the phase-out is correct?

The phase-out targets growth promotion, not treatment.

3. An ionophore acts by

Ionophores are lipid-soluble cation carriers.

4. Gram-negative bacteria are largely unaffected by ionophores because of

The outer membrane stops the ionophore reaching the inner membrane.

5. Which species is exceptionally sensitive to monensin?

Horses are the classical highly sensitive species.

6. The tissues mainly damaged in ionophore poisoning are

Disrupted ion balance damages muscle cells.

7. A common way dogs and horses are poisoned is

Accidental access to cattle or poultry feed is the typical cause.

8. Tiamulin with an ionophore may

Some drugs inhibit hepatic metabolism and raise ionophore toxicity.

9. What is a withdrawal period?

It allows residues to fall below the MRL.

10. After suspected ionophore poisoning the first action is to

Stopping exposure and keeping a sample are essential.

Key points to revise

1. Feed additives range from nutrients to drugs, and regulation depends on purpose.
2. Antibiotic growth promoters select for resistance and are being restricted or banned in many countries.
3. Check the current Indian notifications on antimicrobial use in animal feed.
4. Ionophores move cations across membranes and kill Gram-positive bacteria and coccidia.
5. Horses and dogs are very sensitive to ionophores, and toxicity targets heart and skeletal muscle.
6. Tiamulin and some macrolides can raise ionophore toxicity by slowing metabolism.
7. Medicated feed carries risks of carry-over, uneven intake and residues.
8. Follow labels, keep records and sample suspect feed.

Go deeper on this site

- Ch 7. Drug use in poultry and aquaculture (in this book)
- Ch 5. Nutraceuticals, herbal and ethnoveterinary medicine (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Concepts
- Veterinary Drug Concepts Clearly Explained

Sources

- WHO: Antimicrobial resistance fact sheet
- WHO: One Health
- WOAH: Codes and Manuals

CHAPTER 7 OF 7

Drug use in poultry and aquaculture

Why treating a flock or a pond differs from treating one animal: group dosing, water and feed medication, the practical limits of each route, withdrawal for eggs, meat and fish, and the main rules and cautions for fish and shrimp medicines.

After this chapter you can

- Explain the logic of flock-level treatment and its limits
- Describe how water and feed medication work and what can make them fail
- Apply withdrawal logic to broilers, layers, fish and shrimp
- Explain why temperature, water quality and the environment matter for aquatic drug use
- Advise a farmer on prudent drug use and banned substances, hedging current Indian rules

Treating a flock or a pond is a population problem

In a poultry house or a fish pond you almost never treat a single animal. The patient is the whole group, and the drug must reach every animal through feed or water. This changes the thinking in four ways.

- Treatment is **delayed** because disease is usually noticed late, after many animals are already affected.
- Dose is only as good as **intake**. A sick bird or fish eats and drinks less, so the animals that most need the drug get the least.
- Cost, labour and the long list of withdrawal obligations force you to be selective.
- The same drug exposure reaches healthy animals, which increases the chance of resistance and residues.

For this reason prevention (biosecurity, vaccination, nutrition, stocking density, water quality) is always the first line, and a drug is a last tool used on a diagnosis.

Submit samples or post-mortem findings, and choose a drug on the basis of the likely cause and sensitivity testing where possible. Avoid treating 'cough' or 'mortality' blindly. Many such problems are viral, parasitic or due to management, and an antibiotic does nothing for them.

Water and feed medication in poultry

Water medication is the usual choice for flock treatment because birds still drink when they stop eating, so water reaches sick birds sooner than feed does. It is also quick to start and stop.

Several things can make water medication fail.

- **Water intake varies** with age, temperature and health. In hot weather birds drink more, so they take more drug; in cold or disease they drink less. The medicine concentration must be set with the expected intake in mind, following the label.
- **Solubility and stability.** A drug that does not dissolve fully, or that breaks down in hard water, in sunlight or in the presence of chlorine or minerals, will not deliver the intended dose. Some drugs bind calcium in hard water.
- **Biofilm and pipes.** Drinker lines may hold biofilm that traps drug and bacteria. Clean lines before and after treatment.
- **Dead ends and uneven flow.** Birds at the far end of the line may get less.
- **Competing water sources.** Make sure the medicated water is the only source, and prepare fresh solutions as the label directs.

Feed medication suits longer programmes, such as coccidiostats, but it is slower to start, depends on appetite and has the carry-over problem discussed in the previous chapter. Mixing must be uniform, and medicated feed must be cleared from lines and bins before another type of feed is made.

Do not use antibiotics together with live bacterial vaccines unless the product information permits it, and do not add disinfectant chlorine to vaccine water. Always follow the product label.

Withdrawal and residues in poultry

Poultry are food animals, and drug residues in meat and eggs are a trade and public-health issue. Withdrawal means that the last dose must be given long

enough before slaughter or egg collection for residues to fall to acceptable levels.

Broilers are slaughtered young, so the margin between treatment and slaughter is short. A treatment started late in a short cycle may run into the slaughter date. Plan the timing and consider whether the batch should be held.

Layers. Many antimicrobials are not permitted for use in birds producing eggs for human consumption, and eggs can carry residues. Check the label and the current rules. If a drug must be used in a laying flock for a good reason, the eggs have to be kept out of the food chain for the required time.

Extra-label and unregistered use. If a product has no stated withdrawal time for the species, do not assume that it is zero.

Banned substances. Some compounds, such as nitrofurans and chloramphenicol, are prohibited in food animals in many countries, including India, and no withdrawal time makes them acceptable. Action on colistin in food animals has also been taken in India. Check the current notifications for the complete and updated list.

Always keep a treatment record: product, batch, dates, quantity, house and who gave it. The record protects the farmer and allows traceback.

Aquaculture: why fish are different

Fish and shrimp live *in* the medium that carries the drug, which makes aquaculture different from land-based farming.

- **Temperature rules the pharmacokinetics.** Fish and shrimp are cold-blooded, so absorption, metabolism and excretion all vary with water temperature. A drug cleared in a few days in warm water may take far longer in cool water. Withdrawal times for fish are therefore commonly expressed in **degree-days**, a combination of days and temperature.
- **Routes.** Medicated feed is the main route for systemic treatment. Bath or dip treatments are used for external parasites and skin infections. Injection is used for valuable broodstock and individual fish.
- **Feed intake falls in disease.** As in poultry, sick fish stop eating, so oral medication fails exactly when it is most needed. Uneaten medicated pellets also leach drug into the water.

- **The environment is part of the treatment.** Drugs and disinfectants may kill beneficial microbes in biofilters and ponds, reduce dissolved oxygen, or harm other organisms. Antimicrobial residues in pond water and sediment select for resistant bacteria and can spread beyond the farm.
- **Water quality comes first.** Low oxygen, poor pH, ammonia and crowding cause stress and disease, and correcting them often does more than any drug. Treat the water before the fish.

Medicines used for baths and dips can be dangerous if the concentration, contact time or aeration is wrong, because fish have small safety margins and gill damage is quick. Follow expert advice and the label.

Fish and shrimp medicines and the rules (hedged)

Few drugs are formally approved for use in aquatic species in any country, and approval differs between countries. A veterinarian or aquaculture expert should choose what is used.

The general principles are the same as for poultry. Use drugs only for a diagnosed problem, choose the narrowest effective option, and respect withdrawal times. Probiotics, good feed, vaccines where available and water management are the preferred first measures.

Rules in India. Aquaculture in India is subject to rules on the use of antibiotics and other pharmacologically active substances, with regulation of coastal aquaculture and export residue monitoring. Several substances, including certain antibiotics and dyes such as malachite green, are prohibited in aquaculture in many exporting countries, and shrimp consignments with banned residues may be rejected abroad. The exact list of prohibited and permitted substances and the responsible agencies change, so check the current notification of the relevant Indian authority and the import rules of the destination market before advising on any drug.

The 'zero tolerance' idea is important. For certain banned compounds, detectable residue is a violation, however small the amount, and no withdrawal time helps.

What to tell the fish or shrimp farmer

Give the farmer a short, practical list.

1. Check water quality first and keep records of oxygen, pH, temperature and mortality.
2. Do not use antibiotics by habit, and do not buy 'secret' mixtures from unknown sellers.
3. Use only approved or veterinarian-advised products, at the labelled concentration.
4. Observe the withdrawal time, remembering that cool water lengthens it.
5. Keep treatment records and batch numbers, and do not harvest early.
6. Dispose of used water and medicated feed responsibly.

Concept cleared

Treat the population, but dose depends on individual intake
In flocks and ponds, the sickest animals eat and drink least, so group dosing under-doses the animals that need it most.

Water first, drug second
Water quality and management are the main drivers of fish and poultry disease and often the best treatment.

Withdrawal protects the food chain
Eggs, meat and fish must be free of residues above accepted limits, and banned substances allow no safe period.

Temperature controls fish pharmacokinetics
Cold-blooded animals clear drugs slowly in cool water, so withdrawal is expressed in degree-days.

Memory aid: Before you medicate a flock or pond: DIAGNOSE-DOSE-DEADLINE
Diagnose the cause, check the dose reaches the animals through intake and water quality, and note the deadline set by withdrawal before sale or harvest.

Compare and contrast

Water medication versus feed medication in poultry

Feature	Water medication	Feed medication
Speed of start	Quick	Slower, needs mixing and delivery
Sick birds	Often still drink	Often stop eating
Main risks	Solubility, hard water, biofilm, variable intake	Uneven mixing, carry-over, appetite
Best use	Short-course treatment of an outbreak	Longer prevention programmes

Poultry versus aquaculture drug use

Feature	Poultry	Fish and shrimp
Body temperature	Constant	Follows water, so affects drug handling
Main routes	Water, feed	Feed, bath, occasional injection
Withdrawal basis	Days	Degree-days or days adjusted for temperature
Environmental concern	Litter and manure residues	Direct release into water and sediment
Special trade issue	Residues in meat and eggs	Banned-substance rejection of exports

Species notes

Broiler chickens

Short production cycle leaves little time for withdrawal. Late treatment can conflict with slaughter dates.

Laying hens

Many antimicrobials are not permitted when eggs go for human food. Check the label and current rules, and keep treated eggs out of the food chain.

Ducks, quail and turkeys

Freshwater fish (carps)

Do not assume poultry products are safe for them. Species sensitivity differs, so use products labelled for the species, particularly ionophores.

Pond-based, with medication mostly through feed and water management. Temperature affects drug clearance.

Shrimp

Antibiotic residues are a major trade concern. Focus on pond management, biosecurity and permitted products, and check current rules.

Clinical pearls

Self-test: 10 questions

1. Why is water medication often preferred for treating a sick flock?

Sick birds usually continue to drink, so the drug reaches them sooner than through feed.

2. Which factor can cause water medication to fail?

Biofilm, poor solubility and mineral binding can reduce the delivered dose.

3. A main problem of medicated feed is

Traces remain in mixers and lines and contaminate later feed.

4. For laying hens producing eggs for human food, you should

Eggs carry residues, and many antimicrobials are not allowed for layers.

5. Why is fish withdrawal often given in degree-days?

Cold-blooded animals clear drugs more slowly in cooler water.

6. Which is true for a banned substance in food animals?

Zero tolerance means that detection itself is a violation.

7. Why do sick fish respond poorly to medicated feed?

Reduced appetite lowers drug intake exactly when needed.

8. What is the first step in managing a disease outbreak in a pond?

Poor water quality often causes or worsens disease.

9. Why can broiler treatment be problematic?

Late treatment may leave too little time for residues to deplete.

10. Which record is most useful after treating a flock?

These details allow traceback and correct withdrawal calculation.

Key points to revise

1. In flocks and ponds, prevention and diagnosis come before drugs.
2. Water medication reaches sick birds sooner than feed medication but depends on intake, solubility and clean lines.
3. Feed medication has carry-over and appetite problems.
4. Layers need special care because eggs are food and many drugs are not permitted.
5. Withdrawal times must be respected, and banned substances are never acceptable.

6. Fish pharmacokinetics depend on water temperature, so withdrawal uses degree-days.
7. Aquaculture drugs enter the environment directly and can select for resistance.
8. Check the current Indian notifications for prohibited substances, permitted products and residue limits.

Go deeper on this site

- Ch 6. Feed additives, growth promoters and ionophores (in this book)
- Ch 5. Nutraceuticals, herbal and ethnoveterinary medicine (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Concepts
- Veterinary Drug Concepts Clearly Explained

Sources

- WHO: Antimicrobial resistance fact sheet
- WHO: One Health
- WOAH: Codes and Manuals

How to use Book 4: a short discussion

The first three books taught the science: how drugs move, how they act, which drugs suit which organ system and which drugs fight infection. Book 4 is where that science meets daily practice. The seven chapters cover the products and supportive measures that veterinarians use constantly but that rarely get a full lecture: skin, eye and ear preparations, vitamins and minerals, fluid and electrolyte therapy, herbal and ethnoveterinary remedies, feed additives, and medicines for poultry and aquaculture.

Why supportive care deserves a book of its own

Many animals recover because of what is done around the specific drug: correcting dehydration, restoring a mineral balance, relieving an itch so that the skin can heal, keeping an eye moist while an ulcer repairs. Students often underrate this work

because it feels less dramatic than choosing an antibiotic. Experienced clinicians know that a sound fluid plan or a correct nutritional diagnosis often saves more animals than any single medicine.

Topical drugs and the species problem

Skin, eye and ear products look harmless, yet they cause many avoidable problems. A shampoo that is fine for a dog can be harmful to a cat that grooms itself. A steroid eye drop that calms inflammation can worsen a corneal ulcer. The chapters on dermatology and on eye and ear drugs explain how a topical drug is absorbed, where it can go wrong, and which species deserve extra caution.

Nutrition, fluids and herbal remedies

The chapters on vitamins and minerals and on fluid, electrolyte and acid-base therapy are among the most useful for field work. They show how deficiency and excess both cause disease and why correcting a disturbance too fast can be as dangerous as ignoring it. The chapter on nutraceuticals, herbal and ethnoveterinary medicine takes a fair view. Traditional knowledge in India is valuable and widely used by farmers, but a remedy needs to be judged on evidence, safety and possible interactions, and the veterinarian must be able to explain this respectfully to the owner.

Production animals, residues and regulation

The last two chapters deal with feed additives, growth promoters, ionophores, and medicines for poultry and fish. They connect directly to the residue and stewardship ideas from Book 3. Rules on additives, growth promotion and aquaculture drugs change over time and differ between countries, so the book repeatedly asks you to check the current notification instead of memorising a list that may become out of date.

Talking to owners and farmers

Applied therapeutics is also communication. An owner who cannot give eye drops at the right interval, or a farmer who mixes a water medicine the wrong way, will undo a

correct prescription. Each chapter therefore includes practical points about what to explain, what to warn about and when to ask the animal to be seen again. Clear advice about missed doses, storage, stopping rules and withdrawal periods is part of good prescribing, and examiners increasingly test it through case-based questions as well as through direct drug questions.

How to study this book

Read one chapter at a time, take the ten-question test, and then read the Revise points. Use the Compare tables to set similar products side by side, and read the Species notes before an examination, because species differences are a favourite topic for questions. As in the earlier books there are no dose tables; use the product label or a current formulary for doses. This material is written for education and does not replace the judgement of a registered veterinarian.

BVSC & AH STUDY BOOK 5 OF 7

Veterinary Anaesthesiology and Analgesia

Fourteen chapters on safe anaesthesia and pain relief: assessment, sedation, injectable and inhalation agents, equipment, local blocks, monitoring, special patients, species and field practice, wildlife capture, record keeping and emergencies. Each chapter ends with a 10-question self-test.

14 chapters | **140** practice questions | **No** dose tables

By Dr. Rameez Bloch, BVSc & AH, MVSc

Start here

Pick a chapter from the list on the left (or the top bar on a phone). The chapters follow the path of an anaesthetic from assessment to recovery: preparation, sedation, induction, maintenance, equipment, local blocks, analgesia, monitoring, special patients and species, field work, safety, and emergencies. Each chapter has six parts: Learn, Concepts, Compare, Species, Quiz and Revise. Your quiz progress is saved on this device only.

CHAPTER 1 OF 14

Principles of anaesthesia and pre-anaesthetic assessment

Anaesthesia is a planned, monitored reversible loss of awareness, sensation and movement, and most anaesthetic deaths trace back to poor assessment or preparation. This chapter covers the stages and planes of anaesthesia, ASA grading, history and examination, fasting by species, consent and the equipment checklist.

After this chapter you can

- Describe the stages and planes of anaesthesia and the signs used to recognise them
- Assign an ASA physical status grade and explain how it guides risk discussion
- List the key points of history and physical examination before anaesthesia
- Explain why fasting advice differs between dogs, cats, ruminants, horses and small mammals
- Prepare an equipment and drug checklist and obtain informed consent

Why assessment comes before the drug

General anaesthesia produces unconsciousness, muscle relaxation and loss of reflex response to pain, but every anaesthetic drug also depresses the heart, the lungs or both. The margin between a useful depth and a dangerous one is narrow. For this reason the safest anaesthetic begins **before** any drug is drawn up.

Surveys of small animal and equine practice repeatedly show that anaesthetic deaths are not mainly due to a single bad drug. They arise from unrecognised disease, poor preparation, inadequate monitoring and delayed response to a problem. A good pre-anaesthetic routine is therefore a patient safety tool, not paperwork.

The aim is to answer four questions: how sick is this animal, which drugs suit its condition, what could go wrong, and are we ready to deal with it.

Stages and planes of anaesthesia

The classical description by Guedel was made with ether, but the idea still helps students recognise depth. Modern injectable and balanced techniques pass through the early stages so quickly that they can be hard to see.

1. **Stage I, analgesia.** The patient is conscious but drowsy, and pain sense is reduced.
2. **Stage II, excitement or delirium.** Consciousness is lost but the brain's inhibitory control is lost first, so the animal may struggle, vocalise, paddle, have irregular breathing and an unpredictable heart rate. This is the stage that smooth

induction and good premedication try to avoid. Vomiting and regurgitation are likely here.

3. **Stage III, surgical anaesthesia.** Divided into light to deep planes. Breathing becomes regular, muscles relax and reflexes fade as the plane deepens.
4. **Stage IV, overdose.** Respiratory and then cardiac failure. This is an emergency: reduce or stop the anaesthetic, ventilate with oxygen and support circulation.

In practice the clinician judges depth by a group of signs, not one. Eye position, jaw tone, palpebral and corneal reflexes, response to surgical stimulus, heart rate, blood pressure and respiratory pattern are read together. A common confusion is to treat a lost palpebral reflex as proof of adequate depth. Signs differ between drugs: ketamine keeps eyes open and reflexes partly present even when the patient is anaesthetised, whereas inhalant agents behave more like the classical scheme.

ASA physical status grading

The American Society of Anesthesiologists (ASA) system, adapted for animals, places each patient in one of five categories before anaesthesia. It describes the animal's health, not the procedure.

- **ASA I**: normal healthy patient, for example a routine elective spay.
- **ASA II**: mild systemic disease without functional limitation, such as a mild, well-controlled condition, an obese animal or a very young or old patient.
- **ASA III**: severe systemic disease with functional limitation, for example anaemia or moderate heart disease.
- **ASA IV**: severe systemic disease that is a constant threat to life, such as decompensated heart failure or severe shock.
- **ASA V**: moribund animal not expected to survive without the procedure.

An **E** is added for emergency surgery. Higher grades carry greater risk, so grading guides drug choice, how much monitoring is needed, whether to stabilise first and what to tell the owner. A frequent mistake is to assume a young animal is automatically ASA I; a puppy with a congenital shunt or a calf with dehydration and acidosis is not. Grading is also a judgement, so two clinicians may differ by one grade.

History and clinical examination

The history should record species, breed, age, weight, current and recent drugs, previous anaesthetic reactions, vaccination and deworming status, exercise tolerance, coughing, fainting, seizures, and any family history of drug problems. Ask specifically about drugs such as ivermectin, steroids, NSAIDs and anything given by the owner or a local practitioner, because these may interact with anaesthetics or affect the kidney and liver.

The physical examination should include demeanour, mucous membrane colour and capillary refill, hydration, heart rate and rhythm, auscultation of heart and lungs, pulse quality, respiratory pattern, temperature and body condition. In ruminants and horses, rumen fill, bloat and colic signs matter. Weigh the animal accurately; drug calculation errors from guessed body weight are a preventable cause of overdose.

Laboratory tests are chosen by the findings and the grade. At minimum, packed cell volume and total protein are cheap and useful; older animals or those with systemic illness benefit from a fuller profile of kidney, liver and electrolytes. Correct dehydration, anaemia, hypovolaemia and electrolyte problems first when the procedure allows it.

Fasting by species

Fasting reduces the volume of stomach contents so that vomiting, regurgitation and aspiration are less likely, and lowers pressure on the diaphragm. But fasting too long causes hypoglycaemia in the very young and small, dehydration and stress. Exact durations vary between textbooks and institutions, so follow your hospital protocol and current guidelines.

- **Dogs and cats**: food is withheld for a limited period, with water allowed until close to premedication. Neonates, toy breeds and diabetics need shorter fasts and glucose awareness.
- **Rabbits, guinea pigs and rodents**: they cannot vomit, so prolonged fasting adds risk without benefit. Rabbits in particular should not be starved long, and food in the mouth should be cleared before induction.
- **Horses**: practices vary. Concentrates are withheld and hay is often reduced; water is usually left available. A full gut presses on the diaphragm and may cause poor ventilation in dorsal recumbency.

- **Cattle, sheep and goats**: the rumen ferments continuously, so complete emptying is not possible. A fasting period lowers rumen volume and bloat, yet regurgitation can still occur. Intubate with a cuffed tube and keep the head lower than the pharynx during recumbency.

Consent, equipment and the final check

Informed consent. The owner should be told in plain language why anaesthesia is needed, the animal's grade, the general risks (including death), the cost of monitoring and the options. Signing a form does not replace the conversation. Record the consent, identification of the animal and the planned procedure. In farm animals, explain the risk for food-producing animals and withdrawal periods for drugs used, and check the current regulations for your region.

Equipment checklist. Before the first drug is given, confirm each item:

1. Oxygen supply with enough reserve, breathing system and anaesthetic machine checked for leaks.
2. Endotracheal tubes in a range of sizes, cuffs tested, laryngoscope working, suction ready.
3. Monitors available: pulse oximeter, blood pressure, ECG, capnograph and thermometer.
4. Intravenous catheter and fluids.
5. Emergency drugs and reversal agents drawn up or labelled and a written emergency plan.
6. Warming equipment, since hypothermia is common and prolongs recovery.

Finally, label every syringe, confirm drugs against the patient record and give a clear start time. Good practice continues after the procedure: recovery needs a trained observer until the animal can protect its airway and hold its own temperature.

Concept cleared

Concept cleared: Planes of anaesthesia

Think of lowering a lift down a building. Each floor is a deeper plane, and the lower you go the quieter the building becomes but the harder it is to get back. The anaesthetist's job is to stop at the floor where surgery is possible and no lower.

Concept cleared: ASA grade

The grade is a weather forecast for the patient, not for the operation. It tells you how rough the journey is likely to be so that you pack the right equipment and warn the owner.

Concept cleared: Excitement stage

When anaesthesia starts, the brain's brakes are switched off before its engine. A struggling, paddling animal is not light, it is disinhibited, and a smooth premedication prevents this.

Concept cleared: Fasting differs by gut

A simple-stomached animal can be emptied, so a short fast helps. A rumen cannot be emptied, so protecting the airway matters more than the length of the fast.

Memory aid: Pre-anaesthetic safety questions

Use SAFE: Status (ASA grade), Animal (history and examination), Fasting and fluids, Equipment and emergency drugs ready. If any letter is missing, pause before inducing.

Compare and contrast

Stages of anaesthesia

Stage	Name	Main features	Clinical aim
I	Analgesia	Conscious, drowsy, reduced pain sense	Starting phase
II	Excitement	Unconscious but disinhibited, struggling, irregular breathing, vomiting possible	Pass through quickly and smoothly
III	Surgical anaesthesia	Regular breathing, relaxation, fading reflexes by plane	Maintain at lightest adequate plane
IV	Overdose	Respiratory then cardiac arrest	Emergency, reverse and support

ASA physical status grades

Grade	Description	Example	Practical meaning
I	Normal healthy	Elective spay	Standard monitoring
II	Mild systemic disease	Obesity, old age	Extra care
III	Severe disease, limits function	Anaemia, moderate heart disease	Stabilise, fuller monitoring
IV	Constant threat to life	Decompensated heart failure	High risk, discuss with owner
V	Moribund	Severe shock	Survival unlikely without procedure

Species notes

Dog

Brachycephalic breeds have narrow airways and are at risk of obstruction and regurgitation during recovery, so keep the tube in until the animal is fully awake. Sighthounds and some herding breeds need drug choice adjusted, covered in later chapters.

Cat

Small body size means rapid heat loss and easy overdose if weight is guessed. Handle gently, since stress raises risk, and take care with the airway because laryngospasm is common.

Horse

Recovery is the dangerous phase: a heavy animal can injure itself standing up. Check footing, padding and assistance, and plan the whole procedure with trained staff.

Cattle, sheep and goat

Regurgitation and bloat are the main risks. Use a cuffed tube, avoid prolonged recumbency and keep the head low. Ruminants can be very sensitive to sedatives.

Rabbit and small mammals

Do not starve them for long, as they cannot vomit. Lose heat fast, and are easily stressed, so keep a quiet warm environment.

Clinical pearls

Self-test: 10 questions

1. Which stage of anaesthesia is characterised by struggling and irregular breathing despite loss of consciousness?

Stage II is excitement or delirium, caused by loss of inhibitory brain control before motor activity is depressed.

2. An animal with decompensated heart failure scheduled for anaesthesia is best graded as:

Severe disease that is a constant threat to life is ASA IV.

3. The letter E added to an ASA grade means:

E denotes emergency procedure, which adds risk.

4. Which statement about fasting is correct?

Rabbits and rodents do not vomit, so long fasting adds risk without benefit; neonates need short fasts.

5. Which is the main airway risk in ruminants under general anaesthesia?

Rumen contents can reach the pharynx; use a cuffed tube and keep the head low.

6. Why is guessing body weight dangerous?

Drug amounts are based on weight, so errors can lead to overdose or underdose.

7. Which sign is unreliable as the only measure of depth during ketamine anaesthesia?

Ketamine often preserves eyelid and eye reflexes, so reflex loss alone is misleading.

8. A young puppy with a congenital shunt is:

Age alone does not define grade; disease status does.

9. Which belongs on the pre-anaesthetic equipment checklist?

Airway equipment, oxygen, monitors, fluids and emergency drugs should be ready before induction.

10. Informed consent for anaesthesia should include:

Owners need to understand benefits, risks and options before agreeing.

Key points to revise

1. Anaesthesia needs assessment, preparation, monitoring and recovery planning.
2. Guedel stages: analgesia, excitement, surgical anaesthesia, overdose.
3. Stage II is avoided by good premedication and smooth induction.
4. ASA grades I to V describe physical status; E means emergency.
5. History should include current drugs, previous reactions and exercise tolerance.
6. Fasting differs by species; follow current protocol and avoid long fasts in small mammals.
7. Informed consent includes the risk of death.
8. Test equipment and have emergency drugs ready before induction.

Go deeper on this site

- Ch 2. Premedication, sedation and tranquillisation (in this book)
- Ch 3. Injectable anaesthetic agents (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

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- Wikipedia: Guedel's classification

CHAPTER 2 OF 14

Premedication, sedation and tranquillisation

Premedication calms the patient, reduces the dose of induction and maintenance drugs and gives early analgesia. This chapter explains phenothiazines, benzodiazepines, alpha-2 agonists and their reversal, opioid combinations, and why cattle and horses respond so differently to the same drug.

After this chapter you can

- State the aims of premedication and distinguish sedation from tranquillisation

- Explain the actions, advantages and cautions of phenothiazines and benzodiazepines
- Describe the effects of alpha-2 agonists and the logic and risks of reversal
- Explain how opioids are combined with sedatives and what to watch for
- Explain why cattle and horses need special care with sedatives

Aims of premedication

Premedication is the drug given before induction. It is not a luxury. A calm animal needs less induction drug, has a smoother induction and recovery, and is safer to handle. Premedication can also provide analgesia, reduce salivation or vagal reflexes, and prevent the pain that would otherwise make anaesthesia harder to manage.

Two terms are often confused. **Tranquillisation** means the animal is calm and unconcerned but still aware and reactive to its surroundings. **Sedation** means drowsiness and reduced response, with the animal often lying down. Neither guarantees analgesia, so a sedated animal may still react sharply to a painful procedure unless an analgesic is added.

The choice of drugs depends on the patient's grade, temperament, procedure and species. Healthy calm animals need light premedication; sick or shocked animals need little, and the doses are reduced. Always give premedication in a quiet place, allow time to work, and monitor heart rate, breathing and temperature afterwards.

Phenothiazines

Acepromazine is the main phenothiazine tranquilliser. It blocks dopamine receptors in the brain, giving calmness, and blocks alpha-1 receptors in blood vessels, causing vasodilation and a fall in blood pressure. It also lowers body temperature.

Its advantages are low cost, smooth calm and an anti-emetic effect. Its disadvantages matter more. It gives **no analgesia**, it has **no specific reversal agent**, and its action is long, often several hours, so a mistake cannot be undone quickly. Hypotension is the main hazard, so avoid it in dehydrated, hypovolaemic, shocked or bleeding animals.

Other cautions: reduce its use in old or debilitated patients; breeds such as boxers and some giant breeds are reputed to be more sensitive; dogs with the MDR1 (ABCB1) mutation, such as collies, may show prolonged and deeper effect, so lower amounts are advised; and its use in animals with a seizure history is debated. In stallions and geldings it can cause penile relaxation and prolapse, so owners must be warned. A common confusion is to expect the drug to "calm pain". It does not.

Benzodiazepines

Diazepam and midazolam act on the $GABA_A$ receptor, making the chloride channel open more often when GABA is present. The result is anxiety relief, muscle relaxation and anticonvulsant effect, with **very little cardiovascular and respiratory depression**. This makes them useful in sick, old or cardiac patients, and as a partner to ketamine or opioids.

Their weakness is that they are poor sedatives alone in healthy animals. A fit dog or cat may become excited, disinhibited or even aggressive, called paradoxical excitement. They are better when combined with an opioid or used in already depressed patients. They provide no analgesia.

Diazepam is dissolved in propylene glycol, which can irritate veins, and it adsorbs to plastic, so it should not be diluted or stored carelessly. Midazolam is water soluble and can be given by more routes. Oral diazepam has been linked to serious liver failure in cats, so check current advice. Benzodiazepine effect can be reversed with flumazenil, a competitive antagonist, though in practice reversal is seldom needed.

Alpha-2 agonists and reversal

Xylazine, medetomidine, dexmedetomidine and detomidine act on alpha-2 adrenergic receptors, reducing noradrenaline release in the brain and spinal cord. They give reliable sedation, muscle relaxation and some analgesia, and they sharply reduce the amount of other anaesthetic drugs required.

The costs are cardiovascular. Blood vessels constrict, causing a brief rise in pressure, then **bradycardia** follows through baroreceptor reflex and the central effect, and cardiac output falls substantially. Mucous membranes may look pale or bluish, which is expected but should not be confused with hypoxia, so confirm with

a pulse oximeter or by other signs. Other effects include hyperglycaemia, increased urine output, vomiting in dogs and especially cats, muscle tremor, bloat risk in ruminants, and uterine stimulation, notably with xylazine in late pregnancy of ruminants.

These drugs are best used in healthy, young to middle-aged patients. Avoid them in animals with heart disease, shock, severe liver or kidney disease, or in patients with a marked bradycardia.

Reversal uses an alpha-2 antagonist such as atipamezole (or yohimbine and tolazoline in some settings). Reversal is a key advantage, but it carries a warning: it also removes the analgesia given by the alpha-2 agonist, so a patient reversed soon after painful surgery may wake in pain. It can also cause sudden vasodilation, hypotension, agitation and tachycardia if given too quickly. Never use anticholinergics routinely to counter bradycardia from alpha-2 agonists, since this can cause hypertension and arrhythmia, unless a clinician has decided it is justified.

Opioid combinations

Combining an opioid with a tranquilliser or sedative is called **neuroleptanalgesia**. The sedative calms; the opioid adds analgesia and stable cardiovascular effect, and the two together allow lower doses of each. Common combinations pair acepromazine or an alpha-2 agonist with butorphanol, buprenorphine, methadone or morphine. Pure mu agonists give more analgesia than butorphanol, which is mainly useful for mild pain and sedation. Opioid side effects include bradycardia, respiratory depression, panting, nausea and vomiting (morphine), and urinary retention. Opioids are reversible with naloxone, but reversal also removes analgesia.

Before giving any opioid combination, check liver function, breathing and the procedure, and have naloxone and oxygen ready. Sedative and opioid effects add together, so reduce each amount in old, sick or very quiet animals.

Horses, cattle and other species

Horses. Horses given an opioid alone may become excited, restless and walk in circles, so opioids are normally given after a sedative such as an alpha-2 agonist. Sedated horses can look calm yet kick suddenly, so approach carefully and stay at the shoulder, not behind. Their head drops and the upper airway may narrow, so

avoid sedation in animals with airway disease. Detomidine is widely used in horses, but doses differ from small animals.

Cattle. Cattle are far more sensitive to xylazine than horses, so much lower amounts are used, and equine amounts can be dangerous. Sedation causes salivation, bloat, regurgitation, recumbency and a fall in oxygen; lie the animal on the sternum and keep the head lower than the pharynx. Sheep and goats are also sensitive. Pregnant cows risk premature calving. Pigs are comparatively resistant to alpha-2 agonists. Always use label and current references for the species, and never extrapolate from dogs or horses.

For all species, begin with the lowest effective plan, wait for full onset before judging effect, and keep the animal under observation until it is fully recovered.

Concept cleared

Concept cleared: Tranquillisation versus sedation
A tranquillised animal is like a person who has stopped worrying but is still listening. A sedated animal is drowsy and may lie down. Neither feels less pain unless an analgesic is given.

Concept cleared: Alpha-2 bradycardia
Alpha-2 drugs squeeze the vessels, pressure rises, and the brain slows the heart in response. When the pressure falls later the heart stays slow and output drops. It is a drug effect, not a fault of dose alone.

Concept cleared: Reversal removes analgesia
If you reverse an alpha-2 agonist with atipamezole, you take away both the sleep and the pain relief. Think of switching off the whole lamp, not only the colour.

Concept cleared: Neuroleptanalgesia
A tranquilliser is the driver who calms the horse, the opioid is the one who removes pain. Together they work better with lower amounts of each.

Memory aid: Premedication drug cautions

Remember ABCD: Acepromazine = hypotension, no reversal; Benzodiazepine = may excite healthy animals; Cattle = very sensitive to xylazine; Dexmedetomidine and kin = bradycardia and reversal removes analgesia.

Compare and contrast

Main premedication drug groups

Group	Examples	Main benefit	Main caution
Phenothiazine	Acepromazine	Calm, anti-emetic	Hypotension, no analgesia, no reversal, long action
Benzodiazepine	Diazepam, midazolam	Minimal cardiorespiratory effect, muscle relaxation	Excitement in healthy animals, no analgesia
Alpha-2 agonist	Xylazine, medetomidine, dexmedetomidine, detomidine	Deep sedation, some analgesia, reversible	Bradycardia, low output, vomiting, species sensitivity
Opioid	Butorphanol, buprenorphine, methadone, morphine	Analgesia, cardiovascular stability	Respiratory depression, vomiting, horse excitement if alone

Reversal agents

Drug reversed	Antagonist	Effect of reversal	Caution
Alpha-2 agonist	Atipamezole	Wakes patient, removes analgesia	Pain, agitation, hypotension if rapid
Opioid	Naloxone	Reverses respiratory depression and analgesia	Short action, renarcotisation possible
Benzodiazepine	Flumazenil	Reverses sedation	Rarely needed, may unmask seizures
Acepromazine	None	Wait and support	Treat hypotension with fluids

Species notes

Dog

Use lower amounts of acepromazine in boxers, giant breeds and MDR1 mutation breeds. Alpha-2 agonists cause vomiting and bradycardia, so use only in healthy patients.

Cat

Alpha-2 agonists often cause vomiting. Opioids can cause excitement or mydriasis in some cats, so combine with a sedative. Be careful with oral diazepam.

Horse

Alpha-2 agonists and opioids are used together, but horses can still kick. Acepromazine can cause penile prolapse in males. Plan a quiet, safe place.

Cattle, sheep and goat

Very sensitive to xylazine. Expect salivation, bloat and regurgitation. Avoid in late pregnancy and use species-specific references.

Pig

Relatively resistant to alpha-2 agonists. Azaperone and combinations are used, but venous access and airway management are difficult, so plan ahead.

Clinical pearls

Self-test: 10 questions

1. Which drug has no specific reversal agent?

Acepromazine has no antagonist, so effects are managed by supportive care.

2. Benzodiazepines act on which receptor?

They enhance GABA action at the GABA-A chloride channel.

3. A healthy dog given a benzodiazepine alone may show:

Fit animals can become disinhibited without another sedative.

4. The main cardiovascular effect of alpha-2 agonists is:

Vasoconstriction triggers reflex bradycardia, and cardiac output falls.

5. Reversing xylazine with atipamezole also:

The analgesia is mediated by the same receptors, so it is lost.

6. Which statement about acepromazine is correct?

Alpha-1 blockade causes hypotension, so avoid in shock.

7. Why are horses usually given an opioid after a sedative?

Opioids alone can cause excitement and restlessness in horses.

8. Compared with horses, cattle are:

Ruminants respond to far lower amounts, so equine amounts can be dangerous.

9. A common risk of acepromazine in male horses is:

Penile relaxation and prolapse may occur, so owners should be warned.

10. Neuroleptanalgesia means:

The combination calms the animal and gives analgesia, allowing lower amounts of each drug.

Key points to revise

1. Premedication calms, reduces other drug needs and provides early analgesia.
2. Tranquillisation is calm with awareness; sedation is drowsiness.
3. Acepromazine blocks dopamine and alpha-1 receptors, causing hypotension.
4. Benzodiazepines act on GABA-A with little cardiovascular depression.
5. Alpha-2 agonists give sedation and analgesia but reduce heart rate and output.
6. Atipamezole reverses alpha-2 agonists, and naloxone reverses opioids.
7. Opioids plus sedatives give neuroleptanalgesia.
8. Cattle, sheep and goats are far more sensitive to alpha-2 agonists than horses.

Go deeper on this site

- Ch 3. Injectable anaesthetic agents (in this book)
- Ch 1. Principles of anaesthesia and pre-anaesthetic assessment (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Wikipedia: Veterinary anesthesia
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- Cornell University College of Veterinary Medicine: Drug sensitivity (MDR1)

CHAPTER 3 OF 14

Injectable anaesthetic agents

Injectable agents induce anaesthesia quickly and can also maintain it as total intravenous anaesthesia. This chapter covers propofol, alfaxalone, ketamine, thiopentone and etomidate, how to give them safely to effect, and the special cautions for sighthounds, cats and ruminants.

After this chapter you can

- Explain how rapid induction occurs and why recovery depends on redistribution and metabolism
- Compare propofol, alfaxalone, ketamine, thiopentone and etomidate by mechanism, advantages and risks
- Describe the principles of induction to effect and of total intravenous anaesthesia
- Explain breed and species cautions in sighthounds, cats and ruminants
- Recognise and respond to common complications of injectable induction

How injectable induction works

After intravenous injection, a lipid-soluble anaesthetic travels with blood to the brain, which receives a large share of cardiac output. Anaesthesia therefore starts within one arm-brain circulation time. Recovery after a single dose is not mainly due to metabolism. It happens because the drug **redistributes** from the brain to muscle and then fat, so brain concentration falls. The drug is later removed by liver metabolism or other routes.

This explains why a repeated dose or a lean, poorly perfused animal behaves differently. When muscle and fat stores fill, or when body fat is low, the drug stays in the blood and brain longer, so recovery is slow.

Safe induction rests on three habits. Give the dose **slowly and to effect**, not as a rapid push, because circulation time is longer in sick or shocked animals. Have the airway equipment, oxygen and a means of ventilation ready, because most induction agents cause apnoea. And pre-oxygenate where possible. Premedication reduces the needed amount, and the calculated dose is only a guide, so always watch the patient. No dose figures are given here; consult current references.

Propofol and alfaxalone

Propofol is a short-acting phenol that enhances $GABA_A$ receptor activity. Induction is rapid and smooth, and recovery is quick because of redistribution and fast

hepatic and extra-hepatic metabolism. This makes it a popular choice for induction and total intravenous anaesthesia.

Its cautions are important. It causes **dose-dependent apnoea**, especially with a fast injection, and vasodilation leading to hypotension. It gives no real analgesia. The lipid emulsion supports bacterial growth, so syringes and opened vials must be handled aseptically and discarded within the time stated by the manufacturer. Pain on injection may occur. In cats, repeated daily use can cause oxidative injury, with Heinz body formation, slower recovery and sometimes appetite loss, so avoid prolonged or repeated infusions in cats unless judged necessary.

Alfaxalone is a neuroactive steroid that also acts on $GABA_A$ receptors. It is now formulated in a cyclodextrin vehicle, which allows a smooth induction with a wide safety margin and little irritation. It can also cause apnoea and some cardiovascular depression, though usually less than propofol at comparable depth. In cats and dogs, recovery without adequate premedication can be rough, with paddling or excitement, so premedicate and recover the animal in a quiet place.

Ketamine

Ketamine is a **dissociative** agent. It blocks the NMDA receptor, which disconnects the cortex from the lower brain, so the animal looks awake with open eyes but is unaware. It gives good somatic analgesia and, unlike most induction agents, tends to **support heart rate and blood pressure** by sympathetic stimulation. Respiration is usually preserved, though the breathing pattern may become irregular.

The same sympathetic drive can be harmful in a heart that is already compromised or an animal that is depleted of catecholamines, since the direct effect of ketamine on the heart is depressant. Other cautions: muscle rigidity and rough recovery if used alone, so it is almost always combined with a benzodiazepine or an alpha-2 agonist; increased salivation; and caution in animals with raised intracranial or intra-ocular pressure, uncontrolled seizures or severe hypertension. In cats, much of the drug leaves unchanged in the urine, so urethral obstruction is a concern. Reflexes such as the palpebral and corneal reflexes stay present, so do not rely on them to judge depth.

Ketamine is widely used in food animals and horses, where combinations with sedatives are standard. Check the current rules on its use and withdrawal in food-

producing species.

Thiopentone and etomidate

Thiopentone is an ultra-short-acting thiobarbiturate acting at the $GABA_A$ receptor. It induces smoothly, but recovery depends on redistribution; in sighthounds and thin animals this is slower and metabolism is also slower, so recovery can be prolonged. Thiopentone depresses breathing and the heart, and it can sensitise the myocardium to catecholamines, producing ventricular arrhythmias. The solution is strongly alkaline, so **perivascular injection causes tissue necrosis**; use a secure catheter. Thiopentone has little analgesia and may cause apnoea. Its availability varies between markets, so check what is available to you.

Etomidate is an imidazole that acts on $GABA_A$. Its main advantage is **cardiovascular stability**, so it is considered in animals with heart disease or shock where little blood pressure fall is tolerated. Its drawbacks: myoclonus and retching on induction, unless premedicated; pain on injection and haemolysis with some solvents; and suppression of adrenal steroid synthesis, even after a single dose. It is therefore avoided for repeated use or infusions and in animals with adrenal disease or critical illness where cortisol response matters. It gives no analgesia.

Induction and TIVA in practice

For induction, premedicate, pre-oxygenate, place an intravenous catheter, give the agent slowly until the jaw relaxes and the animal can be intubated, then connect oxygen. Stop giving the drug once the depth is adequate; the calculated volume may not be needed. In sick animals, a small amount of a benzodiazepine or opioid beforehand lowers the induction requirement and helps stability, sometimes called co-induction.

Total intravenous anaesthesia (TIVA) means maintaining anaesthesia with a continuous infusion or repeated boluses of injectable agents instead of an inhalant. It is useful when inhalant equipment is not available, for short procedures, for field work, and for patients where inhalant side effects should be avoided. The drug must be given by a controlled method, an animal must be intubated and oxygen supplied, and monitoring should be at least equal to inhalant anaesthesia. Agents with short, predictable recovery, such as propofol and alfaxalone, suit TIVA better

than thiopentone or etomidate. Recovery is longer after long infusions in cats, and analgesia must be provided separately.

In large animals, combinations such as guaifenesin, ketamine and an alpha-2 agonist are used to maintain anaesthesia for short procedures, usually after sedation and induction; follow current references.

Sighthounds, cats, ruminants and complications

Sighthounds such as greyhounds and related breeds have little body fat and slower hepatic metabolism of some drugs. Thiobarbiturate recovery can be very prolonged, so propofol or alfaxalone are generally preferred. Give by slow titration, keep warm and observe for longer after recovery.

Cats are sensitive to drug accumulation because of slow glucuronidation. Propofol repeat use, ketamine kidney excretion, and apnoea and laryngospasm at intubation are the main points. Use a small amount of local anaesthetic spray on the larynx and avoid forcing the tube.

Ruminants are at risk of regurgitation, bloat and aspiration. Ketamine combinations are common in cattle, sheep and goats. Intubate quickly with a cuffed tube, position the head low, and avoid long recumbency. Ruminants may also be sensitive to the sedative given alongside, so reduce accordingly.

Complications and responses:

1. Apnoea: provide oxygen and ventilate, and wait for return of breathing.
2. Hypotension: reduce depth, give fluids, and consider supportive drugs.
3. Perivascular injection: stop, aspirate and follow current tissue-protection advice.
4. Excitement or myoclonus: usually temporary; deepen anaesthesia with a safe agent or improve premedication.
5. Prolonged recovery: keep warm, support airway, and observe until the animal can stand and protect itself.

Concept cleared

Concept cleared: Redistribution

Like pouring water from a bucket into a pond, the drug leaves the brain not because it is destroyed but because it spreads into muscle and fat. In a lean animal there is less pond, so waking is slower.

Concept cleared: Dissociative anaesthesia

With ketamine the lights are on, but nobody is home. Eyes are open and reflexes remain, yet the animal is unaware, which is why normal depth signs can mislead.

Concept cleared: Induction to effect

Give a little, wait for circulation time, assess, and give more only if needed. A fixed calculated dose is a guide, not an order.

Concept cleared: TIVA

TIVA is like running a tap at a steady, adjustable flow instead of vapour from a machine. The airway and oxygen are still your responsibility.

Memory aid: Induction agent memory hook

PAKTE: Propofol and Alfaxalone are smooth, Ketamine is dissociative, Thiopentone needs a clean vein, Etomidate protects the heart but suppresses the adrenal.

Compare and contrast

Injectable induction agents

Agent	Mechanism	Main advantage	Main caution
Propofol	GABA-A enhancement	Rapid smooth induction and recovery, suits TIVA	Apnoea, hypotension, no analgesia, contamination, cats on repeated use
Alfaxalone	Neurosteroid at GABA-A	Smooth induction, wide margin	Apnoea, rough recovery if unpremedicated
Ketamine	NMDA antagonist	Analgesia, supports heart rate and pressure	Rigidity, poor in cardiac or raised pressure cases, cat renal excretion
Thiopentone	Barbiturate at GABA-A	Rapid induction	Necrosis if perivascular, arrhythmia, slow recovery in sighthounds
Etomidate	GABA-A modulation	Cardiovascular stability	Myoclonus, adrenal suppression

Species and breed cautions

Group	Main concern	Preferred approach
Sighthounds	Prolonged recovery from thiobarbiturates	Propofol or alfaxalone, warmth, careful monitoring
Cats	Slow drug clearance, laryngospasm, kidney excretion of ketamine	Avoid repeat propofol, protect airway
Ruminants	Regurgitation, bloat, sedative sensitivity	Cuffed tube, head low, reduce sedative
Cardiac or shocked patients	Hypotension	Consider etomidate or co-induction, give slowly

Species notes

Dog

Titrate induction slowly. Brachycephalic breeds need airway readiness. Sighthounds recover slowly from thiobarbiturates.

Cat

Avoid repeated propofol over days. Ketamine is eliminated unchanged in urine, so be cautious in urinary obstruction. Laryngospasm is common.

Horse
Induction usually follows sedation, with ketamine and a benzodiazepine commonly used. Control the fall and plan a safe recovery.

Cattle, sheep and goat
Ketamine combinations are standard. Watch for regurgitation, bloat and aspiration, and use a cuffed tube.

Rabbit and small mammals
Injectable combinations are used, but venous access is hard and hypothermia is quick, so monitor and keep warm.

Clinical pearls

Self-test: 10 questions

1. Recovery after a single induction bolus is mainly due to:

The drug leaves the brain for muscle and fat, so brain concentration falls.

2. Which agent is a dissociative NMDA antagonist?

Ketamine blocks NMDA receptors and causes dissociation.

3. A major concern with perivascular thiopentone is:

The solution is strongly alkaline and irritant.

4. Which agent is most noted for cardiovascular stability but adrenal suppression?

Etomidate causes little cardiovascular change but inhibits adrenal steroid synthesis.

5. Which is generally preferred over thiopentone in sighthounds?

Sighthounds recover slowly from thiobarbiturates, so propofol or alfaxalone are favoured.

6. Why must propofol syringes be handled aseptically?

Contamination can cause infection, so discard within the manufacturer's time.

7. A cat concern with repeated daily propofol is:

Cats have limited ability to conjugate phenols, so oxidative injury may occur.

8. Which step is essential for TIVA?

Injectable maintenance carries the same airway and cardiovascular risks as other anaesthesia.

9. Ketamine in cats needs caution in:

Much of the drug is excreted unchanged in urine, so obstruction prolongs the effect.

10. A main complication of induction in ruminants is:

Rumen contents can reach the pharynx, so a cuffed tube and low head position are needed.

Key points to revise

1. Give injectable agents slowly and to effect.
2. Redistribution ends the effect of a single dose.

3. Propofol is smooth but causes apnoea and hypotension and needs aseptic handling.
4. Alfaxalone is a neurosteroid with a wide margin but needs premedication for smooth recovery.
5. Ketamine is a dissociative NMDA antagonist that supports heart rate but is not used alone.
6. Thiopentone causes tissue damage if given outside the vein.
7. Etomidate is cardiovascularly stable but suppresses the adrenal gland.
8. TIVA requires intubation, oxygen and full monitoring.

Go deeper on this site

- Ch 4. Inhalation anaesthesia (in this book)
- Ch 2. Premedication, sedation and tranquillisation (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Wikipedia: Propofol
- Wikipedia: Alfaxalone
- Wikipedia: Veterinary anesthesia

CHAPTER 4 OF 14

Inhalation anaesthesia

How volatile agents are delivered, why potency is measured as MAC, how isoflurane, sevoflurane and nitrous oxide differ, and how breathing circuits, scavenging and ventilation keep patient and staff safe.

After this chapter you can

- Explain why precision vaporisers are agent-specific and how they work
- Define MAC and list factors that raise or lower it

- Compare isoflurane, sevoflurane and nitrous oxide in terms of solubility, side effects and use
- Describe the purpose of waste gas scavenging and the main sources of pollution
- Explain why ventilation support and monitoring are needed during inhalation anaesthesia

Why inhalation anaesthesia is the preferred maintenance method

In inhalation anaesthesia a volatile liquid is turned into vapour, mixed with oxygen and breathed in. The lung is both the entry and the exit route. The anaesthetist can therefore make the patient deeper or lighter within minutes by changing the dial, and most of the drug leaves through the lungs rather than depending on the liver or kidney.

This control is the main safety advantage over injectable-only anaesthesia, especially in sick, young, old or very small patients. The price is that the patient needs a secured airway, an oxygen supply, a machine that works properly, and a person who watches the patient continuously.

Vaporisers

A **precision vaporiser** delivers a known, safe percentage of vapour into the fresh gas flow. Part of the gas passes through the vaporising chamber and part bypasses it, and the dial sets the splitting ratio. Modern vaporisers are temperature compensated, because evaporation cools the liquid and would otherwise reduce output.

Key points for students:

- Most vaporisers are **agent-specific** and **out of circuit**. A vaporiser built for one agent has different vapour pressure characteristics, so using another agent in it can give a dangerously wrong concentration.
- Keyed filling systems exist to prevent filling with the wrong liquid. Always check the label on the vaporiser before filling.
- Keep the vaporiser upright, avoid tilting it, and have it serviced and calibrated as the maker advises.

- Never use a precision vaporiser for an agent it was not designed for. Simple draw-over or in-circuit vaporisers are different devices and give less predictable output.

Remember that the dial setting is the concentration delivered to the circuit, not the concentration in the patient's brain. The two differ for several minutes at the start of anaesthesia.

MAC and agent solubility

MAC (minimum alveolar concentration) is the alveolar concentration of an agent at which half of patients do not move in response to a standard painful stimulus. It is the standard measure of potency: a low MAC means a potent agent. MAC values are broadly additive, and an animal at about 1.3 times MAC is usually considered adequately anaesthetised for surgery, although this is a guide only.

MAC is *lowered*, so the vaporiser can be turned down, by opioids, alpha-2 agonists, benzodiazepines, other sedatives, older age, hypothermia, hypotension, pregnancy and severe illness. It is *raised* by hyperthermia, and values differ between species. This is why a premedicated animal needs less volatile agent, and why an overdose is easy in a cold, hypotensive neonate.

MAC tells you about potency, not about speed. Speed depends on the **blood:gas partition coefficient**, which describes how soluble an agent is in blood. A poorly soluble agent leaves the blood and reaches the brain quickly, so induction, changes of depth and recovery are fast. A very soluble agent is taken up into blood and tissues for longer, so everything is slower. Do not confuse potency (MAC) with speed (solubility).

Isoflurane, sevoflurane, nitrous oxide and others

Isoflurane is widely used in many species. It causes dose-dependent respiratory depression and vasodilation with fall in blood pressure, and little sensitisation of the heart to catecholamines. Its smell is pungent, so mask induction is less pleasant.

Sevoflurane is less soluble, so induction and recovery are faster. It is less irritant to the airway, and is popular for mask or chamber induction in small animals and exotics. It also depresses breathing and blood pressure. It is more expensive, which matters in practice. Sevoflurane can break down with some carbon dioxide

absorbents, forming compound A; its clinical importance in animals is debated, and the manufacturer's guidance on fresh gas flow should be followed. Dry, exhausted or desiccated absorbent can also generate heat and carbon monoxide with modern agents, so absorbent should be changed on schedule and not left with gas flowing through it overnight.

Halothane is an older agent. It sensitises the myocardium to catecholamines, so arrhythmias are more likely, and it is associated with liver injury in some patients. Availability differs by country, so check what is currently marketed. **Desflurane** is very insoluble but needs a special heated vaporiser and is rarely used in veterinary practice.

Nitrous oxide is a weak anaesthetic with a very high MAC, so it cannot anaesthetise on its own and is used only as an adjunct. Its good points are a mild analgesic effect and the *second gas effect*, which speeds uptake of the volatile agent. Its dangers are important: it diffuses into gas-filled spaces faster than nitrogen leaves them, so it is avoided with pneumothorax, gastric dilatation-volvulus, intestinal obstruction, tympany in ruminants and air embolism. At the end of anaesthesia it rushes out of the blood into the alveoli and dilutes oxygen (**diffusion hypoxia**), so the patient should breathe 100 percent oxygen for a few minutes afterwards. Because of these limits, and because it is a greenhouse gas, many clinics no longer use it.

Breathing circuits and scavenging

The volatile agent reaches the patient through a **breathing circuit**. In a **rebreathing (circle) system** exhaled gas passes through a carbon dioxide absorber and is breathed again, so low fresh gas flows save oxygen and agent. In a **non-rebreathing system** a higher fresh gas flow flushes exhaled gas away. The next chapter covers these in detail. Whichever is used, the circuit size must match the patient so that resistance and dead space are acceptable.

Scavenging removes waste anaesthetic gas from the breathing system. Exhaled gas and gas released through the pop-off valve are led away by tubing, either to an *active* system with a fan or to a *passive* system with a charcoal canister. Charcoal canisters do not absorb nitrous oxide and must be weighed and replaced as advised. Passive systems must never be blocked.

Staff are exposed through leaks, poorly fitting masks, chamber induction, spills during filling, and disconnecting the patient while the vaporiser is still on. Good practice is to use a cuffed tube, check the system for leaks, fill vaporisers carefully, turn off the vaporiser before disconnecting and flush the circuit with oxygen at the end. Pregnant staff should discuss risks with their supervisor and check the current local occupational exposure guidance.

Ventilation, monitoring and complications

Nearly all volatile agents depress the respiratory centre. Under anaesthesia, especially in recumbent large animals or obese and brachycephalic patients, breathing becomes shallow and carbon dioxide rises. **Hypoventilation** is therefore the commonest problem. A rise in end-tidal CO_2 shown by capnography is the early warning. The remedy is manual or mechanical **intermittent positive pressure ventilation** (IPPV), used with care because high airway pressures can damage the lung and reduce venous return. Horses are usually ventilated during volatile anaesthesia.

The other main problem is **hypotension**, caused by vasodilation and falling cardiac output. First reduce the vaporiser setting if the plane is too deep; then consider fluids and other supportive measures chosen by the clinician. Monitoring should include heart rate and rhythm, respiration, mucous membrane colour, capnography, pulse oximetry, blood pressure and body temperature. Hypothermia is common and slows recovery.

Remember that a patient that looks "light" may simply be hypoxic or hypercapnic. Check oxygen flow, airway and circuit before deepening anaesthesia. Malignant hyperthermia, a rare inherited trigger condition linked to volatile agents, is described mainly in pigs and also reported in some other species, and needs urgent recognition by rising CO_2, temperature and rigidity.

Concept cleared

Concept cleared: MAC

Think of MAC as the 'price' of anaesthesia in vapour. A potent agent has a low price in concentration terms. Sedatives and opioids are like a discount, so you need less vapour. Cold and low blood pressure also lower the price, which is why a cold, sick animal can be overdosed on a setting that suits a healthy one.

Concept cleared: Solubility and speed

A sponge that soaks up a lot of water takes longer to fill and longer to dry. A very soluble agent is like that sponge, with slow induction and slow recovery. A poorly soluble agent like sevoflurane is like a waxed surface, which fills and empties quickly.

Concept cleared: Diffusion hypoxia

At the end of nitrous oxide use, a large volume of gas pours from blood into the lung. This dilutes the oxygen in the alveoli, like pouring a jug of water into a glass of squash. Breathing 100 percent oxygen for a few minutes replaces the diluted mix.

Concept cleared: Vaporiser setting versus patient

The dial is the concentration in the pipe, not in the brain. Brain concentration rises slowly, like a bath filling from a tap, so a patient that is still light a few minutes after starting is normal and not a reason to open the dial fully.

Memory aid: Low solubility, low delay

Remember: Low blood solubility means Quick control. Low MAC means a Potent agent. Potency and speed are two separate questions.

Compare and contrast

Common volatile agents

Agent	Solubility	Induction and recovery	Main cautions
Isoflurane	Moderate	Moderate	Hypotension, respiratory depression, pungent smell
Sevoflurane	Low	Fast	Respiratory and blood pressure depression; compound A and cost
Halothane	Higher	Slower	Arrhythmias with catecholamines; liver injury; availability
Nitrous oxide	Very low	Very fast uptake	Weak; fills gas spaces; diffusion hypoxia

Potency versus speed

Property	Measured by	Meaning	Affected by
Potency	MAC	How much vapour is needed	Drugs, age, temperature, pregnancy, species
Speed	Blood:gas partition coefficient	How fast depth changes	Solubility, ventilation, cardiac output

Species notes

Dog

Brachycephalic breeds have airway obstruction and are prone to hypoventilation, so secure the airway early, preoxygenate and monitor recovery closely.

Cat

Small body size means rapid heat loss and a greater risk of circuit dead space and resistance, so use a suitable circuit and warm the patient.

Horse

Recumbent horses develop ventilation-perfusion mismatch and hypotension under volatile agents, so ventilation and blood pressure support are usually needed.

Pig

Pigs are the species most associated with malignant hyperthermia; watch for rising CO2, temperature and muscle rigidity.

Ruminants

Nitrous oxide is avoided because of rumen gas, and regurgitation risk means the cuffed tube is essential.

Clinical pearls

Self-test: 10 questions

1. MAC is best defined as the alveolar concentration that

MAC is the alveolar concentration at which half of patients do not move in response to a standard surgical stimulus.

2. Which of the following lowers MAC?

Opioids and other sedatives are additive with volatile agents, so less agent is needed.

3. A low blood:gas partition coefficient means

A poorly soluble agent equilibrates quickly between blood and brain, so depth changes fast.

4. A precision vaporiser for isoflurane should

Vaporisers are calibrated for one agent. Another agent gives an unpredictable concentration.

5. Nitrous oxide should be avoided in

It diffuses into gas-filled spaces and increases their volume.

6. Diffusion hypoxia is prevented by

Oxygen replaces the nitrous oxide that rushes into the alveoli.

7. The commonest respiratory problem under volatile anaesthesia is

Volatile agents depress the respiratory centre, so carbon dioxide rises unless the patient is ventilated.

8. Which agent is associated with myocardial sensitisation to catecholamines?

Halothane makes arrhythmias more likely, especially with adrenaline.

9. The best step if a patient seems light but oxygen supply has not been checked is to

Hypoxia and hypercapnia can mimic light anaesthesia, so deepening without checking may cause harm.

10. A passive charcoal scavenging canister

Canisters become saturated, do not absorb nitrous oxide, and must never be obstructed.

Key points to revise

1. Inhalation anaesthesia gives fine control of depth because the lungs deliver and remove the drug.
2. Precision vaporisers are agent-specific, out of circuit and temperature compensated.
3. MAC is the alveolar concentration that prevents movement in half of patients.
4. Opioids, alpha-2 agonists, sedatives, old age, cold and hypotension lower MAC.

5. Low solubility gives rapid induction and recovery.
6. Sevoflurane is faster and less irritant than isoflurane, and both cause dose-dependent depression of breathing and blood pressure.
7. Nitrous oxide is a weak adjunct that expands gas-filled spaces and causes diffusion hypoxia on withdrawal.
8. Scavenging, leak checks and careful filling protect staff from waste gas.

Go deeper on this site

- Ch 5. Anaesthetic equipment and breathing circuits (in this book)
- Ch 3. Injectable anaesthetic agents (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- WSAVA Global Pain Council Guidelines
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- PubMed search: veterinary anesthesia breathing circuits

CHAPTER 5 OF 14

Anaesthetic equipment and breathing circuits

The parts of an anaesthetic machine, how rebreathing and non-rebreathing circuits differ, how to test for leaks before every case, and how to place and check an endotracheal tube in different species.

After this chapter you can

- Name the main parts of an anaesthetic machine and their functions
- Distinguish rebreathing from non-rebreathing circuits and choose between them
- Perform and interpret a pre-use leak test
- Describe the role and limits of the carbon dioxide absorbent

- Explain endotracheal intubation and tube checks in dogs, cats, horses, ruminants and pigs

Why equipment knowledge is a safety skill

Many anaesthetic accidents are not caused by the drug but by equipment: an empty oxygen cylinder, a disconnected hose, a stuck valve or an exhausted absorbent. The machine delivers oxygen and anaesthetic gas, and the circuit carries them to the patient and removes carbon dioxide. A student who understands the path of the gas can find a fault quickly.

The golden rule is to check the whole system *before* the patient is premedicated, not after the animal is already asleep.

Parts of the anaesthetic machine

Follow the gas from source to patient.

1. **Gas supply.** Oxygen comes from a cylinder or a pipeline. Cylinders are fitted through yoke connections designed so that the wrong gas cannot be attached, and the cylinder pressure gauge shows how much oxygen is left, so a falling gauge means the supply is running out.
2. **Pressure regulator.** It reduces the very high cylinder pressure to a low, steady working pressure.
3. **Flowmeter.** It sets the fresh gas flow of oxygen. Read it at the correct point on the float, with the machine upright.
4. **Vaporiser.** Adds a controlled amount of volatile agent to the oxygen, as described in the previous chapter.
5. **Common gas outlet.** Fresh gas leaves here to the breathing circuit.
6. **Oxygen flush valve.** It delivers a high flow of pure oxygen that bypasses the vaporiser. It is used to fill the circuit quickly and to flush out agent at the end of anaesthesia. Use it with caution while connected to a patient, because the sudden pressure can harm the lungs and it dilutes the anaesthetic.
7. **Breathing circuit** with reservoir bag, pressure manometer, adjustable pressure-limiting (APL or pop-off) valve and a link to the scavenging system.

Rebreathing and non-rebreathing circuits

The purpose of any circuit is to bring fresh gas to the patient and prevent the animal from rebreathing its own carbon dioxide.

A **rebreathing system**, usually the **circle system**, directs exhaled gas through a **carbon dioxide absorber** (soda lime or similar) and returns it to the patient with fresh gas added. One-way valves keep the flow in one direction. The advantages are saving of oxygen and volatile agent, retention of heat and moisture, and less pollution. The disadvantages are more parts that can leak or fail, greater resistance, and slower change in anaesthetic depth when flows are low. It is usually chosen for patients above a certain size, which the maker states for each machine.

A **non-rebreathing system** has no absorber and no one-way valves in the same way. A high fresh gas flow washes exhaled gas out through the pop-off valve. Examples are the Bain coaxial system and the T-piece (Jackson-Rees). Their strengths are low resistance, light weight and quick change of depth, so they suit cats, small dogs, birds and other small patients. The weakness is the high gas use and the greater cooling and drying of the patient and pollution risk. If the flow is too low in a non-rebreathing system, carbon dioxide builds up and the patient becomes hypercapnic, so the flow must follow the maker's or textbook recommendation.

Common confusion: students think that "low flow" is always better. In a circle system low flow is a saving only if the absorber, leaks and monitoring are all in good condition.

The carbon dioxide absorbent

The absorbent chemically binds carbon dioxide and releases heat and water. It has a limited life. Signs of exhaustion include a colour change of the indicator, a warm canister, and rising inspired CO_2 on the capnograph. The indicator may revert to its original colour after a rest, so a pale colour on the next morning does not prove that the granules are fresh, and capnography is the better guide.

Do not leave gas flowing through the absorber overnight, because dry granules can produce heat and unwanted by-products with some volatile agents. Keep the lid closed, store spare absorbent sealed, and replace it on a routine schedule noted in a log. Channeling, where gas runs through a small path in loosely packed granules, reduces absorption, so do not overfill the canister or leave gaps.

Leak and function tests

A **leak test** should be done on every circuit, every day of use, and again after any change of circuit parts.

1. Check oxygen supply, flowmeter and vaporiser level; make sure the scavenging line is connected.
2. Close the APL valve and block the patient end of the circuit (the Y-piece or the open end of the tubing).
3. Fill the system with oxygen by the flush valve until the reservoir bag or manometer shows a moderate pressure, as advised for your machine.
4. Stop the flow and watch. The pressure should hold. A steady fall means a leak, so check tubing, connections, the absorber canister, the bag and the valves.
5. Open the APL valve and confirm that the pressure is released and the gas passes to scavenging.

Test the one-way valves by watching them move on a breath. For a Bain system a separate test checks that the inner fresh gas tube is intact and not disconnected, since a break turns the whole outer tube into dead space and causes rebreathing.

Remember to open the APL valve before connecting to the patient. Leaving it closed is a classic cause of dangerous pressure build-up in the lungs.

Endotracheal intubation by species

The **endotracheal tube** secures the airway, allows delivery of oxygen and volatile agent, permits ventilation and protects the lungs against regurgitated material or blood. A cuff seals the airway, but an overinflated cuff can injure the trachea. Inflate it just until no leak is heard under gentle bag pressure.

General steps: the patient is adequately unconscious, the head and neck are extended in line, the tongue is drawn forward, the larynx is seen with a laryngoscope where needed, and the tube is passed through the open arytenoids. Confirm placement by observing chest movement, listening for breath sounds, feeling breath at the tube, and above all by seeing a normal capnograph trace. Tie the tube in place and check it does not reach beyond the thoracic inlet, since a tube that goes too far enters one bronchus and ventilates only one lung.

- **Dog:** usually straightforward. Brachycephalic breeds have a long soft palate, narrow trachea and swollen tissues, so a smaller tube size is often needed and extubation must be delayed until the animal is fully swallowing.
- **Cat:** prone to laryngospasm, and the trachea is delicate and can rupture if a tube is oversize, forced or the cuff overinflated. Topical laryngeal local anaesthetic may be used by the clinician, and the neck should not be over-flexed or twisted with the tube in place.
- **Horse:** a long cuffed tube is passed through the mouth with a mouth gag to protect the tube from being bitten, often guided by hand. Check the tube is not kinked, and the cuff must be tested before use.
- **Cattle, sheep and goats:** intubation is done to protect the airway because of the real risk of regurgitation. The head is held extended, a gag is used, and it is passed with the larynx located by hand or laryngoscope. Ruminants often need the head positioned lower than the pharynx during recumbency so that saliva drains away.
- **Pig:** the long snout, small mouth opening and laryngeal anatomy make intubation difficult, and laryngospasm is common. A laryngoscope with a long blade and small tubes is needed.

Concept cleared

Concept cleared: Rebreathing
A circle system is like a recycling plant: the used gas is cleaned (CO_2 removed) and returned. If the cleaner is spent, the same dirty gas goes round again and the patient slowly builds up carbon dioxide. A non-rebreathing system is like opening a window: a strong draught of fresh gas pushes the old air out.

Concept cleared: Leak testing
Blowing up a tyre and watching the gauge is the same idea. A tight system holds pressure. If it falls, something leaks, and the patient will lose agent to the room or oxygen to the air.

Concept cleared: Dead space

Dead space is the part of the airway or circuit where gas moves back and forth without exchange. A broken inner tube in a Bain system, or a long connector on a cat, adds dead space and makes the patient rebreathe CO2.

Concept cleared: Tube depth

Putting the tube in too far is like pushing a drinking straw into one branch of a Y. Only one lung gets gas, so oxygen levels fall. The tube tip should stay at or before the chest entrance.

Memory aid: Gas path: GRF-VOC-B

Gas source, Regulator, Flowmeter, Vaporiser, Outlet, Circuit, Breathing patient. Test the machine in that order, and always open the APL valve before connecting the patient.

Compare and contrast

Rebreathing versus non-rebreathing circuits

Feature	Circle (rebreathing)	Bain or T-piece (non-rebreathing)	Practical meaning
CO2 removal	Absorbent	High fresh gas flow	Absorber must be fresh; flow must be adequate
Gas use	Low flows possible	High flows needed	Cost and pollution
Resistance	Higher	Low	Small patients favour non-rebreathing
Heat and humidity	Retained	Lost	Hypothermia risk in non-rebreathing

Intubation concerns by species

Species	Main difficulty	Main risk	Precaution
Dog	Brachycephalic airway	Obstruction after extubation	Smaller tube; delayed extubation
Cat	Laryngospasm	Tracheal injury	Small tube; gentle cuff inflation
Horse	Size and mouth	Tube bitten or kinked	Gag and cuff check
Ruminant	Regurgitation	Aspiration	Cuffed tube; head position
Pig	Long snout, small larynx	Laryngospasm	Long blade and small tubes

Species notes

Dog

Brachycephalic breeds should be kept intubated until they swallow and have a clear airway, and should be recovered with close observation.

Cat

A cat trachea is easily damaged by an oversize tube or an overinflated cuff, so use gentle technique and check the cuff pressure.

Horse

A mouth gag prevents the horse from biting through the tube, and a long, cuffed tube is needed with a stout connector.

Cattle and small ruminants

A cuffed tube is essential to protect against aspiration of rumen fluid and saliva, and the head is kept low during recumbency.

Pig

Laryngospasm is common, and intubation needs a long-bladed laryngoscope and several small tube sizes.

Clinical pearls

Self-test: 10 questions

1. The oxygen flush valve

It bypasses the vaporiser, so it dilutes the anaesthetic and can cause high pressure if used on a connected patient.

2. A main advantage of a circle system is

Exhaled gas is cleaned of CO2 and re-used.

3. Which circuit is usually preferred for a kitten?

Low resistance and low dead space suit very small patients.

4. During a leak test with the APL valve closed and the Y-piece blocked, the manometer pressure steadily falls. This means

A tight system holds pressure.

5. One of the safest ways to confirm tracheal intubation is

A normal capnograph trace shows that exhaled CO2 comes from the lungs and not the oesophagus.

6. Overinflation of the cuff in a cat can cause

The cat trachea is thin, and high cuff pressure or oversize tubes can tear it.

7. Which is a sign of exhausted soda lime?

If CO_2 is not absorbed, the patient inspires CO_2.

8. Why is a cuffed tube essential in ruminants?

Ruminants regurgitate readily when recumbent and sedated.

9. A tube advanced too far in a dog is likely to

Endobronchial intubation gives uneven ventilation and hypoxia.

10. What must be done before connecting a patient to a circle system?

A closed APL valve allows pressure to build up in the lungs.

Key points to revise

1. Gas flows from source to regulator, flowmeter, vaporiser, outlet and circuit.
2. The oxygen flush valve bypasses the vaporiser and should be used with care on a connected patient.
3. Circle systems recycle gas through an absorber, saving oxygen and agent.
4. Non-rebreathing circuits need high fresh gas flow and suit small patients.
5. Absorbent has a limited life and exhaustion shows as rising inspired CO_2.
6. A pressure leak test is done before each day's use.
7. The endotracheal tube cuff should seal without overinflation.
8. Tube position is confirmed by capnography and chest movement.

Go deeper on this site

- Ch 6. Local and regional anaesthesia (in this book)
- Ch 4. Inhalation anaesthesia (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- WSAVA Global Pain Council Guidelines
- PubMed search: veterinary anesthesia breathing circuits
- University of Minnesota Libraries: Principles of Pharmacology study guide

CHAPTER 6 OF 14

Local and regional anaesthesia

How local anaesthetic drugs block nerve conduction, why they can be toxic, and how nerve blocks, epidurals, cattle paravertebral and line blocks and ring blocks are chosen and used safely.

After this chapter you can

- Explain how local anaesthetics block sodium channels and why pH and tissue infection matter
- Compare amide and ester agents and name the main toxicity signs
- Describe the purpose and cautions of epidural anaesthesia
- Explain the paravertebral, line, inverted L and ring blocks used in cattle
- State patient safety rules for any regional technique

Why local and regional techniques matter

Local anaesthetics stop pain signals from reaching the brain by blocking nerve conduction at the site of injection. In veterinary practice, especially in cattle, sheep and goats and in equine standing procedures, they allow surgery with a conscious patient and avoid the risks of general anaesthesia. In small animals they are added to general anaesthesia to reduce the dose of other drugs and to improve pain relief after surgery.

A local block does not provide restraint or calm the animal. A frightened or fractious animal may still need sedation. Sedation and a block together are safer than a deeper general anaesthetic in many field cases.

How local anaesthetics work

Local anaesthetics block **voltage-gated sodium channels** inside the nerve membrane. Without sodium entry the nerve cannot generate an action potential, so the signal is not carried. Small, thin fibres carrying pain and sympathetic signals are usually blocked first, then touch and pressure, and motor fibres last in a lower concentration. This is why an animal may feel less pain but can still move.

These drugs are weak bases. The **non-ionised** form crosses the nerve membrane; the **ionised** form binds the channel inside. In inflamed or infected tissue the pH is acidic, so more drug is ionised outside the nerve, less enters, and the block is weak or fails. This is the reason for the old advice not to inject into an abscess.

Two groups are described. **Amides** such as lidocaine, mepivacaine, bupivacaine and ropivacaine are broken down in the liver and are the common agents. **Esters** such as procaine are broken down by plasma esterases and are used less. Lidocaine acts quickly with moderate duration, and bupivacaine is slower to start and longer lasting. Adrenaline added to some preparations narrows blood vessels, slows absorption, prolongs action and reduces toxicity, but it should **not** be used where the blood supply depends on end arteries, such as ear tips, tail, penis, teats and digits, because it can cause tissue loss.

Toxicity and its management

Toxicity occurs when too much drug reaches the blood, usually by accidental intravascular injection, overdose in a small animal, or rapid absorption from a vascular site. Because many cases are small animals, the dose must be calculated from the body weight, and the total allowed amount should not be exceeded when several blocks are done in one patient.

Signs usually progress from the nervous system to the heart. Early signs are muscle twitching, restlessness, ataxia and then seizures, followed by depression and coma. Cardiovascular signs are arrhythmias, hypotension and collapse. **Bupivacaine** is especially cardiotoxic, and it must never be given intravenously or used for intravenous regional techniques. Cats are generally considered more sensitive to systemic effects of lidocaine, so smaller total amounts are used, and topical benzocaine preparations are avoided in cats because of the risk of methaemoglobinaemia.

Prevention rules: aspirate before each injection and inject slowly in small increments, use the lowest effective volume, avoid injecting into the vein or artery, and keep oxygen, airway equipment and emergency drugs ready. Treatment is supportive: stop injecting, secure the airway, give oxygen, control seizures and treat arrhythmias and low pressure. Intravenous lipid emulsion has been reported as a rescue treatment for severe local anaesthetic toxicity, and the clinician decides on its use. In food-producing animals, a withdrawal period applies to local anaesthetics, so check the current regulatory notification and label advice.

Nerve blocks and epidural anaesthesia

A **nerve block** places local anaesthetic near a named nerve to desensitise the area it supplies. Examples are dental blocks (infraorbital, mental, maxillary and inferior alveolar nerves) in dogs and cats, the brachial plexus block for forelimb surgery, intercostal blocks for thoracic pain, and testicular and spermatic cord infiltration in castration. Block success depends on accurate anatomy, a clean technique, enough waiting time and avoiding vessels.

Epidural anaesthesia places drug in the space outside the dura of the spinal canal. In dogs and cats it is usually given at the lumbosacral space; in cattle and horses the caudal (sacrococcygeal or first intercoccygeal) site is common. Epidural local anaesthetic blocks the nerves of the tail, perineum, rectum, vagina and, with larger volume, hindlimbs. Epidural opioids and alpha-2 agonists can add pain relief with less motor loss; their selection is a clinical decision.

Concerns: spread of drug forward can paralyse the hindlimbs and cause recumbency, a serious problem in standing cattle, or can block the chest nerves and sympathetic fibres, causing hypotension and breathing difficulty. Epidurals are avoided in infection at the site, bleeding disorders, severe hypovolaemia and unstable spinal disease. Strict asepsis is needed because infection of the epidural space can be devastating. The patient must be supported and not allowed to walk until the block has gone.

Cattle paravertebral block

Many cattle operations are done standing under local techniques. For flank laparotomy (caesarean section, rumenotomy), the usual choices are the **paravertebral block** and the **line (infiltration) block**.

A **paravertebral block** deposits local anaesthetic near the spinal nerves emerging between vertebrae (the last thoracic nerve and the first and second lumbar nerves) before they spread into the flank. The skin, muscle and peritoneum of the flank are desensitised, the abdominal wall relaxes, and a warm, pain-free area is created by blood vessel dilation. Various approaches are named after their authors, and which one is used is a matter of training and preference. Advantages are small drug volume and good muscle relaxation; disadvantages are skill needed, possible failure, and temporary curvature of the spine toward the blocked side. The block can be falsely judged successful or unsuccessful if tested too early.

Line, inverted L, ring and cornual blocks

A **line block** is a row of infiltration along the line of the planned incision, and an **inverted L** block places the row along two sides of the area. It is simple and needs little skill, but it needs more drug volume, it blocks only the layers infiltrated, distorts tissue layers, and may delay wound healing if used excessively. Muscle relaxation is less complete than with a paravertebral block.

A **ring block** is a circle of subcutaneous infiltration around a limb, teat, tail or digit to block all nerves entering the area below. It is used for amputation of digits, teat surgery and tail docking. Adrenaline-containing products must not be used for ring blocks. Do not inject too tightly around the structure because the volume can compress its blood supply. Intravenous regional anaesthesia (Bier block) below a tourniquet is a related technique used for digit surgery in cattle, and tourniquet time should be limited.

Also in cattle, a **cornual block** of the cornual nerve is used for dehorning. Animal welfare rules in many countries require pain relief for dehorning and castration, so check the current guidance for your area.

Concept cleared

Concept cleared: Ion trapping at the nerve

Think of the drug as a key that must first pass through a door (non-ionised) and then turn in a lock inside (ionised). In acidic infected tissue most keys arrive in the wrong form to pass the door, so the nerve is not blocked.

Concept cleared: Order of nerve block

Pain fibres are thin and blocked first, like narrow pipes that clog fastest. Large motor fibres need more drug. That is why a block can remove pain and temperature sensation while the animal can still move the limb.

Concept cleared: Why adrenaline is avoided at extremities

Adrenaline narrows vessels to keep the drug in place. At a digit or teat the blood supply is a single thin vessel, so tightening it can starve the tissue and cause death of the tip.

Concept cleared: Line block versus paravertebral block

A line block is like painting each room of the house after the damage is done, with a lot of paint and many layers. A paravertebral block is like switching off the power at the main box before it reaches the rooms, using little drug.

Memory aid: Before every local injection: ASPIRATE

Aspirate for blood, Slow injection, Pause and watch the patient, Inject in small increments, Respect total allowed amount, Avoid adrenaline at extremities, Treat toxicity early, Equipment ready for emergencies.

Compare and contrast

Amide and ester local anaesthetics

Feature	Amides	Esters	Practical meaning
Examples	Lidocaine, bupivacaine, ropivacaine, mepivacaine	Procaine, tetracaine	Amides are the common choices
Metabolism	Liver	Plasma esterases	Liver disease prolongs amides
Allergy	Rare	More common (PABA metabolite)	Esters need more caution in sensitive patients
Use	Most blocks	Limited, topical or older products	Check availability

Cattle flank techniques

Technique	Site	Strength	Limitation
Paravertebral	Spinal nerves near vertebrae	Small volume, good relaxation	Skill needed; spinal curvature
Line block	Along incision	Simple	Large volume; incomplete relaxation; tissue distortion
Inverted L	Two sides of the field	Simple, covers more area	Large volume; same drawbacks
Ring block	Around limb, teat or tail	Quick for distal parts	No adrenaline; avoid compression

Species notes

Cattle

Standing flank surgery under paravertebral or line block is routine, but cranial spread of an epidural can cause recumbency, so be careful with volume and the choice of drug.

Cat

Cats are sensitive to systemic local anaesthetic effects and to methaemoglobinaemia from benzocaine, so calculate the total carefully and avoid benzocaine products.

Dog

Dental and limb blocks reduce the need for general anaesthetic and give postoperative comfort, but bupivacaine must never go into a vein.

Horse

Standing procedures need sedation plus local block, with attention to the safety of the people near the hindlimbs during caudal epidural anaesthesia.

Sheep and goats

Small body size makes overdose easy, so the total dose by weight must be calculated before blocks,

especially when several sites are infiltrated.

Clinical pearls

Self-test: 10 questions

1. Local anaesthetics act mainly by blocking

Blocking sodium entry prevents the action potential.

2. Why does a block fail in an abscess?

Ionised drug does not cross the nerve membrane.

3. Which agent is particularly cardiotoxic if given intravenously?

Bupivacaine binds tightly in the heart and can cause refractory arrhythmias.

4. Early signs of local anaesthetic toxicity are

CNS excitation usually appears first and may progress to seizures.

5. Adrenaline-containing preparations should NOT be used for

Vasoconstriction at an end-artery site can cause tissue necrosis.

6. Which of these is an advantage of paravertebral block over line block?

It blocks nerves proximally, using less drug and relaxing the wall.

7. A risk of cranial spread of an epidural in a standing cow is

Motor nerves to the hindlimbs may be blocked.

8. Before injecting local anaesthetic, you should

Aspiration detects intravascular needle placement, a main cause of toxicity.

9. A topical agent to avoid in cats because of methaemoglobinaemia is

Cats are particularly sensitive to benzocaine-induced methaemoglobinaemia.

10. A cornual block is used for

It desensitises the cornual nerve supplying the horn base.

Key points to revise

1. Local anaesthetics block voltage-gated sodium channels.
2. Pain fibres are blocked before motor fibres.
3. Amides are metabolised by the liver, esters by plasma esterases.
4. Acidic infected tissue reduces effect.
5. Toxicity progresses from CNS excitation to cardiovascular collapse.
6. Epidural anaesthesia carries a risk of hindlimb weakness and hypotension.
7. Paravertebral block gives flank anaesthesia with a small volume of drug.
8. Ring blocks must avoid adrenaline and tight circumferential injection.

Go deeper on this site

- Ch 7. Analgesia and pain management (in this book)
- Ch 5. Anaesthetic equipment and breathing circuits (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- WSAVA Global Pain Council Guidelines
- PubMed search: local anesthetic systemic toxicity and lipid emulsion
- University of Minnesota Libraries: Principles of Pharmacology study guide

CHAPTER 7 OF 14

Analgesia and pain management

How pain signals travel from tissue to brain, why combining drug classes works better than one drug, and how opioids, NSAIDs, ketamine and gabapentinoids fit into a plan. Includes pain scoring in dogs, cats, horses and farm animals, with species cautions.

> **After this chapter you can**
>
> - Trace the nociceptive pathway through transduction, transmission, modulation and perception
> - Explain peripheral and central sensitisation and why pre-emptive analgesia matters
> - Justify multimodal analgesia by matching each drug class to a point on the pathway
> - Describe the actions, benefits and cautions of opioids, NSAIDs, ketamine and gabapentinoids
> - Choose a suitable pain scale for a species and interpret behaviour changes

Why pain control is a patient safety issue

Pain is not only a welfare problem. Untreated pain raises catecholamines, increases heart rate and blood pressure, slows wound healing, suppresses appetite and delays recovery. In the anaesthetised patient, nociception that is not blocked causes autonomic responses that can be mistaken for light anaesthesia, and the usual reaction is to give more inhalant. This deepens anaesthesia and lowers blood pressure. Good analgesia therefore allows a lighter, safer plane of anaesthesia.

Animals cannot report pain, so the clinician must assume that any procedure painful to a human is painful to the animal. Prey species such as sheep, goats and cattle

often hide pain, and cats show it in subtle ways. Absence of crying is never proof of comfort.

The pain pathway and where drugs act

Nociception has four steps, and each is a drug target.

1. **Transduction.** Tissue damage releases prostaglandins, bradykinin and other mediators that excite nociceptors. NSAIDs act here by blocking cyclo-oxygenase. Local anaesthetics also prevent the nerve ending from firing.
2. **Transmission.** The signal travels along A-delta fibres (sharp, fast) and C fibres (dull, slow) to the dorsal horn of the spinal cord. Local anaesthetics block conduction in these fibres.
3. **Modulation.** In the dorsal horn, signals can be amplified or dampened. Opioids, alpha-2 agonists and gabapentinoids act here. The NMDA receptor, blocked by ketamine, drives amplification.
4. **Perception.** The brain interprets the signal as pain. Opioids, alpha-2 agonists and general anaesthetics act at this level.

Because no single drug acts on all four steps, combining drugs gives broader control.

Sensitisation and pre-emptive analgesia

Repeated or intense nociception changes the system. In **peripheral sensitisation**, inflamed tissue lowers the threshold of nociceptors, so normal touch becomes painful. In **central sensitisation**, sustained C-fibre input activates NMDA receptors in the dorsal horn and the spinal neurons become hyperexcitable. This is called wind-up. The result is hyperalgesia (exaggerated response to a painful stimulus) and allodynia (pain from a normally painless stimulus).

Once sensitisation is established it is harder to treat and may become chronic pain. This is the reason for **pre-emptive analgesia**: giving analgesics before the surgical insult so that the spinal cord never becomes sensitised. A common confusion is to think pre-emptive means a bigger drug amount. It means earlier timing and continued cover afterwards, not a larger exposure.

Multimodal analgesia

Multimodal analgesia combines drugs from different classes, often with local or regional blocks, so that each acts at a different site. The benefit is better pain relief with less of each drug, so the side effects of any one drug are reduced. A typical plan might pair an opioid, an NSAID where safe, a local anaesthetic block and, for selected cases, ketamine or a gabapentinoid.

Two cautions apply. First, combining drugs also combines their risks, so patient selection still matters; an NSAID is not suitable for a hypovolaemic or hypotensive patient. Second, drugs from the same class should not be stacked. Two NSAIDs together do not add analgesia but do add gastric and renal injury.

Local and regional anaesthesia deserve special mention in this plan. A nerve block or a local infiltration stops transmission before the signal reaches the cord, so it also reduces the amount of inhalant and opioid needed. Always check the maximum safe exposure for the species and body weight, because cats and small patients are easily overdosed with local anaesthetics. Signs of toxicity include tremors, seizures and arrhythmias, and the response is to stop, support ventilation and call for senior help.

Opioids, NSAIDs, ketamine and gabapentinoids

Opioids act on mu, kappa and delta receptors, which are G-protein-coupled and reduce neurotransmitter release and neuronal firing. Full mu agonists give the strongest analgesia. Partial agonists and agonist-antagonists such as buprenorphine and butorphanol are milder; butorphanol is short acting and better for visceral than for severe somatic pain. Common effects are sedation, bradycardia, respiratory depression, vomiting and defecation in dogs, and constipation or urine retention with prolonged use. Respiratory depression is usually modest in conscious animals but is additive with anaesthetics, so ventilation must be watched. Opioids are controlled substances; follow the current Indian narcotic rules, which should be checked in the latest notification.

NSAIDs block cyclo-oxygenase and reduce prostaglandins at the site of injury and in the cord. They are excellent for inflammatory and post-operative pain. The risks are gastric ulceration, renal injury (especially with hypotension or dehydration) and effects on platelets. COX-1 protects stomach and kidney; COX-2 is induced in inflammation, so COX-2 preferential drugs are considered safer. Never give an

NSAID together with a corticosteroid, and allow a washout between different NSAIDs.

Ketamine is an NMDA receptor antagonist. At low sub-anaesthetic exposure it dampens wind-up and reduces opioid need, which is useful in severe or chronic pain. It does not replace an opioid. Watch for tachycardia and, in some patients, dysphoria.

Gabapentinoids (gabapentin, pregabalin) bind the alpha-2-delta subunit of voltage-gated calcium channels and reduce release of excitatory transmitters. They are used for neuropathic and chronic pain, and gabapentin is also valued for calming cats before handling. The main effect is sedation and ataxia. They are cleared by the kidney, so reduced function needs caution. Gabapentin is not a quick rescue drug for acute severe pain.

Pain scoring and reassessment

Pain must be measured repeatedly, because analgesia is adjusted to the score and not to a fixed routine. Scales combine behaviour, posture and response to touch.

- **Dogs:** the Glasgow Composite Measure Pain Scale (short form) uses behaviour, response to gentle touch and posture, and gives a score at which rescue analgesia is advised.
- **Cats:** the Feline Grimace Scale scores ear position, orbital tightening, muzzle tension, whisker position and head position. Hiding, reduced grooming and loss of appetite are common signs.
- **Horses:** the Horse Grimace Scale and composite scores look at ears, eyes, nostrils and facial muscle tension, along with posture, weight shifting and reluctance to move.
- **Cattle, sheep and goats:** scoring is less standardised; look at facial expression, head carriage, rumination, feeding and willingness to move.

A common error is to score only when the animal is disturbed. Observe quietly first, then approach, then palpate. A sedated animal can still be in pain, and sedation should not be read as analgesia. Always follow a dysphoric, whining, hypotensive or vomiting patient back to the cause: pain, drug effect, or both.

Concept cleared

Concept cleared: Wind-up

Think of a crowded stairwell alarm. A single press of the button rings once. If the button is pressed again and again, the alarm becomes louder and starts to ring even when lightly touched. Repeated C-fibre input makes spinal neurons overreact in the same way, which is why early analgesia keeps the alarm calm.

Concept cleared: Multimodal analgesia

To stop water flowing through a pipe, closing one tap works but needs great force. Closing several taps along the line, each a little, works easily. Different drug classes close different taps on the pain pathway, so each is needed in a smaller amount.

Concept cleared: Sedation is not analgesia

A quiet animal is not always a comfortable animal. Alpha-2 agonists and acepromazine produce calm, but acepromazine gives no pain relief at all. Score pain separately from sedation.

Concept cleared: Rescue analgesia

Every pain plan needs a pre-agreed score above which extra analgesia is given. This turns pain control into a measured loop: score, treat, rescore.

Memory aid: TTMP

Transduction, Transmission, Modulation, Perception: the four steps of nociception. Match a drug to each one when planning multimodal analgesia.

Compare and contrast

Analgesic classes at a glance

Class	Main site of action	Best for	Key caution
Opioid	Spinal cord and brain receptors	Moderate to severe acute pain	Respiratory depression, bradycardia, vomiting
NSAID	Peripheral COX at injury site	Inflammatory and post-operative pain	Gastric and renal injury, hypovolaemia
Ketamine (low level)	NMDA receptor in dorsal horn	Severe, chronic or wind-up pain	Tachycardia, dysphoria; adjunct only
Gabapentinoid	Calcium channel alpha-2-delta	Neuropathic and chronic pain	Sedation, ataxia, renal clearance
Local anaesthetic	Sodium channel on nerve	Block of transmission	Systemic toxicity, especially cats

Pain pathway steps and drugs

Step	What happens	Drug that acts here
Transduction	Tissue injury excites nociceptor	NSAIDs, local anaesthetics
Transmission	Signal along A-delta and C fibres	Local anaesthetics
Modulation	Dorsal horn amplifies or dampens	Opioids, alpha-2 agonists, ketamine, gabapentinoids
Perception	Brain interprets pain	Opioids, general anaesthetics

Species notes

Dog

Opioids commonly cause vomiting and slowed heart rate. Herding breeds with the ABCB1 (MDR1) variant may be more sensitive to some opioids such as butorphanol, so check breed history. Dogs are prone to NSAID gastric injury; avoid

Cat

Cats clear many NSAIDs slowly because of limited glucuronidation, so only drugs licensed or well documented for cats should be used, with great care over repeat exposure. Pain signs are subtle; use a facial scale. Opioids may cause

combining NSAIDs and corticosteroids.

excitement in some cats, so selection and monitoring matter.

Horse

Opioids may cause excitement or reduced gut motility, so colic and post-operative patients need careful monitoring. NSAIDs are the mainstay for musculoskeletal pain, but gastric and right dorsal colon ulceration and renal injury remain risks.

Cattle, sheep and goats

Ruminants hide pain and are often under-treated. Drugs used in food animals must respect withdrawal times, and there are Indian rules for residues, so check the current notification before choosing any analgesic in a milk or meat animal.

Pig

Pigs show pain by vocalisation, isolation and reluctance to move. Procedures such as castration should include analgesia and local anaesthesia; also confirm local legal requirements for food animals.

Clinical pearls

Self-test: 10 questions

1. Which step of nociception is mainly blocked by NSAIDs?

NSAIDs reduce prostaglandin formation at the injury site, which lowers the excitation of nociceptors (transduction).

2. Wind-up in the dorsal horn is mainly driven by which receptor?

Sustained C-fibre input activates NMDA receptors and makes spinal neurons hyperexcitable. Ketamine blocks this receptor.

3. Pre-emptive analgesia means:

The aim is to stop sensitisation by timing, not by larger exposure.

4. A dog under anaesthesia has rising heart rate and blood pressure during incision. The best first thought is:

Autonomic response to surgery often signals inadequate analgesia, and simply deepening the inhalant adds hypotension.

5. Which pairing is unsafe?

Two NSAIDs add gastric and renal risk without extra analgesia.

6. Gabapentin is mainly useful for:

It acts on calcium channel alpha-2-delta and is slow; it is not a rescue drug.

7. Which statement about acepromazine is correct?

Acepromazine is a phenothiazine tranquilliser without analgesic action.

8. Common sign of pain in a cat is:

Cats show pain subtly; facial scales and behaviour change are more reliable than vocalisation.

9. Which patient is the least suitable for an NSAID?

Prostaglandins maintain renal blood flow in low-perfusion states; NSAIDs may cause kidney injury.

10. Opioids act through which receptor type?

Mu, kappa and delta opioid receptors are G-protein-coupled and reduce transmitter release.

Key points to revise

1. Nociception has four steps: transduction, transmission, modulation, perception.
2. Central sensitisation (wind-up) involves NMDA receptors and makes pain harder to treat.
3. Pre-emptive analgesia protects the spinal cord from sensitisation.
4. Multimodal analgesia uses drugs from different classes at different sites.
5. Opioids act on mu, kappa and delta receptors; side effects are respiratory depression, bradycardia and vomiting.
6. NSAIDs reduce prostaglandins; risks are gastric, renal and platelet effects.
7. Ketamine blocks NMDA receptors; gabapentinoids act on calcium channel alpha-2-delta.
8. Use a species-appropriate pain scale and reassess repeatedly.

Go deeper on this site

- Ch 8. Monitoring and neuromuscular blockade (in this book)
- Ch 6. Local and regional anaesthesia (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- WSAVA Global Pain Council Guidelines
- University of Minnesota Libraries: Pharmacology, G protein-coupled receptors
- Cornell University College of Veterinary Medicine: Drug sensitivity (MDR1)

CHAPTER 8 OF 14

Monitoring and neuromuscular blockade

The core monitors of anaesthesia, what each one measures and where it misleads, and how to read them together. Also covers neuromuscular blocking drugs, how their action is monitored and reversed, and the rule that a relaxed patient must always be ventilated and kept unconscious.

After this chapter you can

- Explain what pulse oximetry, capnography, blood pressure, ECG and temperature each measure and their limits
- Interpret abnormal capnograph findings and decide on a first response
- Distinguish oxygenation from ventilation and perfusion
- Compare non-depolarising and depolarising neuromuscular blockers by mechanism
- Describe how block is monitored and reversed, and the safety rules that apply

Why we monitor

Anaesthetic drugs depress the cardiovascular and respiratory systems, so the safe depth is a balance between enough anaesthesia and too much. Monitoring detects drift before it becomes an emergency. The most important monitor is a trained person who stays with the patient. Machines add information but do not replace observation of colour, pulse quality, chest movement, jaw tone and eye position.

Monitoring should begin before induction, continue through recovery, and be recorded on a chart at regular intervals so that trends are visible. A single normal value matters less than a changing one.

Before starting, check the equipment as well as the patient: oxygen supply, vaporiser level, absorber, breathing circuit leak test, suction and a working emergency drug and intubation kit. Many serious events trace back to a missed circuit fault or an unreadied rescue tool. Set alarm limits for the species and size, and treat an alarm as information to investigate, never as noise to silence. Hand-over between staff during a case should be explicit, so that the person watching the patient always knows the drugs given and the plan for recovery.

Oxygenation: pulse oximetry

A pulse oximeter shines two wavelengths of light through tissue and compares absorption by oxygenated and deoxygenated haemoglobin. It reports SpO_2 and pulse rate. It measures **oxygenation**, not ventilation.

Important limits: it reads poorly with poor perfusion, vasoconstriction (for example after alpha-2 agonists), movement, pigmented or thick tissue, and a cold probe site. It can read falsely normal with carbon monoxide poisoning, and methaemoglobin pushes the reading towards a fixed value. Also, an animal breathing high oxygen can have a normal SpO_2 even while hypoventilating badly, because the extra inspired oxygen masks the problem. This is why SpO_2 cannot replace capnography. A falling SpO_2 is a late sign, so act early: check the airway, circuit and oxygen supply first, then the patient.

Ventilation: capnography

A capnograph measures carbon dioxide in exhaled gas. The end-tidal value ($ETCO_2$) approximates alveolar and arterial CO_2 in a healthy lung and shows **ventilation**. The waveform also tells a story.

- **High $ETCO_2$** means hypoventilation, increased CO_2 production (malignant hyperthermia, fever), or rebreathing from an exhausted absorber or faulty valve.
- **Low $ETCO_2$** means hyperventilation, falling cardiac output or poor lung perfusion, or a leak or sampling problem.
- **Sudden loss of the trace** may mean disconnection, oesophageal intubation, tube obstruction or cardiac arrest. Check the patient first, then the machine.
- **A baseline that does not return to zero** suggests rebreathing.

Capnography also confirms correct tracheal intubation, because a regular waveform appears only when gas comes from the lungs. A common confusion is to think a normal $ETCO_2$ proves a good circulation. It does not; a patient in shock can have a low value for that reason alone.

Perfusion: blood pressure and ECG

Blood pressure reflects perfusion of vital organs. Mean arterial pressure matters most because organs, especially the kidney and brain, are perfused according to it.

Anaesthetic drugs usually lower it through vasodilation and reduced cardiac output. Hypotension is common and dangerous, particularly in sick, young, old or hypovolaemic patients. Non-invasive methods (Doppler and oscillometric) are common; direct arterial measurement is the most accurate and is used in high-risk cases. Cuff size must suit the limb, because a cuff that is too small reads falsely high and one too large reads falsely low.

The **ECG** shows rhythm and rate but not whether the heart is pumping blood. A patient in pulseless electrical activity has an ECG trace and no output, so always feel the pulse. It is used to detect bradycardia, tachyarrhythmia, ventricular premature complexes and conduction block. Check the cause before treating a rhythm change: pain, hypoxia, hypercapnia, light anaesthesia, electrolyte problems and drug effects are common reasons.

Do not attribute hypotension to anaesthetic depth alone. Reduce inhalant if appropriate, give fluids if hypovolaemic, and use supportive drugs on indication. Alpha-2 agonist effect, bradycardia and vasodilation need different responses.

Temperature

Anaesthesia inhibits thermoregulation, and a patient in a cold theatre with exposed skin and clipped hair loses heat quickly. Small patients, neonates and the old are most at risk. Hypothermia lengthens recovery, reduces drug clearance, prolongs the effect of agents, impairs clotting and increases infection. Measure core temperature, usually oesophageal or rectal, and begin warming early with warm air blankets, insulation, warmed fluids and a warm room. Avoid direct contact with heating pads that can burn skin. Hyperthermia is less common but can follow some drugs in cats, or a very warm environment, and malignant hyperthermia, though rare, must be remembered.

Neuromuscular blockers and reversal

Neuromuscular blocking drugs paralyse skeletal muscle at the nicotinic receptor of the motor end plate. They have **no sedative or analgesic effect**. A paralysed animal that is not adequately anaesthetised can be fully aware and in pain while unable to move, so the plane of anaesthesia must be secured first, and the patient must be ventilated because the diaphragm is also paralysed.

Non-depolarising agents (atracurium, cisatracurium, rocuronium, vecuronium) compete with acetylcholine at the receptor. They are used to give relaxation for eye, thoracic and orthopaedic surgery and to allow controlled ventilation. Their effect is reversed by increasing acetylcholine at the junction with an **anticholinesterase** such as neostigmine or edrophonium, usually given with an antimuscarinic (atropine or glycopyrrolate) to prevent bradycardia and excess secretions. Rocuronium and vecuronium can also be reversed with sugammadex, a binding agent, where it is available. Atracurium and cisatracurium break down spontaneously in plasma (Hofmann elimination), which is helpful in patients with kidney or liver disease.

Depolarising agents (suxamethonium) act like acetylcholine, causing initial fasciculations then a persistent depolarisation. They cannot be reversed with anticholinesterases, which would worsen the block. Their use in veterinary practice is limited, with risks including hyperkalaemia, muscle pain and raised intraocular pressure.

Block is monitored with a **peripheral nerve stimulator**, usually the train-of-four pattern. Fade, meaning progressively weaker twitches, indicates a non-depolarising block. Reversal should not be given until at least some twitches return, or it may fail. Before extubation, confirm recovery by return of spontaneous breathing, strong twitches and normal muscle tone. Residual block leads to hypoventilation, regurgitation and airway obstruction, so keep ventilating until recovery is certain. Hypothermia, acidosis, low potassium and some antibiotics prolong block.

Concept cleared

Concept cleared: Oxygenation versus ventilation

Oxygenation is how much oxygen sits on the haemoglobin; ventilation is how well air moves in and out and removes CO2. A patient breathing 100 per cent oxygen can have a normal pulse oximeter reading while CO2 climbs dangerously. Use the pulse oximeter for oxygenation and the capnograph for ventilation.

Concept cleared: Monitor the patient, not the machine

A trace can look normal when the animal is in trouble, and look alarming when a probe has slipped. Always confirm an abnormal reading by examining the patient, then correct the cause rather than the number.

Concept cleared: Paralysis is not anaesthesia

Neuromuscular blockers stop movement only. They do not affect consciousness or pain. Think of a locked door: the person inside is still awake. Never give a blocker without adequate anaesthesia and ventilation.

Concept cleared: Why reversal works

A competitive blocker occupies receptors, and acetylcholine cannot reach them. An anticholinesterase stops acetylcholine breakdown, so its level rises until it outcompetes the blocker. Because it also raises acetylcholine elsewhere, an antimuscarinic is given with it.

Memory aid: VOP-T

Ventilation (capnograph), Oxygenation (oximeter), Perfusion (blood pressure and ECG), Temperature. Check all four before blaming one.

Compare and contrast

What each monitor tells you

Monitor	Measures	Shows	Main limitation
Pulse oximeter	Haemoglobin saturation	Oxygenation	Late sign; poor in low perfusion; masks hypoventilation
Capnograph	Exhaled CO2	Ventilation, circuit problems, perfusion trend	Low value can reflect poor circulation
Blood pressure	Arterial pressure	Perfusion	Wrong cuff size gives false values
ECG	Electrical activity	Rhythm and rate	Does not show pumping or output
Temperature	Core heat	Heat loss or gain	Probe site affects reading

Neuromuscular blockers

Feature	Non-depolarising	Depolarising
Example	Atracurium, rocuronium	Suxamethonium
Mechanism	Competes with acetylcholine	Mimics acetylcholine, persistent depolarisation
Fasciculations	No	Yes
Reversal	Anticholinesterase or sugammadex	Not reversed by anticholinesterase
Train-of-four	Fade present	No fade (phase I block)

Species notes

Dog

Brachycephalic and obese dogs hypoventilate easily, so capnography and readiness to assist ventilation are essential. Small dogs lose heat quickly.

Cat

Cats have small tidal volumes, so capnograph sampling may under-read, and heart rate under anaesthesia can drop substantially. Their small size makes cuff size and probe site important.

Horse

Large horses commonly hypoventilate and develop hypotension and poor muscle perfusion when recumbent, so blood pressure is best measured directly and ventilation assisted. Poor recovery can injure the animal, so recovery must be supervised.

Cattle and small ruminants

Regurgitation and bloat occur in recumbent ruminants, so a cuffed tube and a head-down position protect the airway. Salivation is profuse and should be allowed to drain.

Pig

Pigs are prone to malignant hyperthermia in susceptible lines, so rising ETCO2 and temperature should alert you early. Peripheral vessels are hard to access and probe placement is difficult.

Clinical pearls

Self-test: 10 questions

1. A pulse oximeter measures:

It reports haemoglobin saturation, which reflects oxygenation, not CO2 removal.

2. A rising ETCO2 with a baseline that does not return to zero suggests:

An exhausted absorber or faulty valve returns exhaled CO2 to the patient.

3. Sudden loss of the capnograph trace should first prompt:

Possible causes include disconnection, tube obstruction, oesophageal intubation or arrest.

4. Which is a late sign of hypoventilation?

Oxygen supplementation delays SpO2 changes, so other signs appear earlier.

5. A blood pressure cuff that is too small gives:

A narrow cuff needs extra pressure to occlude the vessel.

6. The ECG alone cannot tell you:

Pulseless electrical activity shows a trace with no output.

7. Which statement on neuromuscular blockers is correct?

They paralyse muscle only, so adequate anaesthesia and ventilation are needed.

8. Neostigmine is usually given with an antimuscarinic because:

Raised acetylcholine acts on muscarinic receptors as well.

9. Train-of-four fade indicates:

Progressive weakening of the four twitches characterises competitive block.

10. Which drug breaks down by Hofmann elimination?

Atracurium breaks down spontaneously in plasma, useful in renal or hepatic disease.

Key points to revise

1. The best monitor is a trained person who stays with the patient.
2. Pulse oximetry measures oxygenation; its readings fail with poor perfusion.
3. Capnography measures ventilation and confirms tracheal intubation.
4. Blood pressure reflects perfusion; use a suitable cuff size.
5. ECG shows rhythm only; always check the pulse.
6. Anaesthesia causes hypothermia, so monitor core temperature and warm early.
7. Non-depolarising blockers compete with acetylcholine and are reversed by anticholinesterases with an antimuscarinic.
8. Suxamethonium is depolarising and is not reversed by anticholinesterases.

Go deeper on this site

- Ch 9. Anaesthesia of special patients (in this book)
- Ch 7. Analgesia and pain management (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- WSAVA Global Guidelines
- University of Minnesota Libraries: Pharmacology, G protein-coupled receptors
- FDA Center for Veterinary Medicine: Animal and Veterinary

CHAPTER 9 OF 14

Anaesthesia of special patients

Why neonates, old animals, caesarean patients and animals with heart, kidney or liver disease or a flat face need a changed approach. The emphasis is on physiology, drug choice reasoning, monitoring and what to do when things go wrong.

> **After this chapter you can**

- Explain why neonatal and paediatric patients respond differently to anaesthetic drugs
- Describe the age-related changes that make geriatric patients more vulnerable
- Outline anaesthetic principles for caesarean section, for the dam and the newborn
- Apply the reasoning for cardiac, renal and hepatic disease to drug and fluid choice
- List the airway risks of brachycephalic breeds and how to manage them from premedication to recovery

A general approach to the high-risk patient

Special patients have less physiological reserve, so the margin between enough anaesthesia and too much is narrow. The same plan works every time: assess the problem, stabilise before induction where possible, choose drugs that are titrated and reversible, use balanced anaesthesia to reduce inhalant needs, monitor more closely, keep the patient warm, and plan the recovery as carefully as the induction.

Always ask three questions. What does this disease do to drug uptake, distribution, metabolism and excretion? What does it do to circulation and breathing? Which drug and technique do the least harm? Prefer drugs with an antagonist or a short action, and take extra care to maintain blood pressure, oxygen delivery and body temperature. Choose the senior person for the case and do not hurry.

Complications are best met early. Falling blood pressure calls for a check of depth, volume and heart rate before any drug is added. Hypoxia calls for airway, oxygen supply and ventilation first. Hypothermia is prevented rather than treated. If cardiac arrest occurs, begin basic life support at once, call for help and follow a current veterinary resuscitation guideline.

Neonates and paediatric patients

Neonates differ from adults in several ways. Their heart rate, not stroke volume, drives cardiac output, so bradycardia reduces output sharply. The liver enzymes that metabolise many drugs are immature, and renal clearance is lower, so drug effects last longer. Plasma protein is low, which leaves more free drug. Body fat is

low and water content high, which changes distribution. Their temperature control is poor and heat is lost quickly because of a high surface area. Glycogen stores are small, so prolonged fasting risks hypoglycaemia. Oxygen consumption is high and the respiratory reserve small, so hypoxia develops fast.

The practical approach is short fasting, active warming, careful fluid and glucose management, a reversible and short-acting drug plan, and attention to airway size and tube choice. Avoid drugs that depend on hepatic metabolism for termination where possible. Monitor closely and expect slower recovery than in an adult. Fluid overload is a risk in small bodies, so measured fluids are needed.

Geriatric patients

Ageing reduces cardiac output, renal and hepatic function, lung elasticity and thermoregulation. Many older animals also have unrecognised disease, such as a heart murmur, early kidney disease, or endocrine disease. Anaesthetic requirement falls with age, so the same drug amount can produce a deeper effect. The response to hypotension is slower, and recovery is longer.

Good practice is a full pre-anaesthetic work-up, correction of dehydration and anaemia, titration of every drug to effect, careful choice of agents with a minimum of cardiovascular depression, and multimodal analgesia. NSAIDs need caution if kidney function is uncertain. Warm the patient and use supported recovery. A frequent mistake is to treat old age as a disease; it is a risk factor that is managed with preparation.

Caesarean section

There are two patients, the dam and the offspring, and the aim is a stable mother and vigorous newborns. Pregnancy increases oxygen demand and reduces lung reserve because the uterus pushes on the diaphragm. Anaesthetic requirement is reduced, gastric emptying is slowed so regurgitation risk is high, and blood volume is raised but the dam can still become hypotensive, especially when lying on her back, because the uterus compresses the vena cava. Drugs cross the placenta readily, so anything that depresses the dam may depress the newborns.

The principles: pre-oxygenate, keep the dam tilted rather than flat on her back, shorten the time from induction to delivery by preparing the surgeon and theatre

first, protect the airway with early intubation, and use agents with rapid onset and short action. Maintain blood pressure with fluids. Use opioid and other drugs with a reversal available for the newborns where appropriate, and local anaesthesia (line or epidural block) may reduce the general anaesthetic need. Prepare warmed towels, suction and resuscitation help for neonates, with drying and stimulation the first step. In cattle and small ruminants, caesarean is often done standing with local or regional blocks, which avoids recumbency risks.

Cardiac, renal and hepatic disease

Cardiac disease. The aim is to maintain cardiac output and avoid sudden changes in heart rate, preload and afterload. Stabilise heart failure and arrhythmia first. Avoid drugs that cause marked bradycardia or vasodilation, or raise heart rate and myocardial oxygen demand sharply. Alpha-2 agonists are usually avoided in significant disease because they cause bradycardia and a rise in afterload. Fluids are given cautiously, because volume overload causes pulmonary oedema. Use an ECG and direct blood pressure, and keep hypoxia and pain from adding stress. A short, steady induction technique is better than a rapid large bolus.

Renal disease. The kidney is vulnerable to hypotension. Correct dehydration, electrolyte and acid-base disturbances before anaesthesia. Maintain blood pressure and perfusion, and keep urine production under watch. Avoid NSAIDs while hydration or function is uncertain. Drugs that depend on renal excretion last longer, so choose agents with other routes of elimination.

Hepatic disease. The liver metabolises many anaesthetics and makes albumin and clotting factors. Low albumin raises free drug levels, and clotting problems increase bleeding risk with blocks and surgery. Watch for hypoglycaemia. Prefer drugs that depend less on liver metabolism or that have an antagonist, and titrate to effect. In portosystemic shunt patients, sedatives and hepatically metabolised drugs may have prolonged effects.

Brachycephalic patients

Brachycephalic breeds (bulldogs, pugs, Pekingese, Persian cats and others) have shortened skulls with stenotic nares, an elongated soft palate, narrow trachea in some, and often everted laryngeal saccules. Together they are called

brachycephalic obstructive airway syndrome. They are prone to airway obstruction, regurgitation, and hypoventilation, and they also have high vagal tone.

Management starts before induction. Avoid excess stress and heat. Give oxygen before induction, and keep it ready afterwards. Use light sedation that is titrated, because heavy sedation can cause obstruction. Pre-oxygenate, induce with a drug that allows rapid intubation, and have several tube sizes, including smaller ones, ready. Keep a laryngoscope and suction available. Monitor with capnography and oximetry.

The greatest danger is at recovery. Extubate late, only when the animal is awake with a strong swallow and can hold its head up, and keep it in sternal position with oxygen and observation. Be ready to re-intubate. Obstruction on recovery, with noisy breathing and respiratory effort, is an emergency: restore the airway, give oxygen, and call for help.

Concept cleared

Concept cleared: Reduced reserve
A healthy patient is like a car with a large fuel tank and spare tyre. A special patient has less in both. A small problem such as a drop in blood pressure or oxygen quickly becomes serious, so the plan needs earlier detection and correction.

Concept cleared: Two patients in caesarean
A drug that reaches the dam reaches the fetus through the placenta. The ideal plan therefore keeps the dam stable and uses agents that are short acting or can be antagonised, so the newborns are born breathing.

Concept cleared: Why neonates are slow to clear drugs
The enzymes and kidney function that clear drugs in adults are still maturing, so drug effect lasts longer. Short-acting, reversible drugs are favoured to make up for that.

Concept cleared: Recovery is the dangerous phase for flat-faced breeds

The airway is narrowest and sedation is wearing off at the same time. A breed that cannot hold its airway open needs the tube kept in place until it is fully awake, and oxygen and close observation until it breathes easily.

Memory aid: SPECIAL: titrate and prepare

Stabilise first, Plan the recovery, Evaluate the organs, Choose reversible drugs, Intubate and oxygenate, Always warm, Look closely (monitor). Use it as a checklist for any special patient.

Compare and contrast

Special patients: main problem and main response

Patient	Main problem	Core response
Neonate	Immature clearance, poor temperature control, low glucose reserve	Short fasting, warmth, reversible drugs, careful fluids
Geriatric	Reduced organ reserve, hidden disease	Work-up, titrate, support blood pressure, supported recovery
Caesarean	Placental drug transfer, regurgitation, vena cava compression	Pre-oxygenate, tilt, rapid delivery, protect airway
Cardiac	Limited output	Avoid sudden rate and afterload changes; careful fluids
Renal	Hypotension injury, delayed excretion	Correct dehydration, maintain pressure, avoid NSAIDs
Hepatic	Reduced metabolism, low albumin, clotting	Titrate, choose less liver-dependent drugs, watch glucose
Brachycephalic	Airway obstruction, regurgitation	Pre-oxygenate, tubes ready, late extubation

Why each system matters for drug effect

Factor	Neonate	Geriatric	Liver disease	Renal disease
Metabolism	Immature	Reduced	Reduced	Normal
Excretion	Reduced	Reduced	Normal	Reduced
Protein binding	Low	Often lower	Low	Variable
Heat control	Poor	Reduced	Variable	Variable

Species notes

Dog

Brachycephalic breeds need airway-first planning, and sighthounds are often sensitive to some drugs because of low body fat and slow metabolism of some induction agents; titrate carefully. Herding breeds with the MDR1 variant may react strongly to some sedatives and opioids, so check breed history.

Cat

Cats have limited hepatic glucuronidation, so many drugs act longer. Cardiomyopathy is often silent in cats, so a murmur or gallop calls for assessment. Persian and similar breeds are brachycephalic and need airway planning.

Horse

Foals and geriatric horses need warmth, glucose and blood pressure support. Pregnant mares can be hypotensive when recumbent; plan for careful recovery in a padded area.

Cattle, sheep and goats

Caesarean often uses local or regional blocks, which avoids regurgitation and recumbency. Check withdrawal times and the current Indian rules for residues before choosing drugs in food animals.

Pig

Obese or pregnant pigs have limited respiratory reserve and are slow to recover. Temperature and ventilation

need attention, and difficult airways make intubation harder.

Clinical pearls

Self-test: 10 questions

1. Why is bradycardia especially harmful in neonates?

Neonatal stroke volume is limited, so a slow rate reduces output sharply.

2. Which statement about neonatal anaesthesia is correct?

Immature enzymes and kidney function slow clearance; short fasting and warmth are needed.

3. In a caesarean patient, lying on the back may cause hypotension because:

The gravid uterus reduces venous return when the patient is supine.

4. A key principle for caesarean is to:

Because drugs cross the placenta, a short induction-to-delivery interval protects the newborns.

5. Which drug class is generally avoided in significant cardiac disease?

They cause bradycardia and increase afterload, reducing output.

6. In renal disease the most important protective step is to:

Kidney injury from hypotension is the main risk during anaesthesia.

7. Hepatic disease may lead to:

Reduced metabolism and protein synthesis raise free drug levels and cause bleeding risk.

8. The most dangerous period for brachycephalic breeds is:

Airway narrowing and fading sedation coincide, so obstruction can follow extubation.

9. For a brachycephalic dog, extubation should be:

The tube protects the airway until the animal can maintain it.

10. A geriatric patient should be managed by:

Reduced reserve and hidden disease call for assessment and slow titration.

Key points to revise

1. Special patients have less physiological reserve and need careful titration and monitoring.
2. Neonates clear drugs slowly, lose heat quickly and have small glucose reserves.
3. Geriatric patients need a work-up and often have hidden disease.
4. Caesarean section: pre-oxygenate, avoid back-lying, protect the airway, and prepare for newborn resuscitation.
5. Cardiac disease: maintain output and avoid abrupt rate or afterload changes.
6. Renal disease: correct dehydration and avoid hypotension and NSAIDs.
7. Hepatic disease: lower drug metabolism, low albumin and clotting problems.
8. Brachycephalic patients: airway kit ready, late extubation, oxygen and observation in recovery.

Go deeper on this site

- Ch 10. Species-specific anaesthesia (in this book)
- Ch 8. Monitoring and neuromuscular blockade (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- WSAVA Global Pain Council Guidelines
- Cornell University College of Veterinary Medicine: Drug sensitivity (MDR1)
- WSAVA Global Guidelines

CHAPTER 10 OF 14

Species-specific anaesthesia

Why one anaesthetic plan cannot be copied from species to species. The chapter covers the main anatomical, physiological and metabolic differences in dogs, cats, horses, cattle and buffalo, small ruminants, pigs, birds and exotic pets, and the complications each difference invites.

After this chapter you can

- Explain why species and breed change drug choice, monitoring and recovery planning
- Describe the main anaesthetic risks of dogs (including sighthounds, brachycephalic and herding breeds) and of cats
- Explain why horses and ruminants need special attention to recumbency, recovery and regurgitation
- Identify the pig-specific risks: difficult intubation, malignant hyperthermia and vascular access
- Describe how avian and reptile respiratory anatomy and body temperature alter anaesthetic management

Why species matter

An anaesthetic drug is only as safe as the animal it is given to. Species differ in body size, airway shape, stomach design, liver enzymes, temperature control and temperament. A plan that is routine in a Labrador can be hazardous in a cat, a buffalo or a parrot.

Three questions help in every species. What is the **main threat to life** in this animal (airway, regurgitation, hypotension, hypothermia, recumbency injury)? Which **drug properties** suit it (reversible, short acting, little metabolism needed)? How will I **monitor and recover** it safely? This chapter answers these questions species by species. Only concepts are given; doses must always be taken from a current formulary or the product label.

Remember also that breed within species matters, and that the individual patient (age, hydration, pregnancy, liver or kidney disease) can outweigh the species rule.

Dog and cat

Dogs show the widest breed variation of any domestic species.

- **Brachycephalic breeds** (Pug, Bulldog, Boxer) have narrow nostrils, a long soft palate and often a small trachea. Heavy sedation can cause airway obstruction. Give oxygen before induction, keep the airway under watch until the animal is fully awake, and extubate late.
- **Sighthounds** (Greyhound and similar) have little body fat and slower recovery from ultra-short barbiturates, so propofol or other redistribution-independent choices are favoured. Their normal laboratory values also differ from other dogs.
- **Herding breeds** with the MDR1 (ABCB1) mutation can show exaggerated, prolonged sedation from some drugs such as acepromazine and butorphanol; use cautious titration.

Cats are not small dogs. Their small body mass means rapid heat loss and easy overdose from small measurement errors. The larynx is prone to **laryngospasm** on intubation; topical local anaesthetic on the larynx and gentle technique reduce this. Cats are slow at glucuronidation, so some drugs (paracetamol is toxic; many NSAIDs need a cat-specific label) accumulate. Ketamine is largely cleared unchanged through the kidney in cats, so it is a poor choice in a cat with urinary obstruction. Alpha-2 agonists commonly cause vomiting in cats, which matters if the airway is unprotected.

Horse

The horse is a large, flighty animal with an unusual recovery risk. Most serious injuries (fractures, head trauma, spinal damage) happen not at induction but in **recovery**, when a heavy, uncoordinated animal tries to stand.

Key concepts:

- **Planned induction**: a quiet area, adequate sedation first (usually an alpha-2 agonist), then an induction agent, and a padded, well-lit box with an assistant controlling the head.
- **Recumbency effects**: a lying horse has a large V/Q mismatch because lung under its own body weight collapses; hypoxaemia is common and oxygen supplementation is standard in prolonged cases.
- **Hypotension and myopathy**: low arterial pressure and prolonged recumbency cause poor muscle perfusion and postanaesthetic myopathy or neuropathy. Good padding, positioning and blood pressure support reduce the risk.
- **Colic risk**: alpha-2 agonists and opioids slow gut motility. Pre-existing colic patients are high-risk.

A common confusion: horses are not fasted in the same way as ruminants. Fasting is usually brief and tailored, and clinic policy and case type decide it.

Cattle and buffalo

The ruminant stomach explains most anaesthetic hazards. Under sedation or general anaesthesia, rumen fermentation continues, gas cannot be belched, and the animal may **bloat** and **regurgitate** rumen fluid. Fluid in the pharynx is easily aspirated, and aspiration pneumonia can follow days later.

Practical consequences:

- Withhold feed (and sometimes water) before elective procedures, following local practice, to reduce rumen load.
- Use a **cuffed endotracheal tube** for general anaesthesia and keep the head and neck lower than the rumen so fluid drains out of the mouth.
- Cattle are very **sensitive to xylazine** and need much lower doses per kilogram than horses. A heavily sedated cow often lies down, which is itself a risk.

- Xylazine can stimulate uterine contraction, so it must be used carefully in late pregnancy.

Buffalo are generally managed like cattle, but they are often more nervous when handled by strangers and can overheat easily in hot weather, so avoid the afternoon sun and keep water available. Because published guidance is mostly for cattle, apply it cautiously and monitor closely. Both species are food animals, so check drug approval and withdrawal times under current Indian rules.

Small ruminants and pigs

Sheep and goats share the ruminant risks of bloat and regurgitation. Some additional points:

- Sheep can develop hypoxaemia and pulmonary changes after alpha-2 agonist sedation, so many clinicians use low-dose, reversible protocols with oxygen available.
- Goats are more sensitive to the toxic effects of local anaesthetics than many species, so total volume must be calculated carefully, especially in kids and thin animals.
- Small ruminants are easily handled, which tempts people to skip monitoring. Do not.

Pigs are a different problem. The IV route is difficult (the ear vein is the usual site), the larynx is long and prone to spasm, and the neck is short. Fat adds a thick layer through which intramuscular injections may not reach muscle. Some pigs, particularly stress-susceptible lines, are prone to **malignant hyperthermia** triggered by halogenated volatile agents and succinylcholine; the signs are rapidly rising temperature, muscle rigidity and tachycardia. Prevention is to avoid triggers in at-risk animals and to have cooling, oxygen and specific treatment ready. Pigs also squeal and struggle when restrained, so a calm approach with sedation first is better than forcing.

Birds and exotics

Birds do not have a diaphragm. They breathe by moving the sternum, and gas flows in one direction through the lungs, with air sacs acting as bellows. So anything that **restrains the sternum** (a tight hand, a heavy drape, dorsal positioning) can stop

ventilation. Birds under anaesthesia often need **assisted ventilation**, as their breathing can slow fast. Small birds lose heat and glucose quickly, so fasting must be short and warmth is vital. Isoflurane or sevoflurane delivered by mask or tube is a common choice, as these allow quick changes in depth. Tracheal rings in birds are complete, so overinflated cuffs can injure the trachea.

Reptiles are ectotherms: drug metabolism and recovery depend on body temperature, so the animal must be kept within its preferred range. They can hold their breath and have intracardiac shunts, which changes the speed of gas induction.

Rabbits and small mammals are prone to stress-related deaths. Rabbits are obligate nasal breathers, have a small mouth opening that makes intubation hard, and their long hind legs and light skeleton may fracture the spine during struggling. Rabbits cannot vomit, so prolonged fasting is not needed and may do harm. Always handle exotics gently, warm them, and record every sign. If unsure about a species, consult an exotic-animal specialist.

Concept cleared

Concept cleared: Why ruminants regurgitate
Think of a large fermentation tank that never stops bubbling. When the animal is lying down and sedated, the gas cannot be released and the liquid can flow back up. A cuffed tube and a head-down position let the liquid run out instead of into the lungs.

Concept cleared: Brachycephalic airway
Imagine breathing through a narrow straw with a floppy flap at the end. Sedation relaxes the flap further. The breed was bred for a short face, but the soft tissue stayed long, so airway control comes first.

Concept cleared: Avian ventilation
A bird breathes like a bellows pumped by its breastbone. If you press on the keel, you take away the pump. That is why birds need to be held loosely and often need assisted ventilation under anaesthesia.

Concept cleared: Recovery risk in horses

Anaesthesia is like landing an aeroplane: the take-off is easy, but the landing is where accidents happen. A padded box, a calm assistant and a patient plan protect the horse as it relearns to stand.

Memory aid: Species risk shortcuts

Dog = Dental and Direction of the airway (brachycephalic). Cat = Cold. Horse = Hit on recovery. Ruminant = Regurgitate and bloat. Pig = Pyrexia (malignant hyperthermia). Bird = Breastbone must move.

Compare and contrast

Main anaesthetic hazard by species

Species	Main hazard	Key precaution
Dog (brachycephalic)	Airway obstruction	Oxygen, late extubation, careful sedation
Cat	Hypothermia, laryngospasm, drug accumulation	Warmth, topical laryngeal local anaesthetic, cat-specific drugs
Horse	Injury in recovery, hypotension, myopathy	Padded recovery, blood pressure support, assisted recovery
Cattle and buffalo	Bloat, regurgitation, aspiration	Cuffed tube, head low, reduced alpha-2 sensitivity
Pig	Malignant hyperthermia, difficult intubation	Avoid triggers, cooling ready
Bird	Ventilation failure, heat loss	Free sternum, assisted ventilation, warmth

Breed and species sensitivities

Group	Sensitivity	Practical meaning
Sighthound	Slow recovery from some barbiturates	Prefer propofol-type drugs
MDR1 herding breeds	Prolonged sedation with some drugs	Titrate carefully
Cat	Slow glucuronidation	Avoid paracetamol; NSAID only per cat label
Cattle	Very sensitive to xylazine	Use much lower doses than horses
Goat	Sensitive to local anaesthetic toxicity	Calculate total volume carefully

Species notes

Dog

Check breed: brachycephalic, sighthound and MDR1 herding breeds all change drug choice and recovery watching.

Cat

Keep warm, use topical local anaesthetic on the larynx, and avoid ketamine if the urinary tract is blocked.

Horse and ruminants

Horses need a safe recovery; ruminants need a cuffed tube, head position and fasting plan to prevent aspiration.

Sheep, goat and pig

Small ruminants may be sensitive to alpha-2 agonists and to local anaesthetic toxicity; pigs risk malignant hyperthermia.

Birds and exotics

Free the sternum, support ventilation, and warm the patient. Rabbits are stress-prone and cannot vomit.

Clinical pearls

Self-test: 10 questions

1. Which complication is most closely linked to ruminant general anaesthesia?

Rumen contents can flow back and enter the airway when the animal is recumbent and sedated, so a cuffed tube and head-down position are used.

2. Why do brachycephalic dogs need special airway care?

Their airway anatomy predisposes them to obstruction, worsened by sedation.

3. Which drug choice is generally favoured in sighthounds for induction?

Sighthounds have little fat and recover slowly from barbiturates that depend on redistribution.

4. In which phase do many horse fractures occur?

The heavy horse tries to stand before it is coordinated, so recovery needs planning.

5. Why can birds stop breathing if held tightly across the chest?

Birds lack a diaphragm, so restraining the sternum stops the bellows action.

6. Malignant hyperthermia in pigs is typically triggered by:

Susceptible pigs react to these triggers with rigidity, heat and tachycardia.

7. Goats are particularly sensitive to which drug class?

Total dose and volume of local anaesthetic must be calculated carefully in goats.

8. Which statement about rabbits is correct?

Because they cannot vomit, long fasting is not needed, and intubation is technically difficult.

9. Why is ketamine a poor choice in a cat with urethral obstruction?

Reduced urine flow prolongs the effect and may lead to a longer recovery.

10. Compared with horses, cattle are:

Cattle need much lower doses per kilogram of xylazine and may lie down when sedated.

Key points to revise

1. Species, breed and individual condition all change anaesthetic risk.
2. Brachycephalic dogs need airway control and oxygen.
3. Sighthounds are slow with some barbiturates; propofol is often preferred.
4. Cats lose heat fast and are prone to laryngospasm.
5. Horses are most at risk in recovery and from hypotension and myopathy.
6. Ruminants bloat and regurgitate, so use a cuffed tube and head-down position.
7. Pigs may develop malignant hyperthermia with some triggers.
8. Birds lack a diaphragm, so sternal restraint stops ventilation.

Go deeper on this site

- Ch 11. Field anaesthesia and standing sedation in livestock (in this book)
- Ch 9. Anaesthesia of special patients (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Tranquilizers, Sedatives, and Analgesics for Treatment of Animals
- University of Wisconsin-Madison RARC: Species Guidelines on Anesthesia and Analgesia
- Merck Veterinary Manual: Exertional Myopathies in Horses

CHAPTER 11 OF 14

Field anaesthesia and standing sedation in livestock

How to plan safe sedation and pain control for cattle, buffalo, small ruminants and horses when the clinic is a cowshed or a village lane. The chapter covers restraint, standing sedation with regional blocks, handler and animal safety, recovery, and the mistakes that most often cause field accidents.

> **After this chapter you can**
>
> - Explain why standing sedation with local or regional analgesia is preferred for many livestock procedures
> - Describe safe restraint and handler positioning for large animals
> - List the monitoring and emergency items needed even in a basic field kit
> - Explain how to manage recovery and avoid bloat, aspiration and injury
> - Identify common field mistakes and how to avoid them

Why standing sedation is often better in the field

In rural practice there is usually no operating table, no oxygen cylinder, no ventilator and no assistant trained in anaesthesia. The patient may be a milch cow, a working bullock, a buffalo or a pony. In such conditions general anaesthesia of a large animal is risky. A heavy animal lying on a hard floor can suffer nerve and muscle damage, and a ruminant can bloat or aspirate.

The safer approach for many procedures is **standing sedation plus local or regional analgesia**. Sedation controls behaviour and fear. Local analgesia blocks pain at the site. Together they permit procedures such as wound repair, teat surgery, rumenotomy through the flank, caesarean section in cattle, and many dehorning or castration cases, with the animal on its feet.

The aim is not to make the animal unconscious but to make it **calm, pain-free and safe**. Choose the lightest plan that works and be ready to change it.

Planning, restraint and handler safety

Assess before drugs: species, temperament, body condition, hydration, pregnancy, heart and respiratory disease, and the procedure planned. A shocked, dehydrated or very thin animal needs a lighter plan, and perhaps fluids first.

Choose a **safe place**: a non-slip floor, shade, space to work, and a way to get out. Use a crush or a stout post and secure the head with a halter or rope. Tie the animal short enough to control it, but with a quick-release knot so a falling animal does not choke.

Know where animals kick. Horses kick backward but can strike forward; cattle kick forward and sideways with a hind leg in a wide arc; buffalo may be quick and unpredictable. Stand close to the body rather than at full leg-length, with a hand on the animal so you can feel movement, and never kneel or stand directly behind. Keep onlookers and children well away. Wear sturdy footwear and avoid working alone.

Sedation does not remove danger. A sedated animal can wake at a sudden noise or pain, so treat it as unpredictable until recovery is complete.

Sedation and local or regional analgesia

The usual sedative class in field practice is the **alpha-2 agonists** (xylazine and related drugs). They give sedation, muscle relaxation and some analgesia, are cheap and reversible with an alpha-2 antagonist. Side effects include bradycardia, an initial rise then fall in blood pressure, reduced gut motility, salivation, drooling, and in ruminants a tendency to lie down and bloat. Cattle are far more sensitive than horses, so horse protocols must never be copied.

Where available, a benzodiazepine or other adjunct can reduce the alpha-2 requirement, and an opioid can add analgesia, but choice depends on law, access and species. Dose and route must come from a current formulary or the product label.

Local and regional techniques include:

- **Line and inverted-L blocks** for flank surgery.
- **Paravertebral blocks** for the flank in cattle, which give wider desensitisation but need anatomical skill.
- **Cornual nerve block** for horn procedures.
- **Caudal epidural** for tail, perineal, vaginal or rectal procedures and for obstetrics. A high-volume epidural can spread forward and cause hind-limb weakness and collapse, so keep the standing animal supported.

Local anaesthetics are limited by total dose, especially in small ruminants and thin animals, so calculate before drawing up. Always aspirate before injecting to avoid intravascular injection.

Monitoring and emergencies in a basic kit

Monitoring in the field relies on the senses and a few simple tools. Watch **breathing rate and pattern**, **mucous membrane colour**, **heart rate** (stethoscope or femoral/facial pulse), **eye position and reflexes**, **jaw tone** and **body temperature**. In hot weather, sedated cattle and buffalo can overheat, so keep them shaded and cool.

A basic emergency kit should contain: the **reversal agent** for the sedative used, an anticholinergic if bradycardia is dangerous, fluids, a cuffed endotracheal tube or a way to secure the airway where possible, a rope for emergency positioning, and a plan for calling help. If the animal goes down unintentionally, lift the head, check the airway, position it in **sternal recumbency** with the head and neck extended, and treat bloat or regurgitation at once.

Record the drug name, time given and animal weight estimate. These records help if you must repeat treatment or if the animal develops late problems.

Recovery and withdrawal

Recovery is part of the procedure. Keep the animal in a quiet, shaded, non-slip place until it is fully steady. Do not let it walk or return to herd, road or water until the sedation has worn off or been reversed and the gait is normal.

Watch for **bloat**, which can develop within hours after alpha-2 agonist use because the animal cannot belch while sedated. Left unchecked, bloat compresses the lungs

and heart. Ensure the animal is upright and offer no feed until it is alert and the gut is working.

If an animal is down, keep it in sternal position, propped with bales or sacks if needed. Avoid lateral recumbency with the head level with the body, as this encourages regurgitation.

Livestock are food animals. Many sedatives, analgesics and anaesthetics have **withdrawal periods** for milk and meat, and some are not permitted for use in food animals. Check the current product label and the latest Indian regulations or notifications before using any drug, and advise the owner clearly on when milk and meat can be used.

Common field mistakes

Most field accidents come from a short list of errors.

- **Guessing weight and copying horse protocols.** Overdosing causes collapse, bloat and respiratory depression. Estimate weight with a tape or chart, and use species-specific references.
- **Relying on sedation alone for painful work.** Without local analgesia, the animal will kick, and the surgeon will be tempted to give more sedative.
- **Not waiting for onset.** Starting early leads to repeat dosing and overdose. Allow time for the drug to act.
- **Ignoring pregnancy, dehydration and heat.** Late-pregnant, shocked or overheated animals are less tolerant.
- **No reversal agent and no plan for a downed animal.**
- **Too much epidural volume**, causing hind-limb collapse.
- **Poor casting practice.** Casting on hard ground, or leaving the animal on one side too long, causes nerve and muscle injury.
- **Forgetting withdrawal times** and failing to tell the owner.
- **Working alone or allowing crowds.**

A short checklist before every case (weight, health, drug, reversal, restraint, helpers, escape route, recovery area, withdrawal advice) prevents most of these.

Concept cleared

Concept cleared: Sedation versus analgesia

Sedation is like turning down the animal's volume and fear; analgesia is like cutting the wire that carries pain. A calm animal can still feel a knife, so painful work needs a block as well.

Concept cleared: Why cattle lie down

Cattle are very sensitive to alpha-2 agonists. Think of an adjustable dimmer switch that is already close to the maximum in a cow, whereas the same turn gives only half the effect in a horse.

Concept cleared: Bloat after sedation

A cow belches thousands of times a day to release rumen gas. Sedation switches off this reflex, so the gas builds up like a balloon pressing on the chest.

Concept cleared: Standing is safer

An animal on its feet keeps its airway, rumen and muscle circulation working as nature designed. Lying down a heavy animal removes these advantages, so only do it when needed.

Memory aid: Field checklist: WHERE-SAFE

Weight, Health, Equipment, Reversal, Escape route, Sedation level, Analgesia block, Food withdrawal, Environment (shade and floor). Run through it before every case.

Compare and contrast

Standing sedation versus field general anaesthesia

Feature	Standing sedation with block	Field general anaesthesia
Airway control	Animal protects its own	Needs tube and assistance
Risk of bloat and aspiration	Lower	Higher
Muscle and nerve injury	Low	Higher on hard ground
Equipment needed	Simple	Oxygen, tube, monitoring
Best for	Flank surgery, teat, wound, obstetrics	Short lying procedures when unavoidable

Common regional blocks

Block	Area desensitised	Caution
Line or inverted-L	Flank incision line	Uneven depth; large volume
Paravertebral	Flank wall	Needs skill; scoliosis and hypotension if misplaced
Cornual	Horn base	Check withdrawal and species
Caudal epidural	Tail, perineum, vagina	Too much volume may cause collapse

Species notes

Cattle
Very sensitive to xylazine, so use cattle-specific references. Watch for bloat and regurgitation; keep head and neck extended.

Buffalo
Handle quietly, avoid heat and prolonged restraint, and plan for stress. Apply cattle guidance cautiously.

Sheep and goat
Easy to restrain but small margin for local anaesthetic overdose and

Horse and donkey
Less sensitive than cattle but may kick or strike; donkeys and mules

alpha-2 effects on breathing. Keep monitoring.

can be stoic, hiding pain and sedative depth.

Pig
Seldom handled standing; use calm approach and sedation before restraint. Beware malignant hyperthermia in susceptible lines.

Clinical pearls

Self-test: 10 questions

1. Why is standing sedation preferred in many field procedures?

A standing animal avoids many dangers of recumbency such as bloat, aspiration and muscle damage.

2. A calm sedated cow is still kicking during a flank incision. The main reason is:

Sedation does not guarantee analgesia; a block is needed for painful work.

3. Which hazard is especially linked to alpha-2 agonist sedation in ruminants?

The animal cannot belch when sedated and recumbent.

4. A too large caudal epidural volume may cause:

Spread forward blocks nerves to the hind limbs.

5. If a sedated cow goes down, the best position is:

Sternal position allows eructation and reduces aspiration risk.

6. Which should be in every field emergency kit?

Reversal allows rapid correction of overdose, such as respiratory depression or collapse.

7. Why should horse protocols not be copied for cattle?

Cattle need much lower doses per kilogram; overdose causes recumbency and bloat.

8. Which animal handling error is most hazardous?

This is the range of the kick.

9. Before treating a dairy cow, which extra step is essential?

Residues in food are a public health concern and rules apply.

10. Which is a common cause of late recovery injury?

A partly sedated animal may fall or wander onto hazards.

Key points to revise

1. Standing sedation with local or regional analgesia is often safer than general anaesthesia in the field.
2. Assess the animal before choosing a plan.
3. Handler position and escape routes prevent kick injuries.
4. Alpha-2 agonists cause sedation but also bradycardia, salivation and bloat risk.
5. Calculate local anaesthetic totals, especially in small ruminants.
6. Caudal epidural overdose can cause collapse of the hind limbs.

7. Recovery needs a quiet place, upright posture and bloat watch.
8. Withdrawal times must be checked and explained to the owner.

Go deeper on this site

- Ch 12. Chemical restraint and capture of wildlife (in this book)
- Ch 10. Species-specific anaesthesia (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Tranquilizers, Sedatives, and Analgesics for Treatment of Animals
- University of Wisconsin-Madison RARC: Species Guidelines on Anesthesia and Analgesia
- WSAVA: World Small Animal Veterinary Association

CHAPTER 12 OF 14

Chemical restraint and capture of wildlife

The concepts behind immobilising free-ranging and zoo animals with drugs: the main drug classes and why potent opioids are used, darting principles, handler safety, and the two great killers, hyperthermia and capture myopathy. It also outlines how zoo and Forest Department work is organised, with legal points hedged.

After this chapter you can

- Describe the main classes of immobilising agents and the reason for combining them
- Explain the principles of darting and the main factors that decide success or failure
- List the hazards to handlers and how to reduce them, including opioid exposure

- Explain the causes, signs and prevention of hyperthermia and capture myopathy
- Outline how zoo and Forest Department practice is organised and regulated in India

Why wildlife is different

Wild and zoo animals cannot be handled like pets or livestock. They are fearful, strong, often dangerous, and they cannot be examined or moved without restraint. **Chemical restraint** uses drugs to immobilise or sedate an animal for examination, treatment, translocation, sampling or rescue.

Two facts define this field. First, the margin of safety is small: the animal's weight is estimated, its health is unknown, and stress alters the drug response. Second, the animal's own struggle and the capture process can kill it even if the drugs are perfect. Good practice therefore means as little chase, noise and handling time as possible, a plan for every foreseeable emergency, and a team in which each person has a role. All doses and combinations must be taken from current wildlife formularies and experienced colleagues; this chapter gives only concepts.

Immobilising agents: the concepts

Wildlife drugs must work in a small volume, act fast, be safe in different species, and ideally be reversible. This explains the main groups.

- **Potent opioids** (etorphine, carfentanil) are extremely potent, so a tiny volume fits in a dart. They produce deep immobilisation in many large hoofed animals and elephants but cause respiratory depression, hypoxaemia and often hypertension and a rise in body temperature. They are reversible with opioid antagonists. They are **dangerous to humans**; a tiny exposure can be life-threatening, and an antagonist and a second trained person must be present.
- **Alpha-2 agonists** (xylazine, medetomidine and related drugs) give sedation and muscle relaxation and are reversible. They are used alone or with other drugs.
- **Dissociative anaesthetics** (ketamine, tiletamine) with a benzodiazepine-like partner are widely used in carnivores and primates. They are not fully reversible, so recovery may be slow and rough.

- **Neuroleptics** (azaperone and similar long-acting tranquillisers) calm animals for transport and are used to reduce stress.
- **Benzodiazepines** add muscle relaxation and a calmer recovery.

Drugs are **combined** to reduce each dose, shorten the time to immobilisation, and lower side effects. The price is more complicated monitoring.

Species matter: a drug that is safe in one family may be dangerous in another. Always follow a species-specific reference.

Darting principles

Delivery is usually by dart fired from a projector (gas, powder or blowpipe for short range). The key principles are:

- **Weight estimate and drug volume**: the dart volume is limited, so concentrated drugs are used. An underestimate means incomplete immobilisation and a long, stressful chase; an overestimate risks overdose.
- **Site**: aim for a large muscle mass such as the hindquarter or shoulder. Avoid the chest, abdomen, spine, head and joints, where the dart can cause serious injury.
- **Distance and angle**: stay within the effective range of the projector; a dart striking at too high a speed or at an angle can bruise or penetrate too deeply.
- **Environment**: choose cool hours of the day, clear ground, away from water, cliffs, dense bush and roads. Many animals have drowned when they entered a pond or river as they went down.
- **Tracking**: note the direction of flight, keep the animal in sight, and know the expected time of effect. A lost darted animal can be in danger and dangerous.
- **Minimise excitement**: no crowds, no noise, no pursuit on vehicles if avoidable.

Every dart should be accounted for, because a lost or misfired dart is a risk to humans and animals.

Handler safety

Wildlife work endangers people in three ways: from the animal, from the drugs, and from the environment.

- **Opioid exposure**: potent opioids can be absorbed through broken skin, mucous membranes, needle-stick or splash. Wear gloves and eye protection, handle

darts with care, never recap needles, and keep the antagonist and medical support ready. Never work alone with these drugs, and ensure the local hospital knows of the risk.

- **Approach to the animal**: do not assume it is fully immobilised. Approach from behind after the expected time, check for a response to a gentle touch of a long stick, and protect the head and eyes. Many animals recover suddenly.
- **Team roles**: one person leads, one handles drugs, one monitors the animal, one controls the crowd and others deal with transport. Practise before the real event.
- **Environment**: heat, terrain, darkness and conflict situations with a crowd or village increase risk. Police or forest staff should control the site.

Never allow untrained persons to hold, photograph or crowd an immobilised animal.

Hyperthermia, capture myopathy and monitoring

Hyperthermia is the commonest killer after capture. Heat comes from muscle activity during the chase or struggle, from the drug (potent opioids and some combinations raise body temperature), from a hot day, and from restricted heat loss when the animal lies on hot ground. Signs include fast, shallow breathing, high rectal temperature, a rapid pulse and weakness. Action: move to shade, wet the animal with cool water, fan it, and reverse the drug if needed. Never cool so fast that you cause shock.

Capture myopathy is a non-infectious muscle disease caused by exertion, struggling and stress during capture, restraint or transport. It is often fatal. Muscle breaks down, the blood becomes acidic, and the kidneys can be damaged by muscle pigment. Signs may appear during capture or hours to days afterwards: stiffness, weakness, an abnormal gait, collapse, dark urine and sudden death. Treatment is mainly supportive and results are often poor, so **prevention** is the key: short pursuit, short handling time, cool conditions, minimal noise, adequate sedation and a quiet recovery.

During immobilisation, monitor breathing, heart rate, temperature and oxygen saturation, and supply oxygen if the animal is hypoxic. Keep the animal in sternal position if possible, with the head and neck extended and the eyes protected.

Zoo and Forest Department practice in India

In India, immobilisation of wild animals is usually done by veterinarians working with the Forest Department, zoo authorities, rescue centres or research bodies. Most species are protected under wildlife law, so capture, treatment, translocation and release generally need formal permission from the competent authority, and the rules and procedures are updated from time to time. **Check the current Wildlife (Protection) Act provisions, rules, guidelines and orders** for the exact process in your state.

Potent opioids and several other immobilising drugs are controlled substances. Their purchase, storage, record keeping and use are regulated under narcotic and drug laws; **check the current notifications and local authority requirements** before holding or using them.

Common practice includes a written plan with the team roles, a risk assessment, notification of the local officers, a veterinary kit with antidotes, a transport vehicle and a destination or release plan. Post-event reports record the drug, time, response, complications and outcome. Human-wildlife conflict captures (for example of leopards or tigers near villages) add crowd control and public safety issues, and good communication with local people is part of the job.

Release should be at a suitable site and time of day, after full recovery. If an animal is not fit, it should go to a rescue centre or receive veterinary care.

Concept cleared

Concept cleared: Why use potent opioids
A dart can only carry a small volume, like a thimble. A very potent drug fits a full dose into the thimble, whereas a weaker drug would need a bucket. The cost is that a tiny splash on a human is also a full dose.

Concept cleared: Capture myopathy
Imagine running a sprint until your muscles burn, and then continuing for hours. The muscle cells break down and leak into the blood, which can damage the kidneys. A wild animal's chase does the same, but it cannot stop or ask for help.

Concept cleared: Heat from struggle

Muscle work turns fuel into heat. A darted animal that runs 20 minutes on a hot day is already close to its limit before the drug even acts. That is why cool hours and a short chase matter.

Concept cleared: Reversibility

A reversible drug has an undo button. When an animal is in trouble, the antagonist can bring it back quickly. Drugs without an antagonist demand more careful planning and longer monitoring.

Memory aid: DART safety

Distance and site, Antidote ready, Rehearsed team roles, Temperature watch. Before every capture, check each letter.

Compare and contrast

Immobilising drug groups

Group	Main advantage	Main concern	Reversal
Potent opioids	Tiny volume, deep effect in large hoofed animals	Respiratory depression, heat, human danger	Opioid antagonist
Alpha-2 agonists	Sedation and relaxation	Bradycardia, hypotension, respiratory effects	Alpha-2 antagonist
Dissociatives (with partner drug)	Wide use in carnivores and primates	Rough recovery, seizure risk	No specific antagonist
Neuroleptics	Calming for transport	Hypotension, slow onset	No specific antagonist
Benzodiazepines	Muscle relaxation, smoother recovery	Weak alone	Specific antagonist exists

Hyperthermia versus capture myopathy

Feature	Hyperthermia	Capture myopathy
Main cause	Heat from exertion, drug and weather	Muscle damage from exertion and stress
Timing	During or soon after capture	During capture to days or weeks later
Signs	Fast breathing, high temperature	Stiffness, weakness, dark urine, collapse
Key action	Cool, reverse, oxygen	Prevent; supportive care
Prevention	Cool hours, short chase	Short chase, calm, quick handling

Species notes

Elephant

Large size and potent opioids are common; protect the airway and avoid long lateral recumbency, as heavy weight compresses the lungs.

Big cats (tiger, leopard)

Often immobilised for rescue or conflict. Protect the eyes, monitor breathing and temperature, and keep the crowd away.

Deer and antelope

Highly prone to capture myopathy and stress. Reduce chase time and keep recovery quiet.

Rhinoceros and other large hoofed animals

Opioid-induced hypoxaemia and hyperthermia are common; oxygen and cooling should be ready.

Primates and bears

Dissociative combinations are common; handle carefully, as recovery may be rough and the animal may suddenly rouse.

Clinical pearls

Self-test: 10 questions

1. Why are very potent opioids used in dart drugs for large animals?

Darts hold limited volume, so high-potency drugs make immobilisation possible.

2. Which is the preferred dart site?

Muscle absorbs the drug and avoids injury to vital organs.

3. What must be ready when potent opioids are used?

Human exposure can be life-threatening and rapid treatment is needed.

4. Which feature best describes capture myopathy?

It is a non-infectious muscle disease and signs can appear after capture.

5. A darted animal runs toward a pond. The main risk is:

Drugged animals may collapse in water; choose sites away from water.

6. Which action helps a hyperthermic immobilised animal?

Cooling reduces temperature and prevents organ damage.

7. Why are drugs combined in wildlife immobilisation?

Combinations give effect with a smaller volume and fewer effects.

8. Which statement about legal rules is best?

Rules change and state processes vary.

9. Which group of drugs is typically not fully reversible?

Dissociatives have no specific antagonist, so recovery may be slow and rough.

10. When is the best time for most captures?

Cool conditions reduce hyperthermia and capture myopathy risk.

Key points to revise

1. Chemical restraint carries risk to the animal and to people.
2. Drug combinations reduce volume and side effects.
3. Potent opioids need antagonists and extreme care.
4. Dart site, distance and environment affect safety.
5. Hyperthermia needs rapid cooling and reversal where possible.
6. Capture myopathy is best prevented by reducing stress and exertion.
7. Monitor breathing, heart rate, temperature and oxygen.
8. Legal permission and drug control rules must be checked in current notifications.

Go deeper on this site

- Ch 13. Anaesthesia safety, records and controlled drugs (in this book)
- Ch 11. Field anaesthesia and standing sedation in livestock (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Pennsylvania Game Commission: Capture Myopathy
- Merck Veterinary Manual: Tranquilizers, Sedatives, and Analgesics for Treatment of Animals

- WOAH: Animal welfare

CHAPTER 13 OF 14

Anaesthesia safety, records and controlled drugs

Safe anaesthesia depends on systems as much as on drugs: checklists before use, a continuous anaesthetic record, honest risk assessment, secure handling of controlled drugs, and a culture that reports near-misses. This chapter explains why each habit exists and how it protects the patient and the team.

After this chapter you can

- Describe the purpose and content of pre-anaesthetic and pre-use equipment checklists
- Explain why a continuous anaesthetic record is both a safety tool and a legal document
- Outline how patient risk is assessed and reduced before induction
- State the principles of secure storage, issue and logging of controlled drugs, with Indian rules hedged
- Explain why near-misses should be reported and how a no-blame culture improves safety

Why systems matter more than single drugs

Most anaesthetic deaths in animals are not caused by a rare drug reaction. They follow ordinary, preventable events: a flat oxygen cylinder, a disconnected breathing circuit, an undetected fall in blood pressure, a mislabelled syringe, or a patient left unwatched. Safety therefore rests on **habits and systems** that catch errors before they reach the animal.

Three tools do most of this work: **checklists** (before the case), the **anaesthetic record** (during the case) and **reporting** (after the case). Controlled-drug procedures add a fourth layer that protects the public and the clinic from misuse.

Checklists before the animal is touched

A checklist is a short, fixed list checked item by item, every time. Its value is that it does not depend on memory on a busy day. Aviation uses the same idea. There are

two linked checks.

1. **Equipment check.** Confirm oxygen supply and reserve, vaporiser fill and secure fitting, correct breathing system for the species and size, leak test of the circuit and bag, working valves, soda lime that is not exhausted (for rebreathing circuits), scavenging connected, suction working, a range of endotracheal tubes with cuffs tested, a laryngoscope that lights, and monitors switched on and probes available.
2. **Patient and plan check.** Confirm identity, procedure, weight, fasting status, pre-anaesthetic examination and any tests, existing disease, current medicines, allergies, owner consent, and the drugs planned with the reasoning for each.

Also prepare the **emergency kit** before induction: reversal agents, emergency drugs drawn up or ready to draw, an airway kit and a clear plan for who does what. Many emergencies are survivable only because the equipment was already within reach.

A common confusion is to treat the checklist as paperwork. It is a thinking tool: the pause makes the team ask whether the plan really fits this animal.

Assessing and reducing risk

Risk is the chance that anaesthesia harms this particular patient. It depends on the animal, the procedure, the drugs and the people. Many practices use a simple physical-status grading (such as the ASA system, from healthy to moribund) to summarise the animal's condition and to communicate it. The grade guides how much preparation and monitoring are needed. It does not replace clinical judgement.

Patient factors that raise risk include extremes of age (neonates and geriatrics), obesity, dehydration, anaemia, cardiac, respiratory, renal or hepatic disease, emergency surgery, and breed features. Brachycephalic dogs and cats have airway obstruction risk; sighthounds respond differently to some drugs because of low body fat and different metabolism; some herding-breed dogs carry the MDR1 mutation and may be sensitive to certain sedatives and opioids; horses and ruminants carry special risks of positioning injury, myopathy and regurgitation.

Risk is reduced by **stabilising before anaesthetising** (correct dehydration, treat pain, delay non-urgent cases), choosing drugs for the patient rather than by habit,

using the lowest-risk plan that still gives safe conditions, securing the airway, and monitoring continuously. Owners should be told honestly that anaesthesia always carries some risk, higher in sick animals, and consent should reflect this.

The anaesthetic record

The anaesthetic record is a written or electronic chart made **during** the case, not reconstructed afterwards. It serves three purposes. It shows **trends**, because a single heart rate means little but a steady downward drift is a warning. It forces the person monitoring to look at the patient and the monitors at regular intervals. It is also a **medical and legal record** of what was given and what happened.

A good record contains: patient identification and weight; physical status; pre-anaesthetic findings; every drug given with route and time (premedication, induction, maintenance, analgesics, fluids, reversal); airway details; and then regularly timed entries of heart rate and rhythm, respiratory rate, oxygenation, end-tidal carbon dioxide where available, blood pressure, temperature, depth of anaesthesia and vaporiser or infusion settings. Events (start of surgery, position changes, complications, treatments) and recovery details are also noted.

Two cautions. First, record values you actually observed; do not fill in the chart to look normal. Second, the monitor shows numbers but the **trained person** interprets them. A designated person whose only job is the patient should be present until the animal is fully recovered.

Controlled drugs: storage, logs and responsibility

Several drugs used in anaesthesia and analgesia, especially opioids and some sedatives and dissociatives, can be abused or diverted. Rules in most countries therefore require secure storage and traceable records. The details in India depend on the drug and change over time: opioids and some psychotropic substances fall under narcotic and psychotropic legislation, while other drugs are controlled under drug and prescription rules. **Check the current notifications and your State licensing requirements** for which drugs are covered and what is required.

The principles are the same everywhere.

- **Locked, limited-access storage**, with named key holders. Keys are not left in the lock.

- **A running register** for each drug: date, patient, amount used, amount wasted, the person who gave it, and the balance remaining. Entries are made at the time and corrected by a visible, signed amendment, never by erasing.
- **Regular stock reconciliation**, comparing the physical stock with the register, with any discrepancy investigated and documented promptly.
- **Witnessed wastage** of any unused drug, and safe disposal.
- **Authorised prescribers only**, and drugs are used only for patients under the veterinarian's care.

These steps also protect staff. Needle-sharing, diversion and accidental self-injection are real hazards, and a clear audit trail protects honest staff from suspicion.

Near-misses, reporting and a learning culture

A **near-miss** is an error or unsafe condition that was caught before it harmed the patient: a syringe drawn from the wrong vial and noticed, an empty cylinder found at induction, a circuit connected wrongly. A **critical incident** reached the patient and caused or could have caused harm. Both teach the same lessons, and near-misses are far more common than harm.

Units that learn from near-misses write them down in a simple, brief form: what happened, what helped catch it, and what could change. The review looks for **system causes** (poor labelling, similar-looking vials, crowded drug trays, rushed turnover, missing checklist) rather than a person to blame. A no-blame, just culture makes staff more willing to report, and unreported errors repeat.

Practical measures include clear drug labelling, colour-coded or syringe labels, separating look-alike drugs, double-checking high-risk drugs, a standard drug concentration policy, and regular review meetings. For students, the habit to build is simple: say what you see, ask when unsure, and record what happened honestly.

Concept cleared

Checklists catch errors that memory misses

A fixed pre-use checklist for equipment and for the patient removes reliance on memory and is repeated for every case, however routine.

The record shows trends

A continuously charted anaesthetic record turns isolated numbers into trends, prompts regular observation and serves as a medical and legal document.

Risk is assessed and then reduced

Physical-status grading and patient factors guide the plan. Stabilise first, choose drugs for the individual animal and monitor continuously.

Controlled drugs need an audit trail

Locked storage, a contemporaneous register, reconciliation and witnessed wastage prevent diversion and protect staff. Indian specifics must be checked against current notifications.

Memory aid: Before every induction: ARMS

Airway kit and tubes, Reversal and emergency drugs, Monitors on and working, Supply of oxygen and suction. Then confirm the patient and plan.

Compare and contrast

Near-miss versus critical incident

Feature	Near-miss	Critical incident
Reached the patient	No, caught in time	Yes
Harm	None	Harm or potential for harm
Value for learning	High and more frequent	High but costly
Action	Report, find system cause	Treat, report, review and inform owner

Equipment check versus patient check

Feature	Equipment check	Patient and plan check
Focus	Oxygen, circuit, vaporiser, suction, monitors	Identity, weight, fasting, disease, consent
When	Start of the day and before each case	Before premedication and again before induction
Typical failure caught	Leak, empty cylinder, exhausted soda lime	Wrong patient, missed disease, wrong drug plan

Species notes

Dogs
Check breed cautions in the plan: brachycephalic airways, sighthound drug handling and the MDR1 mutation in some herding breeds.

Cats
Small size makes dead space, circuit choice and heat loss important to check. Record temperature carefully.

Horses
Plan padding, positioning and a safe recovery area. Large body mass makes equipment and personnel checks essential.

Ruminants
Record fasting status and plan for regurgitation and bloat. Cuffed tubes and positioning are part of the checklist.

Pigs and exotics
Heat loss, difficult airways and species-specific risks need pre-planned equipment and a named person to monitor.

Clinical pearls

Self-test: 10 questions

1. What is the main purpose of a pre-use checklist?

A fixed list ensures essential checks are done every time, whatever the workload.

2. When should the anaesthetic record be filled?

Contemporaneous charting shows trends and keeps the observer engaged.

3. Which finding is best caught by a circuit leak test?

Leak testing is part of the equipment check and is done before the animal is connected.

4. What does physical-status grading do?

It communicates risk, but clinical judgement still decides the plan.

5. How should an error in a controlled-drug register be corrected?

Register integrity requires that the original entry remains legible.

6. What is a near-miss?

Near-misses show system weaknesses without patient harm.

7. Which approach best encourages reporting of errors?

People report more when review aims at fixing systems.

8. Which is a patient factor that raises anaesthetic risk?

Dehydration and anaemia reduce reserve, so stabilise them first when possible.

9. Why is reconciliation of controlled-drug stock done regularly?

Comparing physical stock with the register shows losses promptly.

10. Who should monitor an anaesthetised animal?

Monitors give numbers, but a trained person interprets them and acts.

Key points to revise

1. Most anaesthetic harm follows preventable system failures rather than rare drug reactions.
2. Use a fixed checklist for equipment and another for the patient and plan.
3. Prepare emergency drugs, reversal agents and airway equipment before induction.
4. Physical-status grading summarises risk and guides preparation, but does not replace judgement.
5. Stabilise the patient before anaesthesia whenever the procedure is not an emergency.
6. A continuous anaesthetic record shows trends and is a legal document.
7. Controlled drugs need locked storage, a contemporaneous register, reconciliation and witnessed wastage; check current Indian notifications.
8. Report near-misses in a no-blame way and fix the system cause.

Go deeper on this site

- Ch 14. Anaesthetic complications and CPR (in this book)
- Ch 12. Chemical restraint and capture of wildlife (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Concepts
- Veterinary Drug Concepts Clearly Explained

Sources

- WSAVA Global Pain Council guidelines
- Merck Veterinary Manual
- FDA Center for Veterinary Medicine, Animal and Veterinary

CHAPTER 14 OF 14

Anaesthetic complications and CPR

Anaesthesia can cause hypotension, hypoventilation, hypothermia, regurgitation, malignant hyperthermia and cardiac arrest. This chapter explains how each arises, how it is recognised early, the logical first response, and the basic sequence of cardiopulmonary resuscitation and safe recovery.

After this chapter you can

- Explain the causes, early signs and first responses to hypotension and hypoventilation
- Describe why hypothermia occurs and why it matters in recovery
- Explain how regurgitation occurs and how it is prevented and managed
- Recognise malignant hyperthermia and outline its emergency management
- Outline the steps of cardiopulmonary resuscitation and the principles of a safe recovery

Think in terms of oxygen delivery

Most anaesthetic complications reduce the delivery of oxygen to tissues. Delivery depends on **ventilation** (oxygen reaching the blood), **circulation** (cardiac output and blood pressure), and **haemoglobin** (oxygen carrying capacity). Any complication can be understood by asking which of these has failed.

The best rule is to **respond to trends, not crises**. Monitoring and the anaesthetic record let you see a problem developing. The first step is almost always the same: check the patient, check the equipment, make sure of the airway, give 100% oxygen, and consider reducing anaesthetic depth. Only then look for the specific cause.

Hypotension and hypoventilation

Hypotension is low arterial blood pressure. It reduces perfusion of the brain, heart and kidneys. Common causes are anaesthetic overdose or excessive depth (most inhalants and injectable agents lower blood pressure by vasodilation and reduced cardiac output), hypovolaemia, bleeding, bradycardia, arrhythmias, sepsis and drug effects. It is often present before it is obvious, so measure blood pressure rather than guess from pulse quality.

The logical response is to treat the cause: reduce anaesthetic depth if it is too deep, use balanced anaesthesia with analgesics so less inhalant is needed, correct volume deficits and bleeding with fluids or blood products when indicated, treat bradycardia or arrhythmia, and use drugs that support the heart or vessels where needed. Avoid treating a number without looking for the reason behind it.

Hypoventilation means too little breathing to remove carbon dioxide. Most anaesthetics and opioids depress the respiratory centre, and chest or abdominal pressure, position, obesity and airway obstruction add to this. The signs are a rising carbon dioxide level (end-tidal measurement, if available) and eventually falling oxygen saturation. Pulse oximetry can look normal on high oxygen while ventilation is poor, so oxygen saturation alone does not exclude hypoventilation.

The response is to confirm that the airway is open and the tube is correctly placed, reduce depth, and assist or control ventilation by manual or mechanical means. Keep the technique gentle, because over-inflation damages lungs and impairs venous return.

Hypothermia

Anaesthesia blunts the temperature-regulating response and causes vasodilation, so heat is lost to cold theatres, wet skin, clipped areas, cold fluids and open body cavities. Small patients such as cats, small dogs, neonates and exotics lose heat fastest. Large animals lose less quickly but take long to rewarm.

Hypothermia is not harmless. It slows drug metabolism so that animals sleep longer, reduces anaesthetic requirement (so a given setting is relatively deeper), slows the heart, impairs clotting, increases infection risk and delays healing. During recovery, **shivering sharply increases oxygen demand** when the animal may have little spare capacity.

Prevention is easier than treatment: measure temperature, keep the animal off cold surfaces, use warm air or insulating covers, limit wetting and warm fluids. Warm gradually. Direct hot-water bottles or heating pads can burn anaesthetised skin, so use insulation between the animal and any heat source.

Regurgitation and aspiration

Regurgitation is the passive backflow of stomach or oesophageal contents into the pharynx, because the muscle tone of the lower oesophageal sphincter falls under anaesthesia. It differs from **vomiting**, which is active. Gastric content reaching the airway causes **aspiration pneumonia**, a serious complication. Stomach acid is damaging to lung tissue.

Risk is higher with a full stomach, emergency cases, obesity, brachycephalic breeds, hiatal hernia, oesophageal disease, certain drugs, and in ruminants, whose rumen produces large volumes of fluid and gas. Fasting protocols differ by species and age, and very young animals should not be fasted for long because of hypoglycaemia.

Prevention: appropriate fasting, a rapid and secure airway with a **cuffed endotracheal tube inflated** as soon as it is placed, positioning with the head slightly higher than the stomach in small animals (in ruminants, keep the head lower than the pharynx so that fluid drains out), and cautious recovery with the tube left in until the swallowing reflex returns. If regurgitation occurs, lower the head to drain, suction the pharynx, protect the airway with the cuff, and monitor for coughing, hypoxia or later pneumonia.

Malignant hyperthermia

Malignant hyperthermia is a rare, inherited, life-threatening reaction in which skeletal muscle goes into uncontrolled hypermetabolism after exposure to **volatile inhalant anaesthetics** or the depolarising relaxant **succinylcholine**. It is best described in pigs and also reported in dogs, horses and people. A defect in calcium handling in muscle allows calcium to flood the cell, so muscle burns energy and produces heat and carbon dioxide.

Early signs: rapid rise in end-tidal carbon dioxide despite adequate ventilation, fast heart rate and breathing, muscle rigidity, and then rapidly rising temperature. Later:

acidosis, high potassium, arrhythmias, and muscle breakdown.

Management is an emergency: **stop the triggering agent**, move to a clean oxygen supply and a circuit free of inhalant, ventilate with 100% oxygen, actively cool the animal, treat acidosis and arrhythmias, and give **dantrolene**, the specific drug that blocks the release of calcium in muscle. Prepare in advance in susceptible patients by avoiding triggers. A common confusion is that fever after surgery is not malignant hyperthermia; the pattern of early carbon dioxide rise and rigidity points to it.

Cardiac arrest, CPR and recovery

Cardiac arrest is the loss of effective circulation. Under anaesthesia, it most often follows unrecognised hypoxia, deep anaesthesia, severe hypotension, arrhythmia or electrolyte disturbance, so prevention depends on monitoring. If it happens, act immediately. The principles of current veterinary guidelines (such as the RECOVER initiative) are:

1. **Recognise** arrest: no palpable pulse, no heartbeat, loss of monitored waveform and no breathing. Call for help and note the time.
2. **Stop anaesthetic delivery** and give 100% oxygen. Check the airway and secure it with a tube if not in place.
3. **Start chest compressions at once**, hard and fast, allowing full chest recoil. Minimise interruptions. Position the hands according to species and chest shape. Rotate the person compressing regularly because fatigue reduces quality.
4. **Ventilate** in coordination with compressions without over-inflating.
5. **Attach the ECG** to identify the rhythm. This guides the use of drugs and, if a shockable rhythm, defibrillation.
6. **Give drugs through IV or intraosseous access** according to the current guideline and reverse any reversible agents.
7. **Look for the cause** (for example hypoxia, hypovolaemia, overdose, tension pneumothorax) and treat it, and reassess regularly.

Outcomes from arrest under anaesthesia are better than from arrest in sick animals, but survival is still limited, which is another reason to prevent it.

Recovery is a high-risk period. Keep monitoring until the animal is awake, breathing normally, warm and able to hold its head up. Maintain analgesia, keep the airway

protected until swallowing returns, avoid stimulation, and place large animals in a padded, quiet area with trained staff.

Concept cleared

Oxygen delivery framework
Ask whether ventilation, circulation or oxygen carrying capacity has failed. Give oxygen and secure the airway first, then find the cause.

Treat causes of hypotension
Hypotension usually reflects depth, volume, rate or drug effects. Treat the underlying reason, not just the number.

Passive regurgitation is prevented by airway protection
A cuffed tube, correct positioning and appropriate fasting are the main defences against aspiration.

Malignant hyperthermia is a muscle calcium disorder
Triggered by inhalants and succinylcholine, it causes a rapid rise in carbon dioxide and temperature, and is treated by stopping triggers, cooling and dantrolene.

Memory aid: Complication check: AVOID
Airway open, Ventilation adequate, Oxygen supply and depth reduced, Intravenous fluids and circulation, Depth and drugs reviewed. Do this before looking for rare causes.

Compare and contrast

Regurgitation versus vomiting

Feature	Regurgitation	Vomiting
Mechanism	Passive backflow	Active reflex with abdominal effort
Under anaesthesia	Common, silent	Rare because reflexes are depressed
Warning	May be unnoticed until fluid at the mouth	Retching and salivation
Main risk	Aspiration pneumonia and oesophagitis	Aspiration if airway unprotected

Hypoventilation versus hypoxaemia

Feature	Hypoventilation	Hypoxaemia
Problem	Too little carbon dioxide removed	Too little oxygen in blood
Best monitor	End-tidal or arterial carbon dioxide	Pulse oximetry or blood gas
Effect of 100% oxygen	May hide it on pulse oximetry	Often improves it
Response	Assist or control ventilation	Find the cause and improve oxygenation

Species notes

Dogs
Brachycephalic breeds regurgitate and obstruct easily. Barrel-chested breeds may need different compression positioning in CPR.

Cats
Lose heat quickly and hypoventilate easily. Compression is often done with one hand or around the chest.

Horses
Hypotension and poor ventilation are common under general anaesthesia and recovery injuries are a major

Ruminants
Regurgitation and bloat are major risks. Use a cuffed tube and keep the

risk, so plan padded, supervised recovery.

head lower than the pharynx so fluid drains outward.

Pigs
Some lines are susceptible to malignant hyperthermia. Avoid triggers and be ready to cool and treat.

Clinical pearls

Self-test: 10 questions

1. What is the first general response to an anaesthetic complication?

Securing oxygenation and reducing depth treat the commonest underlying problems.

2. Why can pulse oximetry mislead during hypoventilation?

Animals breathing high oxygen may keep normal saturation while carbon dioxide rises.

3. A common cause of hypotension under anaesthesia is:

Most anaesthetics cause vasodilation and reduce cardiac output.

4. Why does shivering during recovery matter?

Shivering consumes oxygen when reserves may be limited.

5. Regurgitation differs from vomiting because it is:

Regurgitation is passive backflow due to reduced sphincter tone.

6. Which measure best protects against aspiration?

A cuffed tube seals the airway while positioning helps drainage.

7. Malignant hyperthermia can be triggered by:

These agents release calcium in susceptible muscle.

8. Which drug is the specific treatment for malignant hyperthermia?

Dantrolene blocks calcium release in skeletal muscle.

9. In CPR, what should be started immediately after recognising arrest?

Early, high-quality compressions maintain some circulation.

10. Why should heating pads be insulated from the animal?

Anaesthetised animals cannot move away from heat or signal pain.

Key points to revise

1. Most complications reduce oxygen delivery through ventilation, circulation or haemoglobin.
2. Respond to trends. First check the patient and equipment, give oxygen and reduce depth.
3. Treat the cause of hypotension rather than the number.
4. Hypoventilation raises carbon dioxide and may be hidden by pulse oximetry on oxygen.
5. Prevent hypothermia with measurement, insulation and warming, avoiding direct hot surfaces.
6. Regurgitation is passive; a cuffed tube and positioning protect against aspiration.

7. Malignant hyperthermia: stop triggers, cool, ventilate with oxygen and use dantrolene.
8. CPR needs early, high-quality compressions, ventilation, ECG, drugs per current guidelines and a search for the cause.

Go deeper on this site

- Ch 13. Anaesthesia safety, records and controlled drugs (in this book)
- Ch 12. Chemical restraint and capture of wildlife (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- WSAVA Global Pain Council guidelines
- Merck Veterinary Manual
- FDA Center for Veterinary Medicine, Animal and Veterinary

How to use Book 5: a short discussion

Anaesthesia is the part of veterinary practice where drug knowledge, physiology and careful observation meet in a single hour. A good anaesthetic is not the one with the cleverest drug combination; it is the one in which the animal is assessed beforehand, monitored throughout, and recovered safely. This book follows that path in fourteen chapters, from the first examination of the patient to the management of an emergency.

Preparation comes first

The opening chapter covers pre-anaesthetic assessment, fasting, physical status grading and equipment checks. Most anaesthetic accidents trace back to poor preparation and inadequate monitoring rather than to one dangerous drug, so this chapter is worth reading twice. The chapters on sedation and injectable agents then

explain why premedication lowers the dose of everything that follows and how each drug class suits or harms different species and breeds.

Maintenance, equipment and monitoring

Inhalation anaesthesia, breathing circuits and monitoring are treated as a connected system. You will meet minimum alveolar concentration, vaporisers, absorbers, pulse oximetry, capnography and blood pressure, and you will learn what each number tells you about the patient and what it cannot tell you. The monitoring chapter also covers neuromuscular blocking drugs and their reversal.

Pain relief and regional techniques

Analgesia is part of anaesthesia, not an optional extra. The chapters on pain management and on local and regional anaesthesia explain how pain pathways work, why combining drugs from different classes gives better relief with fewer side effects, and how nerve blocks and epidurals are used in dogs, cats and livestock. They also explain the signs of local anaesthetic toxicity, which every student should be able to recognise.

Species, field practice and wildlife

Dogs, cats, horses, cattle, buffalo, small ruminants, pigs and birds each respond differently, and the species chapter collects those differences. The field chapter deals with the real conditions of Indian rural practice, where equipment is limited and standing sedation with local blocks is often the safest choice. The wildlife chapter covers the principles of chemical restraint and capture, including handler safety and capture myopathy, and it points out that permissions and controlled-drug rules must be checked before any work begins.

Safety, records and emergencies

The last two chapters cover checklists, anaesthetic records, controlled-drug storage and logs, and the management of complications and cardiac arrest. Reading about hypotension, hypoventilation, regurgitation and malignant hyperthermia in advance is far better than meeting them for the first time on the table.

Recovery and the hours after surgery

Many students stop thinking about the patient once the vaporiser is turned off, yet recovery is when airway obstruction, hypothermia, pain and violent emergence are most likely. Throughout the book you will find reminders to keep the airway protected until the animal swallows, to keep it warm, to keep monitoring, and to continue analgesia into the recovery period. Brachycephalic dogs, cats, horses and ruminants each have their own recovery risks, and the chapters point them out so that you can plan for them in advance.

A note on doses

As in the other books, there are no dose tables or infusion rates. Doses depend on the product, the patient and the situation, and they must come from the label, a current formulary or an experienced anaesthetist. The book gives you the reasoning behind a plan so that you can judge a protocol and ask the right questions. Use the self-tests after each chapter, read the Species notes before an examination, and treat this material as education that does not replace the judgement of a registered veterinarian.

BVSC & AH STUDY BOOK 6 OF 7

Veterinary Toxicology

Seventeen chapters on poisons and poisoning: principles, pesticides, rodenticides, plants, metals, feed and gas hazards, photosensitisation, household and pet toxins, venoms, drug toxicities, antidotes, environmental toxicology and medico-legal work. Each chapter ends with a 10-question self-test.

17 chapters | **170** practice questions | **No** dose tables

By Dr. Rameez Bloch, BVSc & AH, MVSc

Start here

Pick a chapter from the list on the left (or the top bar on a phone). Chapter 1 gives the principles and Chapter 15 is a quick reference for antidotes and decontamination. The other chapters group poisons by source: pesticides, rodenticides, plants, metals, feed and gases, household and pet hazards, venoms and drugs. Each chapter has six parts: Learn, Concepts, Compare, Species, Quiz and Revise. Your quiz progress is saved on this device only. In a real poisoning, contact a veterinary poison service or toxicologist at once.

CHAPTER 1 OF 17

General principles of toxicology

How poisons enter, move through and leave the animal, how dose and response are related, and how toxicity is tested. The chapter also sets out the logic of decontamination, supportive care, antidotes and history taking in a poisoned patient.

After this chapter you can

- Describe toxicokinetics in terms of absorption, distribution, biotransformation and excretion, and link them to toxicity

- Explain the dose-response relationship, threshold, LD50 and the limits of LD50 as a measure of safety
- Distinguish acute, sub-acute and chronic toxicity studies and state what each is designed to find out
- Explain the reasoning behind decontamination, supportive care and the use of antidotes
- Take a structured history in a suspected poisoning case and know when to seek urgent specialist help

What toxicology asks

Toxicology studies the harmful effects of chemicals on living animals. The old statement that 'the dose makes the poison' remains the foundation: almost any substance is harmless at a low enough exposure and harmful at a high enough one. A **toxicant** is any substance that causes harm. A **toxin** is a toxicant made by a living organism, such as a plant, fungus, bacterium or snake.

In practice the veterinarian asks four linked questions. What was the exposure? How much reached the body? What is it doing at its target? What can be done to stop it or reverse it? Every section of this chapter answers one of those questions.

Toxicokinetics

Toxicokinetics describes what the body does to the poison. The same four steps as in pharmacokinetics apply, but the amounts are often large enough to overload normal handling.

- **Absorption.** Poisons enter by the gut, skin, lungs, eye or injection. Route matters. A lipid-soluble pesticide can be absorbed through the skin of a dog bathed in it, and inhaled gases act within minutes. Food in the stomach, gut motility and the form of the product (liquid, powder, granule) change the speed.
- **Distribution.** Fat-soluble agents such as organochlorines are stored in fat and released slowly, so signs can appear long after exposure, for example when the animal loses weight. Binding to plasma protein holds a poison in the blood but can be displaced by other drugs.
- **Biotransformation.** The liver usually converts poisons to water-soluble products that can be excreted. Sometimes this makes the agent *more* toxic, which is called

bioactivation. Phosphorothioate insecticides are converted to the more active oxon form. Species differ greatly here: cats are poor at glucuronidation, so phenols and some drugs linger and cause toxicity.

- **Excretion.** Kidney, bile, lungs and milk are the main routes. Compounds that are excreted in bile and reabsorbed (enterohepatic recirculation) stay in the body longer, which is why repeated activated charcoal is sometimes helpful.

Dose-response, threshold and LD50

As exposure rises, more animals in a group respond and the response in each animal becomes more severe. Plotted against the logarithm of dose, the proportion of animals responding forms an S-shaped curve. Many toxic effects have a **threshold**, a dose below which no effect is seen, because the body's defences can cope with small amounts. Some effects, such as certain cancers caused by genotoxic agents, are treated as having no safe threshold.

The **LD50** is the dose calculated to kill half of a group of test animals under stated conditions. **LC50** is the same idea for concentration in air or water. A low LD50 means high acute toxicity. The figure is useful for ranking and labelling products, but it has limits that students should know:

- It describes death only, not illness, organ damage or long-term effects.
- It depends on species, strain, sex, route and vehicle, so a value in rats cannot be applied directly to a cat, a horse or a cow.
- It says nothing about the slope of the curve. Two agents with the same LD50 may differ sharply in how close the lethal dose is to a harmless one.

The related ideas are the **NOAEL** (no observed adverse effect level) and the **margin of safety**, which compare the dose that causes harm with the dose that is intended or likely.

Acute, sub-acute and chronic toxicity

Toxicity is classified by how long exposure lasts and how quickly signs appear.

- **Acute toxicity** follows a single exposure or several within a day. Signs are usually fast. Acute studies give the signs, target organs and the approximate lethal range, and help to choose doses for longer studies.

- **Sub-acute (repeat-dose short-term) toxicity** follows daily exposure for a few weeks. It shows target organs, effects on blood and chemistry values, and a first estimate of a no-effect level.
- **Sub-chronic and chronic toxicity** follow exposure for months to most of the animal's life. They detect cumulative harm, organ damage, effects on growth and reproduction, and cancer. Chronic data underlie decisions on residues in food, such as the acceptable daily intake used to set maximum residue limits. Indian limits are notified by the regulator and change over time, so check the current notification.

Cumulative poisons such as lead and fluoride build up until a threshold is crossed, so chronic cases have a vague history.

Decontamination, supportive care and antidotes

Treatment follows a sequence: stabilise first, then reduce further absorption, then speed elimination, then give a specific antidote if one exists.

Stabilise. Airway, breathing, circulation, seizure control, temperature and fluid balance come before anything else. Supportive care is often the most important part of treatment, because most poisons have no antidote.

Decontamination. The aim is to reduce the amount that reaches the blood.

- *Skin and coat:* wash with water and mild detergent, with the handler wearing gloves, so the animal does not keep absorbing the agent or lick it off.
- *Eye:* flush with clean water or saline.
- *Gut:* emptying the stomach by induced vomiting helps only if done soon after a recent ingestion and the animal is alert. It is wrong in an animal that is convulsing, depressed or unable to protect its airway, after corrosives, and after some petroleum products, because of the risk of aspiration or further injury. Some species, such as horses and ruminants, cannot vomit effectively. In ruminants rumen lavage or rumenotomy may be considered for a large recent load.
- *Adsorbents:* activated charcoal binds many poisons in the gut and prevents absorption. It is less useful for alcohols, metals and corrosives. It carries a risk in animals that are depressed or vomiting.

Enhancing elimination uses fluid diuresis, repeated charcoal for poisons that recirculate in bile, and dialysis in referral centres.

Antidotes. An antidote works by one of a few logical routes: blocking the receptor (atropine against muscarinic over-stimulation), reactivating the enzyme (oximes), binding the poison (chelators for metals), supplying the missing substance (vitamin K_1 for anticoagulant rodenticides), or blocking harmful metabolism (fomepizole for ethylene glycol in dogs). An antidote must match the mechanism, and it does not replace supportive care.

History, examination and urgent help

A careful history often identifies the poison before any laboratory test. Ask in a structured way.

1. What species, age, weight and how many animals are affected, and how many are healthy?
2. What was the possible source: feed, water, pasture, plants, pesticides, drugs, household products, rodent baits, snakebite?
3. When did exposure happen, and by what route? How long between exposure and first signs?
4. Any recent change in feed, dipping, spraying, pasture or new medicines? Were the dosing or dilution instructions followed?
5. What treatment has already been given by the owner, such as home remedies or induced vomiting?

Ask to see the container or label and record the active ingredient, not just the trade name. Keep the packaging, because many brands share an active ingredient.

Examine for patterns: pupils, salivation, tremor, gait, heart rate, temperature, gum colour, breath odour and urine. Collect samples *before* treatment where possible: vomit or stomach contents, feed, water, blood, urine, and tissues at post-mortem.

Seek urgent help from a poison information service, veterinary college toxicology unit or senior colleague when the agent is unknown, when several animals are affected, when signs are progressing, or when human exposure is possible. Protect yourself and the owner while handling contaminated animals.

Concept cleared

Bioactivation

Some poisons are harmless until the liver converts them to an active product. In such cases the liver is the site where toxicity begins, so liver function and species enzyme differences change the outcome.

Threshold and the log dose-response curve

Below a threshold the body's defences cope. Above it the proportion of animals affected rises in an S-shaped curve against log dose. The slope matters as much as the LD50.

Stabilise before decontaminate

A seizing, hypoxic or shocked animal needs airway, circulation and seizure control first. Decontamination that is started too early can itself cause harm, such as aspiration.

Antidote matches mechanism

Antidotes act by blocking a receptor, reactivating an enzyme, binding the poison, replacing a missing factor or blocking toxic metabolism. Without a known mechanism, treatment stays supportive.

Memory aid: Order of treatment: SDEA

Stabilise, Decontaminate, Enhance elimination, Antidote. Think of the order when a poisoned animal arrives, and add history-taking running alongside all four.

Compare and contrast

Acute, sub-acute and chronic toxicity

Feature	Acute	Sub-acute	Chronic
Exposure	Single or within 24 hours	Repeated for some weeks	Months to much of a lifetime
Main aim	Signs, target organs, lethal range	Target organs, early no-effect level	Cumulative damage, cancer, reproduction
Typical use	Labelling and dose selection	Planning longer studies	Residue and safe-intake decisions

Toxicant and toxin

Term	Meaning	Example
Toxicant	Any substance that causes harm	Organophosphate, lead, copper
Toxin	Harmful product of a living organism	Snake venom, aflatoxin, botulinum toxin
Antidote	Agent that counteracts a specific poison	Atropine, vitamin K1, fomepizole

Species notes

Cats

Poor glucuronidation makes cats sensitive to phenols, some drugs and many topical products meant for dogs. Grooming increases oral exposure after skin contact.

Dogs

Scavenging behaviour makes dogs the commonest victims of baits, household chemicals and discarded food. They vomit readily, so emesis is an option only within the right time and condition limits.

Cattle and buffalo

The rumen slows absorption of some poisons, dilutes them, and can also convert some compounds into more toxic ones. Vomiting is not possible,

Horses

Horses cannot vomit and have a delicate gut, so colic and ileus complicate many poisonings. Stomach tube and charcoal are the usual decontamination route.

so rumen lavage may be needed for a recent large intake.

Poultry
Birds are exposed through feed and water, and signs appear in the whole flock. Flock-level history and feed testing are essential.

Clinical pearls

Self-test: 10 questions

1. Which statement about LD50 is correct?

LD50 is a lethality measure for a specific species and route. It does not describe sublethal or chronic effects.

2. Bioactivation means that:

Metabolism can produce a more toxic compound, for example conversion of phosphorothioates to oxons.

3. Cats are particularly sensitive to many phenolic compounds because they:

Deficient glucuronide conjugation slows elimination of phenols and some drugs in cats.

4. Inducing vomiting is inappropriate in which situation?

A convulsing or depressed animal cannot protect its airway, so vomiting risks aspiration.

5. The first priority in a poisoned, collapsing animal is:

Life-support measures come before decontamination and specific therapy.

6. Repeated doses of activated charcoal are most logical for poisons that:

Charcoal in the gut binds poison re-secreted in bile and prevents reabsorption.

7. A 'threshold' in a dose-response relationship means:

Below threshold, body defences cope and no measurable effect occurs for many toxic endpoints.

8. Which study type is mainly used to detect cancer and cumulative damage?

Chronic studies, covering months to much of the lifespan, are designed to find cumulative and late effects.

9. Vitamin K1 is an antidote that works by:

Anticoagulant rodenticides block vitamin K recycling, and vitamin K1 restores the pathway.

10. Which action is most useful in history taking?

Active ingredient, timing, route and group pattern guide diagnosis and treatment, and the container helps confirm the agent.

Key points to revise

1. Toxicity depends on agent, dose, route, duration and the animal's own characteristics.
2. Toxicokinetics covers absorption, distribution, biotransformation and excretion.
3. Bioactivation can make a compound more toxic after metabolism.

4. The dose-response curve is S-shaped against log dose and many effects have a threshold.
5. LD50 measures lethality only and is species and route specific.
6. Acute, sub-acute and chronic studies answer different questions about toxicity.
7. Treatment order: stabilise, decontaminate, enhance elimination, give antidote if available.
8. A structured history, label and sample collection often identify the poison.

Go deeper on this site

- Ch 2. Organophosphate and carbamate poisoning (in this book)
- Ch 3. Pyrethroid, amitraz and other insecticide poisoning (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Overview of Veterinary Toxicology
- Merck Veterinary Manual: Introduction to Poisoning (pet owner version)
- ASPCA Animal Poison Control

CHAPTER 2 OF 17

Organophosphate and carbamate poisoning

Organophosphates and carbamates inhibit acetylcholinesterase and cause cholinergic overstimulation. The chapter explains the mechanism, the muscarinic, nicotinic and central signs, the logic of atropine and oxime treatment, species differences and prevention.

After this chapter you can

- Explain how organophosphates and carbamates inhibit acetylcholinesterase and why acetylcholine accumulates
- Recognise muscarinic, nicotinic and central nervous signs of poisoning

- Explain why atropine and oximes are used and what each can and cannot reverse
- Describe differences between organophosphates and carbamates, and between species
- List practical prevention measures and know when to seek urgent help

Why these insecticides matter

Organophosphates (OP) and carbamates are among the most widely used insecticides, acaricides and ectoparasiticides in farming and household pest control. They are also among the commonest causes of poisoning in Indian dogs, cattle and buffalo, because they are cheap, easy to buy and often stored carelessly or applied at the wrong dilution.

Both groups act on the same enzyme. Understanding one enzyme and one neurotransmitter explains nearly every sign, the logic of the antidotes, and why the two groups behave a little differently in the clinic.

Mechanism of toxicity

Acetylcholine (ACh) is released at parasympathetic nerve endings, at the neuromuscular junction, at autonomic ganglia and at many sites in the brain. Its action is normally stopped within a fraction of a second by **acetylcholinesterase** (AChE), which splits it into choline and acetate.

OP and carbamate compounds attach to the active site of AChE and block it. ACh then accumulates and keeps stimulating its receptors. The result is continuous overstimulation, known as a **cholinergic crisis**.

- **Organophosphates** phosphorylate the enzyme. The bond is very stable and is broken down only very slowly, so inhibition is effectively irreversible. In time the inhibited enzyme undergoes **aging**, a loss of a chemical group that makes the bond permanent. After aging the enzyme cannot be reactivated, and recovery depends on making new enzyme.
- **Carbamates** carbamylate the enzyme. This bond breaks down much sooner, so inhibition is reversible and signs are usually shorter and often milder.

Many OPs, such as the phosphorothioates, are inactive until the liver converts them to the oxon form. This explains why signs may be delayed by some hours after exposure, especially after skin contact, and why the liver's enzyme activity affects the severity.

Routes of exposure include ingestion of baits, treated seed or contaminated feed, skin absorption from dips, sprays and pour-ons, and inhalation. Overdosing or wrong dilution of a veterinary product is a frequent cause in practice.

Clinical signs

Signs fall into three groups, depending on which receptor is overstimulated.

- **Muscarinic** (parasympathetic): salivation, lacrimation, urination, defaecation, vomiting, colic and diarrhoea, bronchial secretion and bronchoconstriction, slow heart rate and constricted pupils. Death usually results from respiratory failure caused by fluid in the airways and bronchospasm.
- **Nicotinic** (neuromuscular junction and ganglia): muscle fasciculations and tremors, then weakness and paralysis. Overstimulation keeps the end-plate depolarised, so the muscle stops responding. Heart rate may rise instead of fall, because ganglia are also stimulated.
- **Central:** restlessness, ataxia, depression, seizures and coma.

Students often remember the muscarinic signs with the word *SLUDGE* or *DUMBELS*. A common confusion is to expect every case to show miosis and a slow heart rate. Pupils and heart rate can be misleading because of nicotinic effects. Look at the whole pattern: wetness, tremor and respiratory distress together point strongly to this poisoning.

Onset may be acute, within minutes to a few hours. Some OPs also cause an **intermediate syndrome** some days later, with weakness of neck and limb muscles, and certain compounds cause **delayed neuropathy**, which damages nerves and appears one to three weeks after exposure. Poultry are the classic model for delayed neuropathy.

Diagnosis

Diagnosis rests on history of exposure, the typical combination of signs and response to treatment. Laboratory support includes measuring **cholinesterase**

activity in whole blood or in brain tissue after death. A marked fall supports the diagnosis, but red cell and plasma enzyme levels vary by species, and carbamate inhibition can reverse in a stored sample, so interpret with care. Identification of the compound in stomach contents, feed or bait is the most reliable confirmation. Many OP signs mimic other conditions such as heat stress, snake or scorpion envenomation and other causes of colic.

Treatment: decontamination, atropine and oximes

Treatment aims to protect the airway, reduce further absorption, block the effects of excess ACh and, for OPs, reactivate the enzyme.

Decontamination. Wash the skin and coat thoroughly, with gloves on, for dermal exposure. For recent ingestion, activated charcoal is used and emesis is not suitable when the animal is convulsing, depressed or secreting heavily. In ruminants, rumen lavage may be considered after a large recent intake.

Atropine is a competitive antagonist at *muscarinic* receptors. It reverses secretions, bronchospasm and slow heart rate, which are the signs that kill. The end point is judged by drying of bronchial secretions and improved breathing, not by pupil size or heart rate alone. Atropine does *not* act on nicotinic receptors, so tremors and muscle weakness continue. It also does not reactivate AChE. Over-treatment causes atropine toxicity, with dry mouth, tachycardia and, in horses and ruminants, ileus. Dose by a veterinary reference or the clinician in charge.

Oximes such as pralidoxime attach to the phosphorylated enzyme and pull the OP group off, restoring the enzyme. They are the only treatment that acts on nicotinic signs. Oximes work only *before aging*, so they are most useful early. They are less useful in carbamate poisoning because carbamylated enzyme recovers spontaneously, and some authorities advise caution with certain carbamates. Oximes enter the brain poorly, so they help mainly at the muscle and peripheral sites.

Supportive care includes oxygen, airway suction, fluids, and seizure control. Drugs that worsen cholinesterase inhibition, such as some muscle relaxants and phenothiazine tranquillisers, are avoided. Check a current veterinary pharmacology reference for the precise list. Animals may need support for days with OPs, because recovery depends on regenerating the enzyme.

Species differences and prevention

Sensitivity varies with species, with the particular compound, and with the product formulation. Cats and young animals are generally more sensitive. Cats are the species most often affected by dog flea and tick products used wrongly, and some OP compounds are far more dangerous in cats than in dogs. Horses show colic and ileus early. Ruminants show salivation, diarrhoea and tremor, and sudden death can occur after dips or sprays used incorrectly. Birds, fish and bees are very sensitive to many compounds, which matters for wildlife and for the environment.

Prevention is the most effective step.

- Use only products labelled for the species, follow the label for dilution and interval, and do not apply dog products to cats.
- Do not combine OP products with other cholinesterase inhibitors, including some dewormers, in the same animal at the same time.
- Store pesticides in original labelled containers, away from feed, water and children. Never reuse empty containers.
- Keep animals off sprayed pasture and crops for the interval stated on the label, and observe the withdrawal periods for milk and meat. Indian rules on banned or restricted pesticides and maximum residue limits are updated from time to time, so check the current notification.
- Wear gloves and protective clothing when dipping, and wash hands after use. Human exposure is a real risk for the farmer and the veterinarian.

Seek urgent help from a poison information service or a senior veterinarian when there is respiratory distress, seizures or multiple animals, or when a person has also been exposed.

Concept cleared

Cholinergic overstimulation

AChE normally ends the acetylcholine signal. When it is inhibited, acetylcholine builds up at muscarinic, nicotinic and central synapses, and all signs follow from that single change.

Aging of the enzyme

After a period, the phosphorylated enzyme loses a chemical group and becomes permanently inactive. Oximes work only before this happens, which is why early treatment matters.

Atropine limits

Atropine blocks muscarinic receptors only. It controls secretions and bronchospasm but does nothing for muscle tremors or paralysis and does not restore the enzyme.

Reversible and irreversible inhibition

Carbamates form a bond that breaks within hours, so recovery is relatively quick. OPs form a stable bond, and recovery depends on reactivation or new enzyme synthesis.

Memory aid: DUMBELS

Diarrhoea, Urination, Miosis, Bronchospasm and bronchorrhoea, Emesis, Lacrimation, Salivation. These are the muscarinic signs. Remember that tremor and weakness are nicotinic and need separate thought.

Compare and contrast

Organophosphates and carbamates

Feature	Organophosphate	Carbamate
Bond with AChE	Phosphorylation, very stable, aging	Carbamylation, spontaneous recovery
Duration	Long, days	Shorter, hours
Oxime use	Useful early, before aging	Often unnecessary, caution with some agents
Delayed neuropathy	Possible with some compounds	Not typical

Atropine and pralidoxime

Feature	Atropine	Pralidoxime
Action	Blocks muscarinic receptors	Reactivates phosphorylated AChE
Reverses	Salivation, bronchospasm, bradycardia	Nicotinic signs such as weakness, plus enzyme function
Limitation	No effect on muscle tremors	Fails after aging, poor brain entry
Main end point	Dry airway secretions, better breathing	Improved muscle strength

Species notes

Dogs

Commonly poisoned by baits, spilled concentrates and wrong use of dips. Salivation, vomiting, diarrhoea, tremor and seizures are typical. Breeds with the MDR1 mutation need extra care with some other drugs used in treatment, so check the current reference.

Cats

Particularly sensitive to many OP compounds, and exposed through grooming after skin application of dog products or flea sprays. Weakness and tremor may stand out more than wetness.

Cattle and buffalo

Poisoned by dips, sprays, treated seed and contaminated fodder. Salivation, diarrhoea, tremor, laboured breathing and sudden death are seen. Milk and meat residues are a food safety issue.

Horses

Colic and ileus appear early. Atropine must be used cautiously because it slows the gut and may worsen colic.

Poultry

Flocks show weakness, diarrhoea, and paralysis. Some compounds cause delayed neuropathy, with

weakness days later, and birds are used as the test model for this.

Clinical pearls

Self-test: 10 questions

1. The primary enzyme inhibited by OP and carbamate insecticides is:

Inhibition of acetylcholinesterase leads to accumulation of acetylcholine.

2. Which sign is mediated by nicotinic receptors?

Fasciculations and weakness arise at the neuromuscular junction, which has nicotinic receptors.

3. Atropine in OP poisoning is mainly effective against:

Atropine blocks muscarinic receptors but does not affect nicotinic receptors or the enzyme.

4. Aging of phosphorylated acetylcholinesterase means:

After aging the bond becomes permanent, so oximes no longer help.

5. Compared with OPs, carbamate inhibition of AChE is:

Carbamylated enzyme hydrolyses spontaneously within hours.

6. The best end point for atropine therapy is:

Bronchial secretion and bronchospasm cause death, so airway drying is the clinical goal.

7. Which statement about oximes is correct?

Oximes restore enzyme and improve muscle function but do not replace atropine.

8. A species in which atropine must be used cautiously because of ileus is the:

Atropine reduces gut motility and can worsen colic in horses.

9. Delayed neuropathy after certain OPs is best demonstrated in:

Hens are the classical test species for delayed OP neuropathy.

10. Which prevention step is correct?

Correct product use, labelled storage and observing withdrawal periods protect animals, handlers and food.

Key points to revise

1. OPs and carbamates inhibit acetylcholinesterase and cause cholinergic crisis.
2. OP inhibition is long lasting and can age, while carbamate inhibition is reversible.
3. Signs are muscarinic, nicotinic and central.
4. Respiratory failure is the usual cause of death.
5. Atropine blocks muscarinic effects only.
6. Oximes reactivate phosphorylated enzyme and work best early.
7. Cats, young animals and horses need special care.
8. Prevention depends on correct product, label use, storage, and protection of handlers.

Go deeper on this site

- Ch 3. Pyrethroid, amitraz and other insecticide poisoning (in this book)
- Ch 1. General principles of toxicology (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Overview of Veterinary Toxicology
- Merck Veterinary Manual: Introduction to Poisoning (pet owner version)
- ASPCA Animal Poison Control

CHAPTER 3 OF 17

Pyrethroid, amitraz and other insecticide poisoning

Pyrethrins and pyrethroids, amitraz and the isoxazoline class are widely used ectoparasiticides with very different mechanisms. The chapter covers their toxicity, with emphasis on cat pyrethrin poisoning, amitraz in dogs and horses, and cautions with isoxazolines.

After this chapter you can

- Explain how pyrethrins and pyrethroids act on sodium channels and why cats are at special risk
- Describe the mechanism and signs of amitraz toxicity in dogs and why horses are particularly vulnerable
- Explain how isoxazolines work and why caution is advised in animals with a seizure history
- Apply decontamination, supportive care and antidote reasoning to these poisonings
- List prevention measures and know when to seek urgent help

Three groups, three mechanisms

Modern flea, tick and mite products rely on compounds that are far more toxic to insects and mites than to mammals. That selectivity is not complete. Poisoning

occurs when the wrong species is treated, when the dose is not matched to body weight, when products are used together, or when animals groom or lick treated coats.

This chapter deals with three groups that are unrelated in mechanism: **pyrethrins and pyrethroids** (sodium channel modifiers), **amitraz** (an alpha-2 adrenergic agonist) and the **isoxazolines** (inhibitors of ligand-gated chloride channels). Organophosphates and carbamates were covered in the previous chapter.

Pyrethrins and pyrethroids

Pyrethrins are natural extracts of chrysanthemum flowers. **Pyrethroids** such as permethrin, cypermethrin, deltamethrin and flumethrin are synthetic and more stable. They are used on dogs, cattle, buffalo, sheep and goats, in sprays, dips, ear tags, collars and spot-on products, and as household insecticides.

Mechanism. They bind to voltage-gated sodium channels in nerve membranes and keep them open for longer than normal. Nerve cells fire repeatedly, giving tremor, hyperexcitability and, with strong exposure, seizures. Type II compounds that contain a cyano group, such as cypermethrin and deltamethrin, produce a more severe syndrome with salivation and choreoathetosis, a writhing movement. Type I compounds, such as permethrin, cause mainly tremor, often called the T syndrome.

Mammals are protected because they have a higher body temperature, which speeds closing of the channel, and efficient breakdown by esterases and liver enzymes. Mammalian toxicity is therefore low in healthy animals when used as labelled.

Why cats are at risk. Cats are poor at glucuronidation, one of the main routes of pyrethroid metabolism, so permethrin lingers. Many cat poisonings come from the owner placing a concentrated dog spot-on product on a cat, or from a cat living with a recently treated dog and grooming it. Signs begin within hours and include hypersalivation, ear and skin twitching, tremor, ataxia, hyperthermia, seizures, and in severe cases death. Cats are more sensitive than dogs, and young, small or debilitated animals are at greater risk.

Dogs and other species usually show milder tremor, salivation and vomiting after an overdose or ingestion. Fish and bees are extremely sensitive, so dips must not be discharged into ponds.

Treatment of pyrethroid poisoning

There is no specific antidote, so treatment is decontamination and supportive care.

- **Skin:** bathe with lukewarm water and a mild liquid detergent, with gloves. Cold water may cause chilling and hot water increases absorption. Prevent the animal from licking the coat.
- **Tremor and seizures:** centrally acting muscle relaxants such as methocarbamol are commonly used for tremor. Benzodiazepines or other anticonvulsants may be added for seizures. Dose by a current veterinary reference.
- **Temperature:** cool the hyperthermic animal gradually and warm the hypothermic one. Provide fluids, and maintain breathing.
- Emesis is considered only for recent ingestion in an alert animal and is avoided when tremor or seizures are present.

Intravenous lipid emulsion is used for severe cases in some centres, but the evidence is limited, so treat it as an option to discuss with a specialist. Because pyrethroids are broken down fairly quickly, most animals recover with good care within a few days.

Do not confuse pyrethroid tremor with organophosphate poisoning. Pyrethroids do not inhibit cholinesterase, and atropine is not the treatment.

Amitraz

Amitraz is a formamidine acaricide used in dips and sprays for ticks and mites, for example in demodectic mange treatment in some regions and in livestock tick control. It is also used as a collar in some countries.

Mechanism. Amitraz and its metabolite act as agonists at **alpha-2 adrenergic receptors**, the same receptors targeted by xylazine and medetomidine. It also has weak monoamine oxidase inhibiting action and effects on octopamine receptors in the mite. Alpha-2 stimulation causes sedation, bradycardia, low blood pressure, reduced gut motility and raised blood glucose, because insulin release is suppressed.

Dogs. Common causes are overdose or wrong dilution of a dip, ingestion of a collar, and licking of treated coats. Signs are depression, ataxia, slow heart rate, hypotension, low body temperature, vomiting, mydriasis, hyperglycaemia and in

severe cases coma. Signs often resolve within a day or two. Small dogs are at higher risk of overdose.

Horses. Horses are very sensitive. Amitraz is not intended for use on equids. Exposure causes marked reduction of gut motility, colic, impaction and sometimes death. The label cautions should be treated as a warning against any use in horses. Ponies, donkeys and foals should be treated with the same caution.

Ruminants are relatively tolerant of properly used products, but sedation and ruminal stasis can occur after overdose. Observe label withdrawal periods for milk and meat, and check current Indian regulations.

Treatment. Decontaminate the skin by bathing and prevent grooming. Alpha-2 antagonists such as atipamezole or yohimbine reverse the sedation and bradycardia and are the antidote logic here, because they compete for the same receptor. In a bradycardic animal, anticholinergic drugs are used with caution because they can raise blood pressure and cause tachycardia, so seek veterinary advice. Monitor heart rate, blood pressure, temperature, blood glucose and gut function. Horses need colic assessment and gut support.

Isoxazolines and other products

Isoxazolines are oral or topical compounds, among them fluralaner, afoxolaner, sarolaner and lotilaner, given to dogs and cats for fleas, ticks and mites. They inhibit insect and mite ligand-gated chloride channels, particularly the GABA-gated ones, so the parasite shows uncontrolled excitation and dies. Binding to the mammalian receptor is much weaker, giving a wide safety margin in most animals.

Regulators, including the United States FDA, have issued cautions that some animals given isoxazolines have shown neurologic signs such as muscle tremor, ataxia and seizures. The cautions advise **care in animals with a history of seizures or epilepsy**. The product label and the current regulatory statement should be checked before prescribing, because wording can change. Reasonable practice is to ask about neurological history, discuss alternatives for such animals, and tell owners what to watch for. Signs when seen are usually managed with supportive care and, if needed, seizure control.

A common confusion is to assume that isoxazolines act on the same channel as pyrethroids, or that they are organophosphates. They are not. They share an effect

on the nervous system but through different targets, so the antidote logic differs.

Other products. Macrocyclic lactones such as ivermectin act on glutamate-gated chloride channels in parasites. Dogs with the MDR1 mutation are at risk of neurotoxicity because less drug is pumped out of the brain, so products for such animals need extra care. Never use fipronil, imidacloprid or similar spot-ons in rabbits or other species not named on the label without advice.

Prevention and urgent help

Prevention for all these groups: use species-specific labelled products, calculate by body weight, avoid overlapping products, separate treated dogs from cats until dry, store products out of reach, wash hands and keep children away from freshly treated animals. Contact a poison information service or specialist promptly for cats with tremor, any seizing animal, horses exposed to amitraz, or any large ingestion.

Concept cleared

Sodium channel prolongation
Pyrethrins and pyrethroids keep voltage-gated sodium channels open, so nerves fire repeatedly. The outcome is tremor, hyperexcitability and seizures, rather than cholinergic wetness.

Cat glucuronidation gap
Cats lack efficient glucuronidation, so permethrin is removed slowly. A dog spot-on applied to a cat is the classic cause of severe tremor and seizures.

Alpha-2 agonism by amitraz
Amitraz acts at the same alpha-2 receptor as xylazine, producing sedation, bradycardia, ileus and hyperglycaemia. Alpha-2 antagonists such as atipamezole reverse these effects.

Selectivity is relative

Isoxazolines bind insect and mite chloride channels more strongly than mammalian ones, but in animals with a seizure tendency the margin may be smaller, so caution is advised.

Memory aid: Match the pattern

Wet and weak means cholinesterase inhibitor. Twitchy and hot means pyrethroid. Sleepy and slow with high glucose means amitraz. Seizure in a treated epileptic means think isoxazoline.

Compare and contrast

Mechanism and clinical picture

Group	Target	Typical signs	Key treatment idea
Pyrethroids	Voltage-gated sodium channel kept open	Tremor, salivation, hyperthermia, seizures	Bathe, muscle relaxant, supportive care
Amitraz	Alpha-2 receptor agonist	Sedation, bradycardia, ileus, hyperglycaemia	Bathe, alpha-2 antagonist, monitor
Isoxazolines	Parasite GABA-gated chloride channel	Rare tremor, ataxia, seizures	Supportive care, caution with seizure history
OP and carbamates	Acetylcholinesterase	Wetness, tremor, respiratory distress	Atropine, oxime for OPs

Species susceptibility

Agent	More vulnerable species	Reason
Permethrin	Cats	Poor glucuronidation, grooming
Amitraz	Horses and ponies	Marked effect on gut motility
Isoxazolines	Animals with seizure history	Possible lowering of seizure threshold
Pyrethroids	Fish, bees	High sensitivity to low concentrations

Species notes

Cats

Highest risk for pyrethroid poisoning, especially from dog spot-ons. Tremor, salivation, hyperthermia and seizures need prompt decontamination and muscle relaxant therapy. Seek urgent help.

Dogs

Amitraz overdose and collar ingestion cause sedation and bradycardia. Small dogs are at higher risk of overdose. MDR1 breeds need care with macrocyclic lactones.

Horses

Amitraz is dangerous, with ileus, colic and impaction. Do not use products labelled for other species on horses.

Cattle, buffalo, sheep and goats

Pyrethroid sprays, pour-ons and dips are common, and mistakes in dilution cause toxicity. Observe milk and meat withdrawal periods, and check current Indian notification.

Rabbits and small mammals

Many ectoparasiticides for dogs are unsafe in these species, so use only products and doses specified for them.

Clinical pearls

Self-test: 10 questions

1. Pyrethroids toxicity arises mainly from:

Pyrethroids keep sodium channels open, leading to repetitive nerve firing and tremor.

2. Which species is at greatest risk from dog spot-on permethrin products?

Cats metabolise pyrethroids slowly because they lack effective glucuronidation.

3. A suitable drug logic for pyrethroid tremor is:

Pyrethroid tremor is central and is treated with muscle relaxants. Atropine and oximes are for cholinesterase inhibitors.

4. Amitraz acts as an agonist at:

Amitraz and its metabolite stimulate alpha-2 receptors, similar to xylazine.

5. Which sign is typical of amitraz toxicity in a dog?

Alpha-2 stimulation causes sedation, bradycardia and suppressed insulin release.

6. Why is amitraz dangerous in horses?

Alpha-2 effects on the equine gut can produce ileus, colic and impaction.

7. The antidote logic for amitraz poisoning uses:

Competitive antagonists at the alpha-2 receptor reverse the sedation and bradycardia.

8. Isoxazolines act on:

They inhibit parasite chloride channels. This differs from pyrethroids and organophosphates.

9. A caution advised by regulators for isoxazoline products concerns animals with:

Neurologic adverse events such as tremor and seizures were reported, so care is advised in animals with seizure history.

10. Which decontamination step is correct for a cat with dermal pyrethroid exposure?

Washing reduces ongoing absorption and licking. Alcohol and hot water can worsen absorption.

Key points to revise

1. Pyrethroids prolong opening of sodium channels in nerve membranes.
2. Type II pyrethroids with a cyano group cause salivation and more severe signs.
3. Cats are especially sensitive to permethrin because of poor glucuronidation.
4. Pyrethroid treatment is decontamination and supportive care with muscle relaxants.
5. Amitraz is an alpha-2 agonist with sedation, bradycardia and ileus.
6. Horses are very sensitive to amitraz, so avoid use.
7. Isoxazolines inhibit parasite GABA-gated chloride channels, with caution in seizure history.
8. Prevention relies on species-specific labelled use and correct dosing by weight.

Go deeper on this site

- Ch 4. Rodenticide poisoning (in this book)
- Ch 2. Organophosphate and carbamate poisoning (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Overview of Veterinary Toxicology
- Merck Veterinary Manual: Introduction to Poisoning (pet owner version)
- ASPCA Animal Poison Control

CHAPTER 4 OF 17

Rodenticide poisoning

Rodenticides are the commonest household poisons met in small-animal practice. This chapter links each group (anticoagulants, zinc phosphide, cholecalciferol, bromethalin, strychnine) to its mechanism, so that signs, timing, antidote and monitoring follow logically.

After this chapter you can

- Explain how anticoagulant rodenticides cause delayed bleeding and why vitamin K1 reverses it
- Describe why zinc phosphide releases phosphine gas and what this means for decontamination and staff safety
- Explain how cholecalciferol causes hypercalcaemia and kidney injury
- Describe the mechanism of bromethalin and strychnine and why no simple antidote exists for bromethalin
- Apply an approach to an unknown rodenticide exposure: history, decontamination, monitoring and when to seek urgent help

Why rodenticides are a veterinary problem

Rodenticides are made to kill mammals, and dogs, cats, pigs, poultry and wildlife are mammals or eat poisoned rodents. Most cases are accidental: a dog eats bait left in a house or godown, a cat eats a poisoned rat, or a farm animal reaches stored grain mixed with bait. Malicious baiting of dogs also occurs, especially with strychnine.

The first task is to learn **which product** was used. Many baits look alike (coloured grain, wax blocks, pellets) but the groups differ in mechanism, in time to onset and in antidote. Ask for the packet or its active ingredient. If it cannot be identified, treat as an unknown exposure and decontaminate, then monitor for all the main groups.

Merck's veterinary overview notes that use has been shifting from anticoagulants towards bromethalin and cholecalciferol in some countries, so an old assumption that every bait is an anticoagulant is unsafe.

Anticoagulant rodenticides

Clotting factors II, VII, IX and X need vitamin K to become active. During activation vitamin K is oxidised to an epoxide, and the enzyme **vitamin K epoxide reductase (VKORC1)** recycles it back. Anticoagulants such as warfarin, coumatetralyl, bromadiolone and brodifacoum block this enzyme. The liver keeps making factors, but they are inactive.

Signs are **delayed** because factors already in blood keep working until they are used up. Factor VII has the shortest half-life, so the prothrombin time (PT) rises first, usually within a day or two, while bleeding appears after several days. Animals present with lethargy, pale gums, breathlessness (bleeding into the chest or lungs), haematomas, nose bleeds, blood in faeces or sudden weakness. The animal is often seen only when bleeding has started.

First-generation compounds (warfarin) act for a short time and often need repeated feeding. **Second-generation** compounds (brodifacoum, bromadiolone, difethialone) are potent, stay long in the liver and may be lethal after a single feed. Their effect lasts weeks, so treatment is long.

Antidote and monitoring. The antidote is **vitamin K1 (phytonadione)**, which supplies active vitamin K and bypasses the blocked enzyme. A common confusion is vitamin K3 (menadione), which is not an adequate substitute. Oral K1 is absorbed better with fat in the meal. Because second-generation agents persist, treatment continues for weeks. PT is measured before treatment, during it, and again a few days after the last dose to confirm that clotting does not fall back. Severe bleeding needs plasma or whole blood, which gives factors at once, because vitamin K takes many hours to act. Avoid unnecessary needle sticks and jugular puncture in bleeding patients.

Early decontamination (induced vomiting if recent and safe, activated charcoal) is useful. Treating after a known ingestion, before signs appear, is easier than treating bleeding. **Secondary poisoning** of dogs, cats and raptors that eat poisoned rodents is possible, mainly with second-generation products.

Zinc phosphide (and related phosphides)

Zinc phosphide is a grey-black powder in baits. Its own toxicity is small until it meets **stomach acid**, which converts it into **phosphine gas**. Phosphine inhibits cellular respiration and damages the gut, liver, kidney, lungs and heart. A full stomach with high acid output produces more gas, and signs begin within hours.

Signs include vomiting (the vomit may smell of garlic or fish), abdominal pain, restlessness, rapid breathing, collapse and sometimes convulsions. There is **no specific antidote**; treatment is decontamination and supportive care. Concepts that matter: keep the stomach less acidic with antacids so that less gas forms; control seizures; support circulation and breathing; and protect staff. Vomitus and stomach contents give off phosphine, so handle them in a ventilated area, not in a closed room.

Aluminium and magnesium phosphide, sold as grain fumigant tablets, act in the same way and release gas on contact with moisture. They are far more dangerous and are a frequent cause of human and animal deaths in India. Check the current notification and local rules on their sale and storage.

Cholecalciferol (vitamin D3)

Cholecalciferol baits do not look dangerous, because vitamin D is a vitamin. In large amounts, however, it is converted to active metabolites that raise calcium absorption and release from bone. The result is **hypercalcaemia and hyperphosphataemia**. Calcium and phosphorus deposit in soft tissues (**mineralisation**) of the kidney, heart, stomach and blood vessels, and the kidneys fail.

Signs are **delayed**, often a day or more after ingestion: vomiting, loss of appetite, excessive drinking and urination, weakness, then signs of acute kidney injury. The common confusion is that the animal looks well on the first day. Monitoring of serum calcium, phosphorus, urea and creatinine is continued for several days even if signs are absent.

Treatment concepts: early decontamination; intravenous fluids to protect the kidney and increase calcium loss in urine; drugs that lower calcium or block bone release (such as calcitonin or bisphosphonates, used under specialist advice); and low-

calcium, low-vitamin-D diet. Recovery can take weeks because vitamin D is stored in fat. Calcium-containing products and vitamin D supplements must be avoided.

Bromethalin

Bromethalin is a neurotoxin. It is converted to a metabolite that **uncouples oxidative phosphorylation** in brain mitochondria. ATP falls, the sodium-potassium pump fails, fluid collects between the myelin layers and the brain and spinal cord swell. Higher doses give an **acute convulsive form** with tremors, hyperexcitability, seizures and death. Lower doses give a **delayed paralytic form** with hindlimb weakness, ataxia, depression and recumbency over days. Cats are especially sensitive.

Merck's manual states plainly that **no antidote exists** for bromethalin. Everything depends on early decontamination and repeated activated charcoal under veterinary advice, plus supportive care, seizure control and nursing. Any pet that may have eaten a bromethalin bait, including a cat, should reach a clinic quickly, before signs begin.

Strychnine and the overall approach

Strychnine blocks **glycine**, the inhibitory transmitter of the spinal cord. Without inhibition, motor neurons fire freely. The animal shows muscle stiffness, an extended posture with arched neck (opisthotonos), and violent seizures set off by touch, light or sound, while it remains **conscious** and in distress. Death comes from exhausted or paralysed breathing muscles. Signs start within a few hours of ingestion. Dogs are the usual victims, often through malicious baiting.

Treatment concepts: control the seizures first (muscle relaxants such as methocarbamol, or sedatives), keep the animal in a quiet, dark place and handle it minimally, then decontaminate once it is stable, and support breathing. Sampling of stomach contents and tissue helps a legal case. Check the current notification on the status of strychnine in India.

Approach to any rodenticide exposure: find the product and time; decontaminate early if safe; do not induce vomiting in a convulsing or already weak animal; arrange monitoring for the likely group; keep baits where pets and livestock cannot reach them; use bait stations; and collect dead rodents. **Seek urgent help** for any

pet with known bromethalin, cholecalciferol or phosphide exposure, any animal with bleeding, tremors or seizures, or when the product is unknown.

Concept cleared

Concept cleared: Delayed bleeding
Think of a shop that stops getting new stock. Shelves look full for a few days because of what is already inside. Only when old stock is used up do shelves empty. Anticoagulants stop new active clotting factors, so bleeding begins only when the old factors have decayed.

Concept cleared: Phosphine and stomach acid
Zinc phosphide is like a sealed gas cylinder that opens only in acid. The powder is harmless on the shelf, but the stomach acid opens it and releases phosphine. Less acid (antacid) means less gas.

Concept cleared: Vitamin K1 as a bypass
Vitamin K recycling is a blocked road. Vitamin K1 given by mouth is a new bypass that reaches the destination without using the blocked road, so clotting factors can be activated again.

Concept cleared: Strychnine and the brake
Glycine is the brake of the spinal cord. Strychnine cuts the brake cable, so every small stimulus sends the motor system into full throttle.

Memory aid: Rodenticide quick code
Anticoagulant = bleeding after Days (Vitamin K1). Phosphide = gas in the stomach (garlic smell). Cholecalciferol = Calcium goes up, kidneys go down. Bromethalin = Brain swells, no antidote. Strychnine = Stiff and Startled by sound, glycine blocked.

Compare and contrast

Rodenticides at a glance

Agent	Main mechanism	Onset	Antidote or key treatment
Anticoagulants	Block VKORC1, inactive factors II, VII, IX, X	Days	Vitamin K1, plasma or blood if severe
Zinc phosphide	Phosphine gas from stomach acid	Hours	No antidote; decontaminate, antacid, support
Cholecalciferol	Hypercalcaemia, soft tissue mineralisation	Delayed, 1 day or more	No antidote; fluids, calcium-lowering drugs, monitor
Bromethalin	Uncoupled oxidative phosphorylation, brain oedema	Hours to days	No antidote; early decontamination, support
Strychnine	Glycine blockade in spinal cord	Within hours	Control seizures, quiet, support

First- versus second-generation anticoagulants

Feature	First generation (e.g. warfarin)	Second generation (e.g. brodifacoum)
Potency	Lower	High
Doses needed for rodents	Often repeated feeding	Often a single feed
Duration in the body	Short	Long, weeks
Treatment with vitamin K1	Short course	Long course, repeat PT

Species notes

Dog

The commonest victim, because it eats baits. Strychnine is often malicious. Dogs may also eat a poisoned rat.

Cat

Especially sensitive to bromethalin, and may be secondarily poisoned by eating poisoned rodents.

Pig

Free-range pigs may eat baits and poisoned rats; pigs also vomit, which can protect or contaminate. Treat as for other monogastrics and seek advice.

Cattle and buffalo

Occasionally exposed through feed contaminated with bait or fumigant residue. Ruminal acid is lower, but gas release can still occur with phosphides, so seek veterinary help.

Poultry

Birds may eat baited grain. Safe baiting practice is to place baits in covered stations out of reach.

Clinical pearls

Self-test: 10 questions

1. Anticoagulant rodenticides act by inhibiting:

They block VKORC1, so vitamin K cannot be recycled and factors II, VII, IX and X remain inactive.

2. Why is bleeding delayed after anticoagulant ingestion?

Active factors already in blood keep clotting until they decay.

3. Which test usually becomes abnormal first after anticoagulant poisoning?

Factor VII has the shortest half-life, so PT rises first.

4. The correct vitamin for anticoagulant rodenticide poisoning is:

Vitamin K1 is the adequate antidote; K3 is not a reliable substitute.

5. Zinc phosphide becomes especially dangerous because it:

Gastric acid converts it into phosphine gas.

6. Which statement about handling phosphide vomitus is correct?

Phosphine can be released from the vomitus and stomach contents.

7. Cholecalciferol poisoning is characterised by:

Excess vitamin D raises calcium and phosphorus and mineralises soft tissue, including kidney.

8. For bromethalin poisoning, which statement is true?

Merck states that no antidote exists; management is decontamination and support.

9. Bromethalin acts mainly by:

ATP loss causes pump failure and brain oedema.

10. A dog is conscious with extended limbs and seizures triggered by noise. Which poison is most likely?

Strychnine blocks glycine in the spinal cord, giving stimulus-triggered rigidity while the animal remains aware.

Key points to revise

1. Rodenticide groups differ in mechanism, onset and antidote.
2. Anticoagulants block VKORC1 and cause delayed bleeding; PT rises first.
3. Vitamin K1 is the antidote; severe bleeding also needs plasma or blood.

4. Second-generation anticoagulants persist for weeks.
5. Zinc phosphide releases phosphine gas in stomach acid and has no specific antidote.
6. Cholecalciferol causes hypercalcaemia, mineralisation and kidney injury.
7. Bromethalin causes brain oedema, with no antidote; cats are very sensitive.
8. Strychnine blocks spinal glycine and causes stimulus-triggered seizures while conscious.

Go deeper on this site

- Ch 5. Herbicide and fungicide poisoning (in this book)
- Ch 3. Pyrethroid, amitraz and other insecticide poisoning (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Anticoagulant rodenticide poisoning in animals
- Merck Veterinary Manual: Phosphide poisoning in animals
- Merck Veterinary Manual: Bromethalin poisoning in animals
- Merck Veterinary Manual: Strychnine poisoning in animals

CHAPTER 5 OF 17

Herbicide and fungicide poisoning

Most herbicides and fungicides are of low toxicity to mammals, but a few, such as paraquat, copper and organomercury compounds, are dangerous. This chapter explains why, with mechanisms, signs, management concepts and prevention.

After this chapter you can

- Explain why glyphosate is of low toxicity to animals and why the surfactant matters
- Describe how paraquat injures the lung and why oxygen and delay in decontamination matter

- Describe the low toxicity of 2,4-D and its indirect hazards
- Explain copper toxicity and species differences, especially in sheep
- Describe organomercury poisoning and the prevention of seed-dressing accidents

General principles

Herbicides are designed to act on plant processes such as amino acid synthesis, hormone control or photosynthesis. Animals lack many of these targets, so most modern herbicides have low acute toxicity to mammals. Poisoning usually follows access to **concentrated product**, contaminated water or feed, spillage, or an animal licking a freshly sprayed surface. Chronic low-level exposure is hard to diagnose.

Fungicides are different. Many contain heavy metals (copper, mercury) that harm animals as well as fungi. Seed treated with a fungicide is a classical hazard when leftover seed is fed to animals.

Common sources of error: assuming that a product that is safe on the label is safe when swallowed as concentrate; forgetting that *formulation* (solvent, surfactant) can be more toxic than the active ingredient; and giving the wrong decontamination. Always get the product name, active ingredient, formulation and time of exposure.

Glyphosate

Glyphosate is a broad-spectrum systemic herbicide. It blocks the plant enzyme **EPSP synthase** in the shikimate pathway, which makes aromatic amino acids. Mammals have no shikimate pathway, so the main target is absent. Merck notes that its immediate toxicity is very low at most environmental concentrations.

A frequent confusion: glyphosate is a phosphorus-containing compound (a phosphonate) but is **not** a cholinesterase inhibitor, so atropine and pralidoxime are not indicated just because the label says "organophosphorus". Concentrated formulations include **surfactants** that irritate the eye, skin and gut and may cause more of the clinical effect than glyphosate itself. Exposure in dogs and cats can cause eye and skin irritation, drooling, vomiting and unsteadiness, which usually resolve when exposure stops. Management is to wash skin and eyes, give fluids

and symptomatic care. Questions about longer-term effects are still being studied, and regulatory status is debated, so check the current notification.

In practice, a poisoning history should include what was sprayed, when, the mixing strength if known, and whether the animals drank from puddles, troughs or ponds near the field. Keep the container and label for the veterinarian and the poison information service. Rinse skin and coat with plenty of water, and prevent the animal from licking itself until it has been washed.

Paraquat

Paraquat is a bipyridyl herbicide and is among the most dangerous. Its toxicity rests on **redox cycling**: inside cells it accepts an electron, then passes it to oxygen, making superoxide and other reactive oxygen species, and the cycle repeats. This consumes NADPH and causes lipid peroxidation and cell death. It is actively taken up into lung cells through a polyamine uptake system, so the lung accumulates it. Damage is greatest in the lung, kidney and liver.

Signs after swallowing: mouth and throat ulceration, vomiting, diarrhoea, then kidney and liver injury. Over days a **progressive pulmonary injury** develops with breathlessness and, in survivors, fibrosis. Merck states that there is no specific treatment and that oxygen therapy and fluids are contraindicated, because extra oxygen increases radical formation. Management is early and aggressive decontamination with adsorbents (activated charcoal, bentonite or Fuller's earth) and cathartics, and supportive care. Because the lung injury is delayed, an animal may look better for a day or two before it deteriorates, and the prognosis for a significant dose is poor.

Paraquat has caused many human and animal poisonings in India. Check the current notification on its sale, restriction or ban, and always handle it as a high-risk product. Seek urgent veterinary and poison-centre help in any suspected ingestion.

2,4-D and phenoxy herbicides

2,4-D is a synthetic plant growth regulator, mimicking the plant hormone auxin, so that weeds grow uncontrollably and die. The group is described as essentially non-toxic to animals at normal exposures, with the exception of one older member (silvex). In very large exposures animals may show vomiting, drooling, weakness

and muscle stiffness or twitching, and some dogs show kidney or liver effects. Treatment is supportive: remove the animal from the source, give fluids, use adsorbents, and monitor.

The more important hazards are indirect. Plants sprayed with growth regulators may become more palatable, so livestock graze poisonous weeds they would normally avoid, and stressed plants may accumulate nitrate, a point that links to the nitrate chapter. Always keep animals off sprayed pasture for the period given on the label.

Copper fungicides

Copper sulfate with lime (Bordeaux mixture) and copper oxychloride are used on grapes, vegetables and other crops. **Species differ greatly**. Sheep are very sensitive because they absorb and store copper in the liver and excrete little. Cattle, goats and pigs tolerate more. Chronic exposure, for example from grazing sprayed orchard or vineyard ground or from feed with too much copper, builds up in the liver for weeks without signs. Then a stressor releases copper suddenly and causes a **haemolytic crisis**: jaundice, dark red-brown urine (haemoglobinuria), weakness, and kidney damage.

Acute swallowing of concentrate is a gastrointestinal irritant, with colic, salivation, green diarrhoea and shock. Management concepts: stop the source, give symptomatic and fluid support, and use a veterinarian's advice on chelators and other copper-lowering therapy. Prevention is the key: keep sheep away from sprayed ground and from feed formulated for other species.

Organomercury fungicides and prevention

Organomercury compounds were widely used as seed dressings. Mercury binds sulfhydryl groups on many enzymes and proteins. Alkyl mercury compounds (such as methyl mercury) cross the blood-brain barrier and cause **neurological signs**: blindness, incoordination, tremor and paralysis, often appearing weeks after exposure. Inorganic and phenyl mercury compounds more often cause gut and **kidney** injury. Human outbreaks have followed the eating of dressed seed grain, and animals fed with it were also affected.

Treatment is difficult once nerve damage is present. Remove the source, give supportive care, and consult a toxicologist about chelating agents such as

dimercaprol or succimer. Most countries have banned or restricted organomercurials, but old seed stocks may still exist. Check the current notification for India.

Prevention in practice: never feed treated seed or the washings of seed to animals; store pesticides in labelled, locked containers away from feed; never reuse pesticide containers for feed or water; observe the withholding period before grazing sprayed fields; wash sprayer equipment away from water sources; and keep poison-centre or veterinary toxicology contacts ready. **Seek urgent help** for any suspected paraquat or mercury exposure, and for sheep with jaundice and dark urine after grazing sprayed ground.

Concept cleared

Concept cleared: Why glyphosate is low toxicity
Glyphosate blocks a factory line that exists in plants but not in animals. Animals buy these amino acids ready-made from food, so the blocked line does not hurt them.

Concept cleared: Redox cycling
Paraquat is like a ball bounced between two walls. Each bounce makes a spark of free radicals, and the ball is not used up, so one molecule can cause damage again and again.

Concept cleared: Oxygen and paraquat
Oxygen is the fuel for paraquat's sparks. Giving extra oxygen to a paraquat-poisoned animal supplies more fuel for radical injury, which is why it is avoided.

Concept cleared: Copper storage in sheep
Sheep keep copper in the liver like a bank deposit that grows quietly. Stress can cause a sudden withdrawal of the whole amount into blood, and red cells burst.

Memory aid: Herbicide and fungicide quick code

Glyphosate = Gentle (no cholinesterase). Paraquat = Pulmonary, Poor outlook, avoid Pure oxygen. 2,4-D = Dull toxicity, but Dangerous weeds eaten. Copper = Chronic store in Sheep. Mercury = Mind and kidney, from Mouldy-treated seed.

Compare and contrast

Herbicide and fungicide poisoning at a glance

Agent	Mechanism	Main signs	Key point
Glyphosate	Blocks plant EPSP synthase; surfactant irritant	Irritation, drooling, vomiting	Low toxicity; not a cholinesterase inhibitor
Paraquat	Redox cycling, free radicals, lung uptake	Mouth ulcers, delayed lung injury	No specific treatment; avoid oxygen; poor prognosis
2,4-D	Plant auxin mimic	Usually mild; vomiting, weakness	Indirect hazards from palatable or nitrate-rich weeds
Copper fungicides	Hepatic copper accumulation, haemolysis	Jaundice, haemoglobinuria; GI signs if acute	Sheep very sensitive
Organomercury	Binds sulfhydryl groups	Neurological or renal signs	Treated seed grain is the main hazard

Glyphosate versus true organophosphate insecticides

Feature	Glyphosate	Organophosphate insecticide
Target	Plant EPSP synthase	Acetylcholinesterase
Cholinergic signs	No	Yes (salivation, miosis, tremor)
Atropine useful	No	Yes
Typical toxicity	Low	Moderate to high

Species notes

Dog

Often exposed by licking sprayed lawns or concentrate. Glyphosate and 2,4-D usually cause mild signs, while paraquat can be fatal.

Cat

Grooming of sprayed fur causes oral exposure. Keep cats indoors during and after spraying.

Sheep

Highly sensitive to copper, including copper fungicide residues; may develop a haemolytic crisis.

Cattle and buffalo

Graze sprayed pasture or eat treated seed. Observe withholding periods and avoid weeds growing after spray, which may hold nitrate.

Pig

May be given waste grain; treated seed is a hazard, including mercury-treated seed.

Clinical pearls

Self-test: 10 questions

1. Glyphosate acts on which plant enzyme?

It blocks EPSP synthase in the shikimate pathway, which animals lack.

2. Glyphosate poisoning should not be treated with atropine routinely because:

Glyphosate does not inhibit cholinesterase, so cholinergic signs are not expected.

3. Much of the irritation from glyphosate products is due to:

Formulation additives can be more irritant than the active ingredient.

4. The main mechanism of paraquat toxicity is:

Paraquat repeatedly accepts and passes on electrons, generating radicals.

5. Paraquat damage is most notable in the:

It is concentrated by lung cells and causes progressive pulmonary injury.

6. Which is advised in paraquat ingestion?

Oxygen worsens radical injury; early adsorption limits absorption.

7. 2,4-D belongs to the group called:

It is a phenoxy acid, a plant auxin mimic of low animal toxicity.

8. Which species is most sensitive to copper?

Sheep accumulate copper in the liver and excrete little.

9. A haemolytic crisis in sheep after chronic copper exposure produces:

Sudden copper release from the liver ruptures red cells.

10. The usual source of organomercury poisoning in animals is:

Seed dressings contained mercury and leftover treated grain can be fed by mistake.

Key points to revise

1. Most herbicides are low toxicity unless concentrate is swallowed.
2. Glyphosate blocks plant EPSP synthase and is not an anticholinesterase.
3. Paraquat causes free-radical injury and delayed lung damage with a poor prognosis.
4. Early adsorbent and cathartic use matters in paraquat poisoning.
5. 2,4-D is of low toxicity but changes plant palatability and may raise nitrate.
6. Sheep are very sensitive to copper; chronic build-up then haemolytic crisis.
7. Organomercury causes neurological and renal damage; treated seed is the hazard.
8. Check current Indian notifications for banned or restricted pesticides.

Go deeper on this site

- Ch 6. Plant poisoning in Indian livestock (in this book)
- Ch 4. Rodenticide poisoning (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Overview of herbicide poisoning in animals
- Merck Veterinary Manual: Organic herbicides toxic to animals
- Merck Veterinary Manual: Toxicology

CHAPTER 6 OF 17

Plant poisoning in Indian livestock

Most livestock plant poisoning follows hunger, drought, flood or a change in feed, not wickedness of the plant. This chapter covers cyanogenic plants, nitrate and oxalate, oleander and related cardiotoxic plants, common toxic weeds, and the seasonal patterns behind outbreaks.

> **After this chapter you can**
>
> - Explain how cyanogenic glycosides release cyanide and how cyanide blocks cell respiration

- Describe nitrate to nitrite conversion and methaemoglobinaemia in ruminants
- Explain how soluble oxalates cause hypocalcaemia and kidney damage
- Describe how cardiac glycoside plants such as oleander affect the heart
- Link outbreaks with season, hunger, drought, rain and fodder practices

Why animals eat poisonous plants

Livestock usually avoid poisonous plants because of taste, but poisoning happens when choice is removed. Typical settings are overgrazed or drought pasture, hungry animals moved to a new field, animals transported and let out hungry, early monsoon flush when only new shoots are green, floods that wash seeds or roots into fields, and garden or roadside cuttings thrown to animals. Animals unfamiliar with a local plant are at greater risk than those raised there.

Toxicity depends on **dose, part of the plant, stage of growth, weather, species and rumen function**. A plant may be safe at one stage and deadly at another. Diagnosis rests on history, plants seen in the field, rumen content examination for plant fragments, and laboratory tests where available. Because specific antidotes are few, prevention and early removal from the source are the foundation. Always contact a veterinarian early.

Cyanogenic plants

Plants such as young or stressed sorghum and Sudan grass, cassava, some Prunus species and certain wild plants hold **cyanogenic glycosides** (for example dhurrin and linamarin). These are harmless while intact. When the plant is wilted, frosted, trampled, chewed or fermented in the rumen, plant enzymes (beta-glucosidases) and rumen microbes split the glycoside and release **hydrogen cyanide**.

Cyanide binds to **cytochrome oxidase** in mitochondria, so cells cannot use oxygen even though blood carries plenty. This is **histotoxic hypoxia**. The blood stays bright red because oxygen is not extracted. Signs begin minutes after eating: distress, rapid laboured breathing, salivation, tremors, staggering, convulsions and sudden death. Ruminants are more susceptible than monogastrics because the rumen provides enzymes and a suitable pH for release.

Risk is highest with **young regrowth, drought-stressed plants and first rain after drought**, with hungry animals, and with fresh cut fodder. Cutting and wilting, then

ensiling or full drying lowers cyanide, though caution is still needed. The antidote concept is two-step: sodium nitrite makes methaemoglobin, which attracts cyanide away from cytochrome oxidase, and sodium thiosulfate supplies sulfur for the enzyme rhodanese to convert cyanide to thiocyanate. Merck also mentions hydroxocobalamin. Treatment must be given fast by a veterinarian, so move animals off the pasture and call for help early.

Nitrate and nitrite

Fast-growing or stressed plants can accumulate **nitrate**, which is not very toxic by itself. Common sources: sorghum, maize, oats, millets, and weeds such as Amaranthus (pigweed) and Chenopodium, especially after drought followed by rain, heavy nitrogen fertiliser, cloudy weather or herbicide stress. Contaminated well water can also contribute.

In the rumen, microbes convert nitrate to **nitrite**. Nitrite oxidises haemoglobin iron to give **methaemoglobin**, which cannot carry oxygen. Blood is a typical **chocolate brown** and mucous membranes look muddy. Signs are weakness, rapid breathing, tremors, staggering, and sudden death. Pregnant animals may abort later. The common confusion is that cyanide gives bright red blood and nitrite gives brown blood, and that nitrite is used therapeutically as an antidote to cyanide, yet nitrite itself is the toxin here.

Merck gives methylene blue as the treatment, to reduce methaemoglobin back to haemoglobin, together with removal of the source. Hungry animals eating suddenly are at highest risk, and feeding grain or gradual introduction can lower risk. Hay does not lose nitrate quickly; silage reduces it.

Oxalate plants

Soluble oxalates occur in Rumex (dock), Oxalis, Amaranthus, Portulaca and some tropical grasses. Oxalate binds calcium, so blood calcium falls (**hypocalcaemia**), producing weakness, tremors and recumbency. Calcium oxalate crystals can also form in kidney tubules and cause **renal failure**.

Rumen microbes of adapted animals break down oxalate, so sudden intake by unadapted, hungry animals is most risky. Treatment is calcium by a veterinarian and supportive fluids. Some tropical grasses with high oxalate cause long-term calcium

imbalance, mainly in horses; this is a different, slower problem from acute oxalate poisoning.

Oleander and other cardiotoxic plants

Oleander (*Nerium oleander*, kaner) and yellow oleander (*Thevetia peruviana*) are common garden and roadside shrubs in India. They contain **cardiac glycosides** that inhibit the sodium-potassium ATPase. Intracellular sodium and then calcium rise, the heart becomes irritable, and potassium rises in blood. Poisoning looks like digoxin overdose: colic, salivation, diarrhoea, weakness, irregular, slow or rapid pulse, heart block and sudden death. A small amount of fresh or dry leaf can be fatal, and drying does not remove toxicity.

Other plants with cardiac glycoside-like action include Calotropis (akand, which also has irritant latex) and other members of the same plant family. Treatment concepts: remove animals from the source, give activated charcoal early, monitor the ECG, correct potassium problems, and use antiarrhythmic drugs under veterinary advice. Antibody fragments for digoxin have been used in selected cases. Prevention is important: never throw oleander prunings into animal enclosures, never use oleander wood for skewers or fodder, and fence off shrubs near sheds.

Toxic weeds and seasonal risks

Several weeds in India are important. **Lantana camara** contains lantadenes that damage the liver and stop bile flow, causing jaundice and **photosensitisation** (sunburn of unpigmented skin) in cattle and buffalo. **Castor** (*Ricinus communis*) contains ricin, a protein synthesis inhibitor that harms gut and organs. **Ipomoea carnea** (besharam) has been reported to cause nervous signs in goats and sheep. **Cassia occidentalis** seeds in feed have been reported to cause muscle degeneration. Plants with pyrrolizidine alkaloids, such as Crotalaria, cause slow, cumulative liver damage. **Parthenium** mainly causes skin allergy and may taint milk and meat, so treat reports with care.

Seasonal pattern, in outline: **early monsoon** flush and first rain after drought (cyanide, nitrate); **summer and drought** (hunger, shortage of fodder, wilting plants); **floods and post-flood** (new weed growth, mouldy fodder); **winter** frost-damaged sorghum; and **festival and garden waste** seasons (oleander, castor). Prevention:

provide adequate clean feed before turnout, avoid grazing hungry animals on risky crops, cut and dry or ensile sorghum, test suspect fodder for nitrate, identify and remove weeds, fence hazardous shrubs, and teach farmers to call early. Treat sudden death in the field as a possible plant poisoning until shown otherwise.

When sudden deaths occur in a herd, collect rumen content, fodder samples and plant specimens in separate clean containers and send them with a full history. Move the survivors to a safe paddock with clean fodder and water. Do not slaughter sick animals for meat or milk use until a veterinarian has advised on withdrawal and safety.

Concept cleared

Concept cleared: Cyanide release
A cyanogenic plant is a locked box. Chewing, wilting or the rumen unlocks the box and cyanide spills out. The animal is not low on oxygen in blood; its cells simply cannot use it.

Concept cleared: Bright red versus chocolate brown
Cyanide stops cells using oxygen, so blood stays red. Nitrite changes haemoglobin so it cannot carry oxygen, so blood turns brown. Same hypoxia, different place in the chain.

Concept cleared: Oxalate and calcium
Oxalate is a thief of calcium. It binds calcium in the gut and blood, leaving muscles short, and the crystals can then clog the kidney.

Concept cleared: Hunger decides
Most plant poisonings are about opportunity. A hungry animal eats what a fed animal ignores, so the cheapest prevention is good feeding.

Memory aid: Plant poisoning quick code

Cyanide = Cherry-red blood, Cells cannot breathe. Nitrate = Nitrite makes Brown blood (methylene Blue). Oxalate = Oxalate Overtakes calcium (hypocalcaemia, kidney). Oleander = Odd rhythm, like digoxin. Lantana = Light-sensitive skin (photosensitisation).

Compare and contrast

Plant poisonings at a glance

Toxin	Example plants	Mechanism	Key sign or test	Treatment concept
Cyanogenic glycosides	Young sorghum, cassava	Cyanide blocks cytochrome oxidase	Sudden death, bright red blood	Sodium nitrite and thiosulfate, or hydroxocobalamin
Nitrate	Sorghum, maize, Amaranthus	Nitrite makes methaemoglobin	Chocolate brown blood	Methylene blue
Oxalate	Rumex, Oxalis	Binds calcium, kidney crystals	Hypocalcaemia, renal failure	Calcium, fluids
Cardiac glycosides	Oleander, Thevetia	Na-K ATPase inhibition	Arrhythmia, colic, sudden death	Charcoal, ECG monitoring, antiarrhythmics

Cyanide versus nitrate poisoning

Feature	Cyanide	Nitrate/nitrite
Site of block	Cytochrome oxidase	Haemoglobin (methaemoglobin)
Blood colour	Bright red	Chocolate brown
Onset	Minutes	Hours
Antidote	Nitrite plus thiosulfate	Methylene blue

Species notes

Cattle and buffalo

Goat

Most often affected by cyanide, nitrate and Lantana because they graze coarse pasture and cut fodder. Rumen conversion makes them more sensitive to cyanide and nitrate.

Browse many shrubs and are exposed to oleander, Ipomoea and other shrubs when grazing is short.

Sheep
Graze close to the ground and are exposed to weeds; oxalate plants and oleander clippings are risks.

Horse
Monogastric, so less affected by cyanide and nitrate from plants than ruminants, but sensitive to oleander and to some oxalate grasses over time.

Dog
Chew garden shrubs and may be exposed to oleander and castor seeds; call a veterinarian early.

Clinical pearls

Self-test: 10 questions

1. Cyanide poisoning blocks:

Cyanide binds cytochrome oxidase and stops cells using oxygen.

2. The colour of blood in acute cyanide poisoning is typically:

Oxygen is not extracted by tissues, so venous blood stays bright red.

3. Which situation raises the risk of cyanide poisoning from sorghum?

Young and stressed plants hold more cyanogenic glycoside.

4. Why are ruminants more vulnerable to plant cyanide?

Rumen enzymes and pH release HCN.

5. In nitrate poisoning of cattle the toxic step is conversion of nitrate to:

Nitrite oxidises haemoglobin to methaemoglobin.

6. Chocolate brown blood suggests:

Methaemoglobin cannot carry oxygen and gives brown blood.

7. The treatment given for nitrite methaemoglobinaemia is:

Methylene blue helps reduce methaemoglobin to haemoglobin.

8. Soluble oxalate plants cause poisoning mainly through:

Oxalate binds calcium, causing hypocalcaemia and kidney crystals.

9. Oleander poisoning is similar to overdose of:

Both inhibit Na-K ATPase and cause arrhythmia.

10. Photosensitisation with jaundice in cattle after grazing is most characteristic of:

Lantadenes damage the liver and bile flow, so phylloerythrin accumulates and sensitises skin.

Key points to revise

1. Plants are most dangerous when animals are hungry or the plant is stressed.
2. Cyanogenic glycosides release HCN, which blocks cytochrome oxidase.
3. Nitrate is reduced to nitrite in the rumen and forms methaemoglobin.
4. Methylene blue treats nitrite methaemoglobinaemia.
5. Oxalate binds calcium and may injure kidneys.
6. Oleander glycosides inhibit Na-K ATPase and cause arrhythmia.
7. Lantana causes liver injury and photosensitisation in cattle.
8. Prevention: feed before turnout, remove weeds, fence shrubs, call early.

Go deeper on this site

- Ch 7. Heavy metals and mineral poisoning (in this book)
- Ch 5. Herbicide and fungicide poisoning (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Cyanide poisoning in animals
- Merck Veterinary Manual: Nitrate and nitrite poisoning in animals
- Cornell University: Plants poisonous to livestock

CHAPTER 7 OF 17

Heavy metals and mineral poisoning

How lead, arsenic, copper, selenium, fluoride, molybdenum and zinc injure animals, why species differ so much, and how chelators work. The emphasis is on mechanism, recognising the pattern, removing the source and preventing exposure.

After this chapter you can

- Explain how lead and arsenic damage cells through sulphydryl binding and enzyme inhibition

- Describe why sheep are especially prone to copper poisoning and how molybdenum and sulphur interact with copper
- Distinguish acute from chronic selenium and fluoride toxicity and name the typical lesions
- Recognise zinc toxicity from foreign bodies in dogs and its haemolytic effect
- Explain the principle of chelation, the main chelating agents and their limitations

Why metals and minerals poison

Metals are not broken down by the body. They bind to proteins, replace essential minerals or sit in tissues for a long time. That is why many metal poisonings are **chronic or cumulative**, and why a single clinical case often points to a problem in the whole herd, feed or water supply.

Two broad groups exist. Classical toxic metals such as lead and arsenic have no useful role in the body. Essential trace minerals such as copper, selenium, zinc and molybdenum are needed in small amounts, but the gap between enough and too much can be narrow. Deficiency and toxicity of the same mineral can occur in the same district.

Always think of three questions: what is the source, which species is exposed, and is the exposure acute (one large intake) or chronic (small repeated intake)?

In practice, a good history is the most valuable test. Ask about recent changes in feed, new mineral mixtures, repainting or renovation, burning of waste, new water sources and access to scrap. Laboratory confirmation (blood, liver, kidney, feed and water analysis) should be arranged through a veterinary diagnostic laboratory, and samples should be collected before treatment where possible. Report herd-level problems to the local animal husbandry authority, because the source may harm other animals and people.

Lead

Lead is among the commonest toxic metals in animals. Sources include old paint, batteries, lead shot, used engine oil, putty, linoleum and pasture contaminated by smelters or burning of lead-containing waste. Young, curious cattle and dogs are most often affected.

Mechanism. Lead binds sulphydryl groups and inhibits enzymes of haem synthesis (such as ALA dehydratase and ferrochelatase). It also behaves like calcium, interferes with calcium-dependent processes, and damages the small blood vessels of the brain, causing oedema and neuronal injury.

Signs. In cattle the picture is mainly nervous: blindness, head pressing, bellowing, muscle twitching, teeth grinding and convulsions. In dogs gastrointestinal signs (vomiting, abdominal pain) often appear together with nervous signs. Nucleated red cells and basophilic stippling without marked anaemia support the suspicion, but diagnosis rests on blood lead measurement and the history.

Management concepts. Stop further exposure first. Chelators are used to bind absorbed lead, and supportive care controls seizures and brain swelling. If lead objects remain in the gut, removal is needed, because chelation alone can leave a continuing source.

Arsenic

Arsenic exists in organic and inorganic forms. **Inorganic trivalent arsenicals** are the more toxic. Sources include old herbicides, wood preservatives, sheep and cattle dips and contaminated water. Arsenic in groundwater is a recognised public health problem in parts of India and neighbouring countries, so check the current local advisories.

Mechanism. Trivalent arsenic binds sulphydryl groups of enzymes, especially those needing lipoic acid, and so blocks cellular energy production. It also damages capillaries, especially in the gut.

Signs. Acute poisoning causes severe abdominal pain, salivation, vomiting in species that can vomit, watery or bloody diarrhoea, weakness, collapse and death, often within a day. Chronic exposure is subtler: poor condition, skin and gut changes.

Antidote reasoning. Dithiol chelators such as dimercaprol and succimer offer competing sulphydryl groups so that arsenic leaves the enzymes. They work best early, before damage is established.

Copper and molybdenum

Sheep are very sensitive to copper because they absorb it efficiently and store it in the liver with poor biliary excretion. Poisoning is often *chronic*: copper builds up silently over weeks, then a stressor triggers a sudden release causing a **haemolytic crisis** with jaundice, dark haemoglobin-stained urine and death. Typical causes are feeds made for cattle or pigs given to sheep, or contaminated pasture.

Molybdenum and sulphur bind copper in the rumen as insoluble thiomolybdates, lowering copper absorption. Excess molybdenum therefore causes *secondary copper deficiency* in cattle (scouring, poor growth, loss of coat colour), while a low molybdenum intake makes sheep copper poisoning more likely. This is a common confusion: molybdenum toxicity is really a copper deficiency state.

Dogs. Certain breeds, such as the Bedlington terrier, inherit a defect in copper handling and develop chronic liver disease.

Prevention depends on correct feed formulation. Treatment aims to bind or reduce liver copper, but advanced haemolysis carries a poor outlook.

Selenium, fluoride and zinc

Selenium. It is essential (part of glutathione peroxidase) yet toxic in excess, with a narrow safety margin. Selenium replaces sulphur in amino acids and promotes oxidative damage. Chronic poisoning in grazing animals, linked to seleniferous soils and accumulator plants, causes hair loss, hoof deformity and lameness. Acute poisoning is usually due to dosing or supplement errors and causes respiratory distress, sudden death or cardiac failure. Some regions of India are reported to have high-selenium soils; check local data.

Fluoride. Sources are high-fluoride groundwater, rock phosphate supplements and industrial emissions. Fluoride enters bone and teeth, forming fluorapatite. Chronic **fluorosis** gives mottled, worn teeth (only if exposure occurred while teeth were forming), bony outgrowths, stiffness and lameness. Fluorosis is reported from several Indian states. There is no specific antidote, so prevention by water testing and low-fluoride supplements is the main tool.

Zinc. Dogs swallow galvanised nuts, bolts, some coins and zinc-containing ointments. Gastric acid releases zinc, which causes **intravascular haemolysis**, and may injure pancreas, liver and kidney. The foreign body should be removed; supportive care follows.

Chelation: principles and cautions

A **chelator** grips a metal ion with several binding sites, forming a stable ring-like complex that is water soluble and excreted, mainly in urine or bile. The choice depends on the metal.

- **Calcium disodium EDTA**: lead and zinc. It is given by injection, and it can injure kidneys. Do not confuse it with disodium EDTA, which can cause dangerous hypocalcaemia.
- **Dimercaprol (BAL)**: arsenic. It is an oily, painful injection.
- **Succimer (DMSA)**: lead, arsenic; oral and generally better tolerated.
- **D-penicillamine**: copper and lead, mainly oral.
- **Tetrathiomolybdate**: reduces copper uptake.

Cautions. A chelator is not a substitute for removing the source. Chelators may also remove essential minerals, and some can increase absorption of metal still in the gut. Dosing must follow a current formulary and veterinary toxicology advice, not a textbook. In any suspected metal poisoning, contact a poison information service or toxicologist early.

Concept cleared

Cumulative toxicity
Metals persist in tissues. Small daily intakes add up until clinical disease appears, often after a stressor.

Sulphydryl binding
Lead and arsenic inactivate enzymes by binding their sulphydryl groups. Chelators with their own sulphydryl groups compete for the metal.

Mineral antagonism
Molybdenum and sulphur lock copper in the gut. Excess of one mineral can produce deficiency of another.

Source control first

Antidotes and chelators cannot work well while the animal is still being exposed. Find and remove the source.

Memory aid: Remember the metal and its target

Lead hits head and heme, arsenic attacks the gut, copper kills sheep, fluoride fixes in bone, zinc breaks blood.

Compare and contrast

Metals at a glance

Agent	Main mechanism	Typical presentation	Antidote concept
Lead	Blocks haem synthesis, vascular and neuronal injury	Blindness, convulsions (cattle); GI plus nervous (dogs)	Calcium EDTA, succimer, source removal
Arsenic (inorganic)	Sulphydryl binding, energy block, capillary damage	Acute haemorrhagic gastroenteritis	Dimercaprol, succimer
Copper	Liver storage then haemolytic release	Jaundice, haemoglobinuria (sheep)	Prevention; tetrathiomolybdate, penicillamine
Fluoride	Replaces hydroxyl in bone and teeth	Dental mottling, lameness	None specific; prevention
Zinc	Haemolysis, organ injury	Anaemia, dark urine (dogs)	Remove object, supportive

Acute versus chronic mineral poisoning

Feature	Acute	Chronic
Exposure	One large intake or error	Repeated small intake
Onset	Hours to days	Weeks to months
Examples	Arsenic, selenium dosing errors, zinc object	Copper in sheep, fluorosis, selenium on pasture
Main aim	Decontaminate and chelate early	Find the source, correct diet and water

Species notes

Sheep

Highly sensitive to copper; chronic accumulation then haemolytic crisis. Avoid feeds meant for other species.

Cattle

Commonest victims of lead (nervous signs); molybdenum excess causes secondary copper deficiency.

Dogs

Lead and zinc from household objects; inherited copper storage disease in some breeds.

Horses

Lead from pasture near contaminated sites can cause laryngeal and nervous signs; fluoride affects teeth and bone.

Pigs and poultry

Sensitive to selenium excess and to arsanilic-type feed additives if overdosed or mixed wrongly.

Clinical pearls

Self-test: 10 questions

1. Which enzyme pathway is a main target of lead?

Lead inhibits ALA dehydratase and ferrochelatase, so haem synthesis is impaired.

2. Typical presentation of lead poisoning in a calf is:

Cattle show predominantly nervous signs.

3. Why do dithiol chelators help in arsenic poisoning?

Competing sulphydryl groups pull arsenic away from enzymes.

4. Which species is most sensitive to chronic copper accumulation?

Sheep absorb and store copper efficiently and excrete it poorly.

5. Excess dietary molybdenum in cattle mainly causes:

Thiomolybdates bind copper in the rumen.

6. Mottled and worn teeth with bony outgrowths suggest:

Chronic fluoride affects developing enamel and bone.

7. A dog that swallowed galvanised nuts develops anaemia and dark urine. The likely mechanism is:

Zinc released in the stomach damages red cells.

8. A caution about calcium disodium EDTA is:

It can damage kidneys; disodium EDTA risks hypocalcaemia.

9. What should come first when managing any metal poisoning?

Antidotes are poorly effective if exposure continues.

10. Selenium excess in grazing animals commonly produces:

Chronic selenosis causes hair and hoof changes and lameness.

Key points to revise

1. Metals bind enzymes and persist, so many poisonings are chronic or cumulative.
2. Lead blocks haem synthesis and injures brain vessels; cattle show blindness and convulsions.
3. Inorganic trivalent arsenic binds sulphydryl groups and damages gut capillaries.
4. Sheep store copper and may suffer a sudden haemolytic crisis after stress.
5. Molybdenum and sulphur reduce copper availability; excess molybdenum causes secondary copper deficiency.
6. Selenium has a narrow margin between need and toxicity.
7. Fluorosis damages developing teeth and bone and has no specific antidote.
8. Chelators are metal specific, can be toxic, and never replace source removal.

Go deeper on this site

- Ch 8. Feed-related toxicities (in this book)
- Ch 6. Plant poisoning in Indian livestock (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Lead poisoning in animals
- Merck Veterinary Manual: Copper poisoning in animals
- Merck Veterinary Manual: Fluoride poisoning in animals

CHAPTER 8 OF 17

Feed-related toxicities

Poisonings that arise from what animals eat or drink: urea and other non-protein nitrogen, salt and water deprivation, nitrate, ionophores and the major mycotoxins. The chapter links each toxin to its mechanism, its species pattern and the practical prevention step.

After this chapter you can

- Explain why ruminal pH and adaptation determine urea toxicity and how acidifying the rumen helps
- Describe salt poisoning as water deprivation sodium toxicosis and the danger of rapid rehydration
- Explain nitrate to nitrite to methaemoglobin and its antidote reasoning
- Describe ionophore toxicity and the species that are most at risk
- Distinguish aflatoxin, ergot and the main Fusarium toxins by source, mechanism and signs

Feed as a source of poison

Many livestock poisonings are not caused by a wild plant or a spilt chemical but by a **feed that is normally safe**. Urea, salt, nitrate and ionophores are useful in the right amount and in the right species. Poisoning follows mixing errors, sudden changes, poor adaptation or feeding a product to the wrong species.

Three themes recur. First, **the rumen** changes both toxicity and safety. Second, **mixing and storage** errors cause herd outbreaks. Third, mycotoxins arise when feed is stored damp or warm, so prevention starts long before the animal eats.

Because many animals share the same ration, a feed problem usually appears as several animals sick or dead within a short period. This pattern is itself a diagnostic clue.

When investigating a suspected feed problem, stop the suspect feed at once, keep a sealed sample of the batch for analysis, and record which animals ate it and when. Check feed mill records for mixing errors and for any recent change of ingredient or supplier. Samples of feed, rumen contents, liver and serum are useful,

but they must be collected and stored correctly. In suspected cases involving milk or meat, ask the authorities about withholding and residue rules and check the current notification.

Urea and non-protein nitrogen

Ruminants can use urea as a cheap nitrogen source because rumen microbes split it with **urease** into ammonia and rebuild it as microbial protein. Poisoning occurs when ammonia is released faster than microbes can use it.

Why ruminal pH matters. Ammonia exists as ammonium ion (poorly absorbed) in an acid rumen, but as free ammonia (readily absorbed) when pH rises. Excess ammonia overwhelms the liver, and the blood ammonia then rises sharply.

Risk factors: unadapted animals, fasted animals eating a large amount quickly, poor mixing, a low-energy diet, and access to fertiliser bags. Non-ruminants do not have the rumen urease and are much less susceptible.

Signs: restlessness, salivation, tremors, bloat, laboured breathing, incoordination, bellowing and rapid death.

Reasoning for treatment: acidifying the rumen with dilute acetic acid and giving cold water slows urease and traps ammonia as ammonium. This is an emergency, because treatment is only effective early. Prevention is gradual adaptation, even mixing and never feeding urea to calves with an undeveloped rumen.

Salt poisoning and water deprivation

Sodium chloride is not very toxic by itself when water is freely available. The true problem is **water deprivation sodium ion toxicosis**. Pigs, poultry and cattle with limited water that eat salty feed, whey, brine or salted waste develop hypernatraemia.

Mechanism. High sodium draws water out of brain cells. The brain protects itself by building up small organic solutes. If water is then given freely and quickly, water follows these solutes into the brain, causing **cerebral oedema**. This is why many animals worsen or die after sudden access to water.

Signs. In pigs: thirst, wandering, blindness, circling, head pressing, then convulsions, often in a dog-sitting posture. Brain lesions with eosinophilic cuffing

are classic in pigs. Ruminants show nervous signs and diarrhoea.

Management and prevention. Withdraw the salt source and restore water slowly and in small amounts, under veterinary supervision. Prevention is constant clean water and care with salty by-products.

Nitrate and nitrite

Nitrate comes from heavily fertilised or drought-stressed plants such as sorghum, oats and some weeds, and from contaminated well water. Nitrate itself is of low toxicity. In the rumen microbes reduce it to **nitrite**, which oxidises the iron of haemoglobin from the ferrous to the ferric state, forming **methaemoglobin** that cannot carry oxygen.

Ruminants are more susceptible than monogastrics because of this ruminal conversion, and a hungry animal eating suddenly is at highest risk.

Signs. Rapid breathing, weakness, muddy or chocolate-brown mucous membranes and blood, tremors, collapse and death. Pregnant cows may abort. The animal appears short of oxygen even though the lungs are normal.

Antidote reasoning. Methylene blue acts as an electron carrier that helps convert methaemoglobin back to haemoglobin. It is used by a veterinarian, because overuse has its own risks. Ensiling reduces nitrate, and testing feed and water before feeding is the best prevention.

Do not confuse nitrate poisoning with cyanide: cyanide blocks tissue use of oxygen and gives bright red blood.

Ionophores

Ionophore antibiotics such as monensin, lasalocid, salinomycin and narasin improve feed efficiency in ruminants and control coccidia in poultry. They carry ions across cell membranes and destroy ion gradients.

Mechanism. In toxic amounts they cause calcium overload and energy failure in muscle cells, with especially severe injury to the heart and skeletal muscle.

Species. Horses are extremely sensitive and may be poisoned by cattle or poultry feed containing monensin, often from a mixing error. Dogs, cats and turkeys are

also sensitive. Cattle tolerate a limited range. Some drugs, notably tiamulin, slow ionophore metabolism and can precipitate toxicity in pigs and poultry.

Signs. Inappetence, colic, sweating, muscle weakness, ataxia, recumbency, fast irregular heart rate, myoglobinuria and sudden death. Survivors may have permanent heart damage.

Management. There is no specific antidote. Remove the feed and give supportive care, and activated charcoal early in recent ingestion. Prevention is strict labelling, dedicated mixing equipment and never feeding ionophore feed to horses.

Mycotoxins: aflatoxin, ergot and Fusarium

Mycotoxins are fungal metabolites produced in the field or in storage. Heat, humidity and damaged grain favour them, and cooking or pelleting does not destroy most of them. Several can occur together.

- **Aflatoxin** (*Aspergillus flavus*, *A. parasiticus*): found in groundnut cake, maize and cottonseed. The liver activates aflatoxin B1 to a reactive epoxide that binds DNA and proteins. Effects: liver damage, poor growth, immunosuppression, bleeding and cancer risk. Ducklings, turkeys and young pigs are very sensitive. Dairy animals excrete aflatoxin M1 in milk, which is a public health issue. Check the current Indian limits for feed and food.
- **Ergot** (*Claviceps* species on grain and grasses): alkaloids act on adrenergic, serotonin and dopamine receptors, causing vasoconstriction and gangrene of tail, ears and feet, and in some cases nervous signs and poor milk.
- **Fusarium toxins:** T-2 toxin and other trichothecenes block protein synthesis (oral and gut lesions, bleeding); deoxynivalenol causes feed refusal and vomiting in pigs; **zearalenone** is oestrogenic (swollen vulva, prolapse, infertility); fumonisins cause leukoencephalomalacia in horses and pulmonary oedema in pigs.

Prevention rests on dry storage, testing, discarding mouldy feed and, where appropriate, binders; no binder works against all toxins.

Concept cleared

Rumen as a reactor

Microbes convert urea to ammonia and nitrate to nitrite. Rumen pH and adaptation decide whether the product is useful or dangerous.

Water deprivation toxicosis

Salt is dangerous when water is short. Rapid rehydration after hypernatraemia can cause brain oedema.

Wrong species, wrong feed

Ionophore feed safe for cattle or poultry can kill horses. Always check the label and the species.

Storage creates toxins

Mycotoxins develop in damp or warm feed and survive processing, so prevention is at harvest and storage.

Memory aid: Feed troubles: U-S-N-I-M

Urea, Salt, Nitrate, Ionophore, Mould: check the feed for each of these when a group of animals falls sick together.

Compare and contrast

Feed toxicities compared

Toxin	Key mechanism	Main species at risk	Characteristic sign
Urea	Rumen ammonia overload	Ruminants	Tremor, bloat, bellowing
Salt	Hypernatraemia, brain oedema on rehydration	Pigs, poultry, cattle	Wandering, convulsions
Nitrate	Methaemoglobin	Cattle, sheep	Brown blood, dyspnoea
Ionophores	Calcium overload in muscle	Horses, dogs, turkeys	Heart and muscle damage

Mycotoxins compared

Mycotoxin	Source fungus	Target	Typical outcome
Aflatoxin	Aspergillus	Liver	Hepatic injury, immunosuppression, milk residue
Ergot alkaloids	Claviceps	Blood vessels, receptors	Gangrene of extremities
Zearalenone	Fusarium	Oestrogen receptors	Vulvovaginitis, infertility
Fumonisin	Fusarium	Brain (horse), lung (pig)	Leukoencephalomalacia, pulmonary oedema

Species notes

Cattle and buffalo
Susceptible to urea and nitrate because of rumen conversion; also exposed to aflatoxin through cake and silage, with M1 in milk.

Sheep and goats
Similar to cattle for urea and nitrate; small body size makes errors in mixing serious.

Horses
Extremely sensitive to ionophores; fumonisin causes

Pigs
Classic salt poisoning with water deprivation; sensitive to

leukoencephalomalacia.

deoxynivalenol and zearalenone.

Poultry

Aflatoxin, ionophore mixing errors and salt excess cause losses; ducklings and turkeys are most sensitive to aflatoxin.

Clinical pearls

Self-test: 10 questions

1. Why is urea toxicity mainly a ruminant problem?

Rumen microbial urease splits urea into ammonia, which is absorbed if released too fast.

2. Which rumen condition increases ammonia absorption?

At high pH more ammonia is in the free, absorbable form.

3. The rationale for giving dilute acetic acid orally in urea poisoning is to:

Acid slows urease and converts ammonia to ammonium.

4. Why can rapid watering be harmful in salt poisoning?

Brain cells have built up solutes; sudden water entry causes swelling.

5. Which species classically show salt poisoning with dog-sitting posture and eosinophilic cuffing?

This is the classic porcine picture.

6. Methaemoglobin forms when nitrite:

Ferric haemoglobin cannot carry oxygen.

7. Which species is exceptionally sensitive to monensin?

Horses are highly sensitive and suffer heart and muscle injury.

8. Aflatoxin M1 is important because it:

M1 is a milk metabolite and a public health concern.

9. Gangrene of the tail and ear tips from contaminated grain suggests:

Ergot alkaloids cause vasoconstriction and dry gangrene.

10. Swollen vulva and prolapse in young gilts suggest:

Zearalenone is oestrogenic.

Key points to revise

1. Urea toxicity depends on ammonia release, rumen pH and lack of adaptation.
2. Acidifying the rumen and cooling it slows urea breakdown and traps ammonia.
3. Salt poisoning is mainly water deprivation sodium toxicosis; rapid water access worsens brain oedema.
4. Nitrite oxidises haemoglobin to methaemoglobin; methylene blue is the antidote concept.
5. Ionophores cause heart and skeletal muscle damage and are especially dangerous to horses.

6. Aflatoxin B1 is hepatotoxic and carcinogenic, and aflatoxin M1 appears in milk.
7. Ergot causes vasoconstriction and gangrene; zearalenone is oestrogenic.
8. Mycotoxin control is dry storage, testing and discarding bad feed.

Go deeper on this site

- Ch 9. Toxic gases and algal toxins (in this book)
- Ch 7. Heavy metals and mineral poisoning (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Nitrate and nitrite poisoning in animals
- WHO: Mycotoxins fact sheet
- Merck Veterinary Manual: Copper poisoning in animals (mineral feed toxicity background)

CHAPTER 9 OF 17

Toxic gases and algal toxins

How carbon monoxide, ammonia, hydrogen sulphide and nitrogen dioxide poison animals in sheds, pits and silos, and how cyanobacterial toxins make water deadly. The chapter stresses mechanism, rescuer safety, ventilation and prevention.

After this chapter you can

- Explain how carbon monoxide produces tissue hypoxia despite normal oxygen in the lungs
- Describe the irritant action of ammonia and its role in poultry and pig housing
- Explain hydrogen sulphide toxicity from manure pits and why smell is an unreliable warning
- Describe silo filler's disease from nitrogen dioxide

- Classify cyanobacterial toxins and describe the clinical pattern, prevention and first response

Gas and water hazards in the animal environment

Animals live and breathe in the same air for hours. Poor ventilation, fermentation and combustion can turn a shed, manure pit or silo into a hazard. Surface water can also turn toxic when cyanobacteria bloom. These poisonings are usually **sudden, affect several animals and sometimes harm people**.

Gases fall into three action types: **asphyxiants** that stop oxygen delivery or use (carbon monoxide, hydrogen sulphide), **irritants** that burn airway lining (ammonia, nitrogen dioxide), and simple oxygen displacement (carbon dioxide, methane).

The most important practical lesson is safety: many human deaths happen when a person enters a pit or silo to rescue an animal. **Never enter a confined space without proper breathing apparatus and trained help.**

Prevention is largely about design and habit: adequate ventilation sized for the number of animals, maintained heaters, covered and ventilated pits, gas detectors where available and a written emergency plan. Staff should be trained to raise the alarm instead of entering confined spaces alone. After any suspected gas event, ventilate fully before re-entry, examine all animals, and seek urgent veterinary and medical advice.

Carbon monoxide

Carbon monoxide (CO) is colourless and odourless. It comes from incomplete combustion: faulty or unvented heaters, charcoal or gas brooders in poultry sheds, engines running in closed spaces, generators and fires.

Mechanism. CO binds to haemoglobin with far greater affinity than oxygen, forming **carboxyhaemoglobin**. This reduces oxygen carrying capacity and also shifts the oxygen dissociation curve so the remaining oxygen is released poorly. CO also binds to cytochrome oxidase and myoglobin. The lungs are normal and the arterial oxygen tension is normal, yet tissues are starved. This is a common confusion: a normal pulse oximeter reading can be falsely reassuring, because it cannot tell carboxyhaemoglobin from oxyhaemoglobin.

Signs. Weakness, headache-like depression, rapid breathing, incoordination, collapse, convulsions and death. Mucous membranes may look bright cherry red, but this is not always seen. Chicks in brooders may die in numbers. Survivors can have delayed brain injury and abortion.

Response. Move animals into fresh air and give high-concentration oxygen, which displaces CO. Prevention: maintenance of heaters, ventilation and CO detectors.

Ammonia

Ammonia is formed by bacterial breakdown of urine and faeces, especially in wet poultry litter and poorly ventilated pig and calf houses. It has a sharp smell that people notice quickly.

Mechanism. Ammonia dissolves in the moist lining of the eyes and airways, forming an alkaline solution that injures cells and paralyses cilia. This allows bacteria and viruses to colonise the respiratory tract. Chronic low-level exposure is therefore a *predisposing cause* of respiratory disease, not just a direct poison.

Signs. Watery eyes, conjunctivitis and corneal damage (including keratoconjunctivitis in chickens), nasal discharge, coughing, reduced growth and increased susceptibility to infections such as colibacillosis. Very high levels cause acute respiratory distress.

Prevention. Good litter management, dry floors, adequate ventilation and sensible stocking density. A simple rule: if a person finds the air irritating at animal height, it is too much for the animals.

Do not confuse airborne ammonia in sheds with ammonia produced in the rumen after urea feeding.

Hydrogen sulphide

Hydrogen sulphide (H_2S) is released when manure or slurry decomposes without oxygen. The risk is highest when a pit is agitated, emptied or stirred, because trapped gas is suddenly released. The gas is heavier than air and collects in low places.

Mechanism. H_2S inhibits cytochrome c oxidase, the final enzyme of the respiratory chain, so cells cannot use oxygen. This is similar to cyanide in effect. At lower levels

it irritates the eyes and airways.

Warning smell. It smells of rotten eggs at low levels, but higher levels *paralyse the sense of smell*, so absence of smell does not mean safety.

Signs. Sudden collapse and death in pigs and other animals in the building (knock-down), with breathing failure. Lower exposure: eye irritation, coughing, nausea and pulmonary oedema. Workers who enter pits to rescue animals are often victims.

Prevention. Ventilate before and while agitating slurry, remove animals and people from the building during pit work, and never enter pits unprotected. Treatment is removal to fresh air and supportive care with oxygen.

Nitrogen dioxide and silo gases

When green forage with high nitrate is ensiled, fermentation produces **nitrogen oxides**, mainly nitrogen dioxide (NO2). The gas appears within hours and may persist for days to a few weeks after filling. It is yellow to brown, heavier than air and may collect at the silo base and near the feed outlet, entering the animal house or a person's lungs.

Mechanism. NO2 is poorly soluble, so it reaches deep into the lungs, where it forms nitric and nitrous acids that damage the air-blood barrier. The result is pulmonary oedema, and some days or weeks later, scarring bronchiolitis may develop. This delayed phase is a typical feature of **silo filler's disease** in people; animals may show coughing, rapid breathing and sudden death if exposed in poorly ventilated spaces.

Silos also fill with carbon dioxide, which displaces oxygen and silently asphyxiates.

Prevention. Keep people and animals away from fresh silage, ventilate adjacent areas, and follow local silo safety guidance. Seek urgent medical or veterinary help after any exposure, even if the first symptoms seem mild.

Blue-green algae and water-borne toxins

Cyanobacteria (blue-green algae) multiply in warm, still, nutrient-rich water, especially in summer. Wind can push a bloom to a shoreline where animals drink or dogs swim and lick their coats. The water may look green, turn like paint, or form scum, but sometimes shows no obvious change.

Main toxin groups:

- **Hepatotoxins** such as microcystins block protein phosphatases, collapsing the liver cell skeleton and causing liver bleeding. Signs appear within hours to a day or two: vomiting, bloody diarrhoea, weakness, pale or jaundiced membranes, shock.
- **Neurotoxins** such as anatoxin-a (nicotinic receptor agonist) and saxitoxins (sodium channel blockers) cause tremors, paralysis, breathing failure and death within minutes to hours. Anatoxin-a(s) is an anticholinesterase, producing heavy salivation.
- **Cylindrospermopsin** injures liver and kidney more slowly.

Response. There is no specific antidote for most. Remove animals from the water at once, provide clean water, decontaminate (rinse coat; activated charcoal or emesis only on veterinary advice) and give supportive care. Boiling does not remove the toxins. Livestock owners should seek urgent help if animals sicken after water contact.

Prevention includes fencing off affected water, providing alternative water and reducing nutrient run-off into ponds.

Concept cleared

Asphyxiant versus irritant
Carbon monoxide and hydrogen sulphide block oxygen delivery or use; ammonia and nitrogen dioxide burn the airway.

Normal lungs, starved tissues
In CO poisoning the lungs work normally but haemoglobin is occupied, so tissues are hypoxic.

Smell is not a safety test
Hydrogen sulphide paralyses smell at high levels, and carbon monoxide has no smell at all.

Rescuer safety

Never enter a pit, silo or enclosed shed without breathing apparatus and trained backup.

Memory aid: Gas safety: CAHN

Carbon monoxide, Ammonia, Hydrogen sulphide, Nitrogen dioxide. Ask for each: where from, how it acts, and how to ventilate and escape.

Compare and contrast

Toxic gases compared

Gas	Source	Mechanism	Main outcome
Carbon monoxide	Faulty heaters, brooders, engines	Carboxyhaemoglobin, tissue hypoxia	Collapse, cherry-red membranes sometimes
Ammonia	Wet litter, manure	Alkaline irritant to eyes and airway	Conjunctivitis, respiratory disease
Hydrogen sulphide	Manure pits, slurry agitation	Cytochrome c oxidase inhibition	Sudden knock-down deaths
Nitrogen dioxide	Fresh silage	Acid injury deep in lung	Pulmonary oedema, later bronchiolitis

Cyanobacterial toxins

Toxin type	Example	Target	Speed and signs
Hepatotoxin	Microcystin	Liver cells	Hours to days; vomiting, bloody diarrhoea, jaundice
Neurotoxin	Anatoxin-a, saxitoxin	Neuromuscular junction, sodium channels	Minutes to hours; tremor, paralysis
Anticholinesterase	Anatoxin-a(s)	Cholinesterase	Salivation, tremor
Cytotoxin	Cylindrospermopsin	Liver, kidney	Slower; organ failure

Species notes

Poultry

Chicks in brooders are vulnerable to carbon monoxide; ammonia from wet litter damages eyes and airways.

Pigs

Slurry pit hydrogen sulphide causes sudden deaths during agitation; ammonia predisposes to respiratory disease.

Cattle and buffalo

Exposed to silo gases and drinking from pond blooms; livestock may die within hours of ingesting toxic algae.

Dogs

Swim in and lick algal scum, with very rapid neurotoxic or hepatotoxic illness; vomiting after water contact is an emergency.

Horses

Poorly ventilated stables with wet bedding build ammonia and contribute to airway disease.

Clinical pearls

Self-test: 10 questions

1. Carbon monoxide causes hypoxia mainly by:

CO occupies haemoglobin and reduces oxygen delivery.

2. Why can a pulse oximeter mislead in CO poisoning?

The device cannot distinguish the two forms and may read normal.

3. The first priority in suspected CO poisoning is:

Oxygen displaces CO from haemoglobin.

4. Chronic ammonia exposure in poultry houses mainly:

It paralyses cilia and injures mucosa.

5. Hydrogen sulphide inhibits:

This blocks cellular respiration.

6. Why is smell an unreliable warning for hydrogen sulphide?

Olfactory fatigue at high concentrations removes the warning.

7. The main hazard during slurry pit agitation is:

Agitation releases trapped gas, causing knock-down deaths.

8. Silo filler's disease is caused by:

NO_2 from fermenting silage damages the deep lung.

9. Microcystins mainly cause:

They inhibit protein phosphatases in hepatocytes.

10. A dog develops tremor and paralysis within an hour of swimming in a green pond. The likely toxin group is:

Anatoxins and saxitoxins act fast on nerves and muscle.

Key points to revise

1. Carbon monoxide binds haemoglobin and causes tissue hypoxia with normal lungs.
2. Ammonia is an irritant that damages eyes and airways and predisposes to infection.
3. Hydrogen sulphide inhibits cytochrome c oxidase and abolishes the sense of smell at high levels.
4. Nitrogen dioxide from fresh silage injures deep lung and can cause delayed bronchiolitis.
5. Silos and pits are confined spaces; never enter without breathing apparatus.
6. Microcystins are liver toxins; anatoxins and saxitoxins are fast neurotoxins.
7. Most cyanobacterial poisoning has no specific antidote, so removal from the water and supportive care are key.
8. Prevention is ventilation, maintenance, water management and supervised access.

Go deeper on this site

- Ch 10. Photosensitisation (in this book)
- Ch 8. Feed-related toxicities (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- CDC: Carbon monoxide poisoning
- CDC NIOSH: Hydrogen sulfide immediately dangerous to life or health documentation
- CDC: Harmful algal blooms

CHAPTER 10 OF 17

Photosensitisation

Photosensitisation is a sunlight-triggered skin disease caused by photodynamic compounds in the skin. This chapter separates primary, hepatogenous and drug-induced forms, links them to common plants and drugs, and explains the management logic of shade, source removal and liver support.

After this chapter you can

- Define photosensitisation and explain the photodynamic mechanism of skin injury
- Distinguish primary, aberrant-pigment, hepatogenous and drug-induced forms
- Explain why liver damage leads to phylloerythrin-based photosensitisation in herbivores
- Name plants and drugs commonly associated with each form
- Outline the management principles and the points that need urgent veterinary help

What photosensitisation is

Photosensitisation is an abnormal reaction of the skin to light. It is not simple sunburn. A **photodynamic agent** must first reach the skin, either from inside the body (through the blood) or by direct contact. When light falls on that agent it absorbs energy and passes it to oxygen, producing reactive oxygen species. These damage cell membranes in the epidermis and the dermal vessels, so the skin becomes inflamed and may die.

Three ingredients are therefore needed: a photodynamic compound, light of the right wavelength, and exposed skin. Take away any one and the disease does not appear. This is the basis of most management advice.

Lesions are seen on **unpigmented or thinly haired skin** that is exposed to sun, such as the white face, muzzle, ears, eyelids, teats, coronets and back. Pigmented skin and well-haired skin are protected because the pigment or coat absorbs or blocks the light. A black cow with a white face and white feet will show lesions only on the white areas.

A common confusion is to treat photosensitisation as an allergy. It is a toxic, dose-related light reaction and does not need prior sensitisation by the immune system, so a first exposure can cause disease. Another is to expect it only in hot weather: bright light on a cool day is enough, and cloud does not block all the relevant light.

Four ways the photodynamic agent arises

Classification depends on where the photodynamic compound comes from.

1. **Primary (type I) photosensitisation.** The animal eats or is exposed to a preformed photodynamic compound. The liver is normal. The compound is absorbed and reaches the skin directly.
2. **Aberrant endogenous pigment synthesis (type II).** An inherited defect in haem synthesis (porphyria) lets porphyrins build up. This is a genetic disease, reported in cattle, pigs and cats, and it is not a poisoning.
3. **Hepatogenous (type III) photosensitisation.** Liver damage or bile obstruction stops the animal clearing **phylloerythrin**, a normal breakdown product of chlorophyll. It builds up in blood and reaches the skin. This is the commonest form in grazing livestock.
4. **Other or unknown causes.** Some classifications keep a group for cases where the mechanism is not understood.

Drug-induced photosensitisation sits mainly with the primary type: the drug or its metabolite is itself the photodynamic agent. The common confusion is to call every photosensitisation 'liver disease'. Only the hepatogenous form is, and a normal liver does not exclude photosensitisation.

Primary and drug-induced forms

In primary photosensitisation the animal's liver can be completely normal, so there is usually **no jaundice** and liver enzymes are not markedly raised. The skin disease appears within hours to a few days of eating the plant and exposure to sun.

Plants usually named include **St John's wort** (*Hypericum perforatum*, hypericin), **buckwheat** (*Fagopyrum*, fagopyrin) and members of the carrot family such as *Ammi* species (bishop's weed), which contain furocoumarins that can act on contact as well as after ingestion. Check regional flora lists for which species are present in your area.

Drugs reported to sensitise skin to light include phenothiazine, tetracyclines, sulfonamides and some other antimicrobials and diuretics. The practical point is that a drug may be safe in a shaded, housed animal and cause lesions in the same animal at pasture in strong sun. Always ask about sun exposure when starting such

a drug and when reviewing an unexplained skin reaction in a treated animal. Reaction is individual and not every treated animal is affected.

Hepatogenous photosensitisation

Ruminants and horses have gut microbes that break down chlorophyll in green forage to **phylloerythrin**. This is absorbed and normally taken up by the liver and excreted in bile. If the liver is damaged or the bile ducts are blocked, phylloerythrin stays in the circulation and reaches the skin. A healthy animal on lush pasture therefore does not react, while a liver-injured animal on the same pasture does.

Plants and toxins that injure the liver or bile ducts include **Lantana camara** (a widespread weed in India, with lantadenes that cause cholestasis), **Tribulus terrestris** (puncture vine) in sheep, certain tropical grasses such as *Brachiaria* and *Panicum* with saponin-containing fungal-linked disease, bog asphodel (*Narthecium*), and blue-green algae (cyanobacteria) in water. The fungal toxin **sporidesmin** from *Pithomyces chartarum* on pasture causes facial eczema in sheep and cattle in some countries. Verify which are relevant locally.

Because the cause is the liver, these animals are often **jaundiced**, may be dull and lose weight, and show raised liver enzymes and bile acids. The prognosis depends on the liver injury as much as on the skin.

Clinical signs and diagnosis

Signs follow the same pattern in every form. Early: restlessness, rubbing, shaking of the head and ears, reddening and swelling of exposed skin. Later: oedema of the face and ears (sometimes called 'big head' in sheep), serous exudate, crusts, cracking, and in severe cases necrosis and sloughing of skin. The eyes may show photophobia, tearing and corneal cloudiness. Animals seek shade and avoid sun.

Secondary problems matter: fly strike and bacterial infection of damaged skin, weight loss because grazing in daylight stops, and in hepatogenous cases the signs of liver failure, including hepatic encephalopathy.

Diagnosis combines the history (plant or drug access, sun exposure), distribution of lesions on unpigmented skin, and tests of liver function when hepatogenous disease is suspected. Differentials include sunburn, contact dermatitis, bacterial or

fungal skin disease, and in cattle certain viral diseases causing teat and muzzle lesions.

Management concepts and when to seek help

Management follows the three ingredients.

- **Remove the light.** Move the animal into a shed or dense shade at once and graze at night or on cloudy days until recovery.
- **Remove the source.** Stop the plant, mouldy or contaminated feed, or the causative drug. Review the pasture and water supply.
- **Treat the skin.** Clean, protect against flies and secondary infection, and give analgesia. Anti-inflammatory treatment is chosen by the clinician.
- **Support the liver** in hepatogenous cases, with good-quality feed and fluids as needed. There is no antidote for most causes.

Call a veterinarian urgently for any animal with swollen face or eyelids, corneal damage, jaundice, neurological signs, or when several animals in a group are affected, because this suggests a pasture or feed problem that will spread. Prevention means weed control (for example removing Lantana from grazing land), avoiding grazing of risky plants during growth stages and sunny periods, and caution with photosensitising drugs in light-skinned animals kept outdoors.

Concept cleared

Concept cleared: Photodynamic reaction

Think of a solar panel connected to a firecracker. The agent in the skin catches the light like the panel and hands the energy to oxygen, which goes off as reactive oxygen species and burns the cells around it. No light, no spark, so shade is a treatment.

Concept cleared: Why the liver matters in type III

The liver is the dustbin for phylloerythrin. If the bin is blocked or broken, the waste piles up in the blood and spills into the skin. A normal grass diet then becomes a source of light-sensitive waste.

Concept cleared: Why only white skin

Pigment and hair act like a sunscreen and a hat. Where they are absent, light reaches the agent in the tissue, so lesions follow the white patches of the animal.

Concept cleared: Primary versus hepatogenous

In primary disease the poison itself is the sensitiser and the liver is healthy. In hepatogenous disease the poison harms the liver and the liver failure creates the sensitiser. Ask: is the liver sick? Jaundice and raised liver enzymes point to type III.

Memory aid: The three ingredients

Think A-L-S: Agent, Light, Skin that is unpigmented. Remove any one and the disease stops. For the four forms remember P-A-H-D: Primary, Aberrant pigment, Hepatogenous, Drug.

Compare and contrast

Forms of photosensitisation

Form	Source of photodynamic agent	Liver	Examples
Primary (type I)	Eaten or applied preformed compound	Normal	St John's wort, buckwheat, Ammi species, some drugs
Aberrant pigment (type II)	Inherited porphyrin defect	Normal function	Congenital porphyria in cattle, pigs, cats
Hepatogenous (type III)	Phylloerythrin retained	Damaged or obstructed	Lantana, Tribulus, cyanobacteria, sporidesmin
Drug-induced	Drug or metabolite in skin	Usually normal	Phenothiazine, tetracyclines, sulfonamides

Sunburn versus photosensitisation

Feature	Sunburn	Photosensitisation
Cause	UV light alone	Light plus a photodynamic agent
Group effect	Any unprotected skin	Only animals exposed to the agent
Systemic signs	Rare	Possible, such as jaundice in type III
Control	Shade and sunscreen	Shade plus removing the agent

Species notes

Cattle

Hepatogenous disease from Lantana is a classic problem in cattle where the weed is common. White-skinned areas of Holstein-type and crossbred animals are most affected; congenital porphyria is also described.

Sheep

Often affected by hepatogenous forms, with facial swelling ('big head') and ear oedema, as with Tribulus and facial eczema; wool covers much of the body, so face and ears show the lesions.

Horse

Can develop photosensitisation on white-marked limbs and muzzle; liver disease from toxic plants or feed contamination should be considered.

Pig

White-skinned breeds are prone to sunburn-like lesions; buckwheat and porphyria are described causes.

Cat and dog

Rare compared with livestock. Light-coated cats on drugs or with porphyria can develop ear and nose lesions; keep indoors in strong sun.

Clinical pearls

Self-test: 10 questions

1. Which three factors are required for photosensitisation to occur?

A photodynamic agent, light and exposed lightly pigmented skin are all required.

2. Phylloerythrin is formed from which dietary substance?

Gut microbes break chlorophyll down to phylloerythrin.

3. A cow with jaundice, raised liver enzymes and skin lesions on white areas most likely has which form?

Liver damage with jaundice points to hepatogenous photosensitisation.

4. Which plant is a common cause of hepatogenous photosensitisation and is widespread in India?

Lantana contains lantadenes that cause cholestasis. The others cause primary forms.

5. St John's wort causes photosensitisation through which compound?

Hypericin is the photodynamic pigment in Hypericum perforatum.

6. Congenital porphyria is best described as

It is a genetic defect that allows porphyrins to accumulate.

7. Which is the most important first step in managing a photosensitised animal?

Removing light interrupts the photodynamic reaction.

8. Why do lesions appear on white-skinned areas?

Pigment and haircoat shield against the light that activates the agent.

9. Which drug group has been reported to cause drug-induced photosensitisation?

Tetracyclines, sulfonamides and phenothiazine are reported photosensitisers.

10. Several animals on the same pasture develop facial swelling and jaundice. What is the best action?

Group outbreaks suggest a feed or pasture source that needs urgent investigation.

Key points to revise

1. Photosensitisation needs a photodynamic agent, light and exposed unpigmented skin.
2. Light activates the agent, which produces reactive oxygen and injures skin.
3. Primary form: preformed agent eaten or contacted, liver normal.
4. Hepatogenous form: liver damage prevents phylloerythrin excretion.
5. Congenital porphyria is an inherited form, not a poisoning.
6. Drugs such as phenothiazine, tetracyclines and sulfonamides may sensitise skin.
7. Management: shade, remove the source, skin care, liver support.
8. Urgent help is needed for jaundice, eye damage, neurological signs or multiple animals affected.

Go deeper on this site

- Ch 11. Household and pet toxins (in this book)
- Ch 9. Toxic gases and algal toxins (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Photosensitization in Animals
- Merck Veterinary Manual: Overview of Veterinary Toxicology
- ASPCA: Toxic and Non-Toxic Plants

CHAPTER 11 OF 17

Household and pet toxins

Many of the commonest poisonings in dogs and cats come from ordinary household items: foods, plants, medicines, antifreeze and cleaners. This chapter explains the mechanism, signs, species differences and decontamination logic for chocolate, grapes, xylitol, onion and garlic, lilies, antifreeze, human painkillers and cleaning products.

After this chapter you can

- Explain the mechanism of toxicity of chocolate, xylitol, onion and garlic, lilies and ethylene glycol
- Recognise the typical clinical signs and their time course for each toxin
- Identify the species that is most at risk for each toxin
- Explain when decontamination is appropriate and when it is harmful
- Describe prevention advice and when to seek urgent veterinary help

Why household toxins matter

Pets explore with their mouths, and homes contain foods, plants, medicines and chemicals meant for people. Pet owners also tend to share human food or leave medicines within reach. In India, additional exposure comes from foods such as raisins in sweets, onion and garlic in cooked household food, and from floor and toilet cleaners and 'phenyl' used on floors.

The approach to any suspected exposure is the same. Identify the product and the animal, estimate how much and how long ago, and ask what signs are present. Then decide whether to decontaminate, which antidote or supportive care is needed, and how long to monitor. The most important lesson is that **timing and the toxin both decide the plan**. A step that helps within an hour (such as induced

vomiting) can be harmful if the animal is already sedated, convulsing or has swallowed a corrosive.

This chapter gives concepts only. Treatment decisions and quantities must come from a veterinarian or a poison information service, which can calculate risk from the product and body weight.

Chocolate, grapes and xylitol

Chocolate contains the methylxanthines **theobromine** and caffeine. They block adenosine receptors, inhibit phosphodiesterase and increase catecholamine effects, so the heart and nervous system are overstimulated. Dogs eliminate theobromine slowly, and it is recirculated through bile, so signs last long. Dark chocolate, cooking chocolate and cocoa powder are more dangerous than milk chocolate because they contain more methylxanthine per gram. Signs: vomiting, restlessness, thirst, rapid heart rate, arrhythmia, tremors, and in severe cases seizures and high temperature. Management uses decontamination when the ingestion is recent, repeated activated charcoal because of the recirculation, and supportive care with heart monitoring.

Grapes and raisins can cause acute kidney injury in dogs. The toxic agent has not been clearly identified, and individual dogs vary unpredictably, so any known ingestion should be taken seriously. Early signs are vomiting and lethargy within hours, followed by reduced urine output and kidney failure over one to three days. Early decontamination and fluid therapy with kidney monitoring are the basis of treatment.

Xylitol is a sweetener in sugar-free gum, sweets and some other foods. In dogs it triggers a large release of insulin, causing sudden **hypoglycaemia** with weakness, ataxia, collapse and seizures. Larger exposures can also cause liver injury. Blood glucose, liver values and electrolytes must be monitored. Do not induce vomiting in a dog that is already weak or dull. Check how xylitol is handled in a poison service protocol, as activated charcoal binds it poorly.

Onion, garlic and lilies

Onion and garlic (the genus *Allium*) contain sulphur compounds that cause **oxidative damage to red cells**. Haemoglobin is denatured into Heinz bodies, the

cells are removed early, and haemolytic anaemia and methaemoglobin can result. The effect is dose-related and cumulative, and signs may appear only after a delay of one to several days: pale or yellow gums, dark urine, weakness, rapid breathing. Cooked, dried and powdered forms are still toxic. **Cats** are very sensitive, and some dog breeds, notably Japanese breeds, are reported to be more sensitive. There is no specific antidote. Treat with decontamination if recent, then supportive care, oxygen and transfusion if needed.

True lilies and daylilies (*Lilium* and *Hemerocallis*) are a major cause of acute kidney failure in **cats**. Leaves, flowers, pollen and even vase water are dangerous, and a small amount can be enough. The toxin is not fully identified, and it injures the renal tubules. Dogs and horses are generally considered not at risk from lilies. Early signs: vomiting, drooling, lethargy and loss of appetite within hours. If untreated, kidney failure follows over a day or two, with changes in urination. Immediate veterinary treatment, with decontamination and intravenous fluids started early, greatly improves the outcome.

Antifreeze and ethylene glycol

Ethylene glycol is found in antifreeze and coolants. It has a sweet taste and attracts animals. The parent compound is only mildly toxic. The harm comes from **metabolism**. Alcohol dehydrogenase converts it to glycolaldehyde, then to glycolic, glyoxylic and finally oxalic acid. Glycolic acid causes a severe metabolic acidosis, and oxalate binds calcium to form **calcium oxalate crystals** that damage the renal tubules.

Signs appear in stages. First, within hours, the animal appears drunk, with ataxia, vomiting and increased thirst. Later, there are cardiopulmonary signs and acidosis. Finally, over one to three days, acute kidney failure with little or no urine develops. Cats progress faster and have a lower tolerance than dogs.

The antidote logic is important for exams. Antidotes such as **fomepizole** (and ethanol where that is not available) compete for alcohol dehydrogenase so that ethylene glycol is not converted to its toxic products. They work only if given early, before most of the compound has been metabolised, and the cat dose differs from the dog dose, so use a protocol. Once kidney failure is established, antidotes are of little use and the outlook is poor. Therefore any suspected ingestion is an **emergency**, and owners should come in at once rather than wait for signs.

Prevention: store antifreeze securely, clean up spills, and consider less toxic products.

Human painkillers and cleaning products

Human **painkillers** are a common source of poisoning. Ibuprofen, naproxen and aspirin inhibit cyclo-oxygenase and cause gastric ulceration and kidney injury. **Paracetamol** is particularly dangerous to cats, which are poor at glucuronidation, and leads to methaemoglobin, haemolysis and facial swelling. Medicines made for people are not scaled for pets, so never advise owners to give human tablets. Chapter 12 covers these in more detail.

Cleaning products divide into groups with different problems. Strong acids and alkalis (some toilet cleaners, drain cleaners) are corrosive and burn the mouth, oesophagus and stomach. Bleach irritates. Cationic detergents and disinfectants can burn tissues. Phenol-based products such as 'phenyl' can be absorbed through skin and by licking, and cats are again vulnerable because of poor glucuronidation. Signs: drooling, pawing at the mouth, vomiting, pain and respiratory distress from fumes.

The golden rule for corrosives is **do not induce vomiting**, because the substance burns twice on the way back up. Rinse the mouth and skin, remove from the area, keep the container and call for veterinary help.

General approach, prevention and urgent help

Decontamination reasoning in brief:

- **Vomiting** may help only when the ingestion is recent, the animal is alert, and the substance is not corrosive or a hydrocarbon. It should be done by or on the advice of a veterinarian.
- **Activated charcoal** binds many toxins in the gut but does not bind everything, and it can be dangerous if the animal is sedated or may inhale it.
- **Antidotes** exist for only a few of these toxins, such as fomepizole for ethylene glycol. For the others, supportive care (fluids, glucose, oxygen, heart monitoring) keeps the animal alive while the body recovers.
- **Monitoring time** depends on the toxin: some, like lily, grapes, ethylene glycol and onion, cause problems days after the exposure, so a well-looking animal is

not safe.

Prevention: keep foods, medicines and chemicals in closed cupboards, keep plants out of reach of cats, use child-proof containers, and educate owners not to share human food. Teach owners to keep the packaging, estimate the amount and time, and phone a veterinarian or a poison information service at once. Do not wait for signs, because signs often start after the best window for treatment has passed.

Concept cleared

Concept cleared: Lethal synthesis

Ethylene glycol is like a harmless-looking parcel that becomes a bomb when opened by the body's own enzyme. Fomepizole blocks the enzyme and the parcel passes out unopened.

Concept cleared: Delayed toxicity

Onion, grapes, lilies and antifreeze look harmless for hours or days. Damage builds quietly in red cells or kidneys. This is why the history, not the current appearance, decides the response.

Concept cleared: Why cats are different

Cats have limited glucuronidation, so drugs and phenols that rely on it, such as paracetamol and phenolic cleaners, linger and cause harm. Add the lily kidney effect and ethylene glycol sensitivity, and cats need extra caution.

Concept cleared: When not to make a pet vomit

If the swallowed substance is corrosive, if the pet is weak, sedated or convulsing, or if inhalation into the lungs is likely, vomiting adds injury. Ask a veterinarian first.

Memory aid: Home hazard list

Think C-G-X-O-L-A-P-C: Chocolate, Grapes, Xylitol, Onion, Lilies, Antifreeze, Painkillers, Cleaners. Keep them away from the pet and the pet away from them.

Compare and contrast

Key household toxins

Toxin	Main target	Key mechanism	Main at-risk species
Chocolate	Heart and brain	Methylxanthines, adenosine block	Dogs
Grapes and raisins	Kidney	Unknown agent, tubular injury	Dogs
Xylitol	Pancreas and liver	Insulin release, hypoglycaemia	Dogs
Onion and garlic	Red cells	Oxidative damage, Heinz bodies	Cats, dogs
Lilies	Kidney	Tubular injury	Cats
Ethylene glycol	Kidney	Metabolites, acidosis, oxalate crystals	Dogs and cats

Decontamination decisions

Situation	Vomiting	Notes
Recent, alert, non-corrosive	May be considered by a veterinarian	Does not work well after a long interval
Corrosive acid, alkali or cleaner	Avoid	Rinse and get veterinary care
Weak, sedated or seizing	Avoid	Risk of inhalation
Xylitol or ethylene glycol	Specific advice needed	Antidote or glucose care may be the priority

Species notes

Dog

Most chocolate, grape and xylitol cases are in dogs, which eat indiscriminately. Dogs are also affected by onion, garlic and antifreeze.

Cat

Very sensitive to lilies, onion and garlic, paracetamol, phenolic cleaners and antifreeze. Cats groom, so skin contamination becomes oral.

Horse

Lilies are not considered a concern in horses, but chocolate by-products, onions and cleaning chemicals in the stable can still cause harm.

Cattle and small ruminants

Antifreeze and household chemicals dumped near yards can be consumed. Onion in large amounts, such as waste, can cause haemolysis in ruminants.

Birds

Avocado, chocolate and fumes from some non-stick or cleaning products are of concern; seek advice for each product.

Clinical pearls

Self-test: 10 questions

1. The main toxic compounds in chocolate are

Theobromine and caffeine are methylxanthines.

2. Xylitol causes which early problem in dogs?

It stimulates insulin release in dogs.

3. Onion toxicity mainly damages which cells?

Oxidative damage leads to Heinz bodies and haemolysis.

4. Which species is most at risk of kidney failure from lilies?

Lily kidney injury is a feline problem.

5. Why is ethylene glycol dangerous?

Metabolites cause acidosis and calcium oxalate crystals in kidney tubules.

6. Fomepizole acts by

It blocks formation of toxic metabolites.

7. Which step is inappropriate after swallowing a strong toilet cleaner?

Corrosives re-injure the oesophagus and mouth on the way up.

8. Why is repeated activated charcoal useful in chocolate poisoning?

Recirculation prolongs exposure, and charcoal traps it in the gut.

9. A dog ate raisins and looks normal. What is correct?

Kidney injury follows after a delay, and early treatment works best.

10. Why are cats particularly sensitive to phenolic cleaners and paracetamol?

Cats clear these compounds slowly.

Key points to revise

1. Household poisoning is decided by the toxin, amount, time and species.
2. Chocolate: methylxanthines, long-lasting signs in dogs.
3. Grapes and raisins: kidney injury of unpredictable risk in dogs.
4. Xylitol: insulin release and hypoglycaemia in dogs.
5. Onion and garlic: oxidative haemolysis, delayed signs.
6. Lilies: kidney failure in cats from small exposures.
7. Ethylene glycol: toxic metabolites; fomepizole works only early.
8. Corrosives: no vomiting; rinse and seek help.

Go deeper on this site

- Ch 12. Recreational drugs and human medicines in pets (in this book)
- Ch 10. Photosensitisation (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Chocolate Toxicosis in Animals
- Merck Veterinary Manual: Ethylene Glycol Toxicosis in Animals
- ASPCA: People Foods to Avoid Feeding Your Pets

CHAPTER 12 OF 17

Recreational drugs and human medicines in pets

Pets are often poisoned by human drugs left within reach or given by well-meaning owners. This chapter covers cannabis, opioids, antidepressants, ADHD stimulants, sleep aids, paracetamol and NSAIDs, with the mechanism of each, the signs to recognise, species differences and a sensible response.

After this chapter you can

- Explain the mechanism of toxicity of cannabis, opioids, antidepressants, stimulants, sleep aids, paracetamol and NSAIDs

- Recognise the characteristic clinical picture of each drug class
- Explain why cats and dogs respond differently to paracetamol and NSAIDs
- Describe the antidote and decontamination reasoning for each class
- Give owners a clear first-response plan and know when urgent help is needed

Why human drugs poison pets

A tablet that is safe for a 60 kg person may be a serious dose for a 5 kg dog or cat. Pets also metabolise drugs differently from humans, so even a normal human dose can behave like an overdose. Common routes of exposure are tablets left on a table, a handbag or a bedside, dogs chewing blister packs and bottles, owners giving human painkillers to relieve pain, and cannabis or edible products dropped or left open.

The first step is always the **history**: which drug, which formulation (immediate or extended-release, or combination products), how many tablets, how long ago, and the weight and species of the animal. Keep the package. Many human medicines contain more than one drug, and some preparations also contain xylitol or chocolate.

Do not try home remedies or induce vomiting without veterinary advice. Some of these drugs cause sedation or seizures within minutes, and vomiting then risks inhalation. This chapter gives concepts only. For quantities, use a veterinarian or poison information service, and check any local rules on controlled substances.

Cannabis and opioids

Cannabis (marijuana, hashish and bhang preparations, and edible products) contains **THC**, which acts on cannabinoid CB1 receptors in the brain. Dogs are the commonly affected species and are very sensitive. Signs appear within hours: wobbling and ataxia, depression or sedation, dribbling urine, slow heart rate, low body temperature, dilated pupils, vomiting, and sometimes agitation or tremors. Severe cases may progress to seizures or coma. Most animals recover with supportive care in a quiet, warm place, but they need monitoring because of the risk of aspiration and low temperature. Edibles are a hazard because of added

chocolate, xylitol or other ingredients. Legal status of cannabis in India is specific and conditional; check the current notification before advising owners.

Owners may be reluctant to admit exposure. Reassure them that treatment depends on honesty, and that clinicians treat the pet, not the owner.

Opioids (morphine, codeine, tramadol, fentanyl patches, buprenorphine, heroin) act on mu receptors. In dogs the typical picture is sedation, slow breathing, slow heart rate, low temperature and small pupils. Cats may be excited with dilated pupils. Tramadol also affects serotonin and noradrenaline, so seizures and serotonin-type signs can occur. The antidote is **naloxone**, which reverses respiratory depression, but its action is shorter than that of many opioids, so the animal may become sedated again and needs prolonged monitoring. Skin patches should be recovered and not left on the animal.

Antidepressants, ADHD drugs and sleep aids

Antidepressants. Selective serotonin reuptake inhibitors and related drugs increase serotonin. Large exposures can cause **serotonin syndrome**: agitation, tremors, increased heart rate, high temperature, dilated pupils, vomiting and diarrhoea, and sometimes seizures. Some animals instead become sedated. Tricyclic antidepressants affect the heart rhythm and the nervous system. Bupropion is known for causing seizures. Treatment is supportive: control of tremors and seizures, cooling, fluids and monitoring of heart rhythm. Drugs that block serotonin, such as cyproheptadine, may be used by a clinician. Avoid vomiting if signs are developing.

ADHD stimulants (amphetamines, methylphenidate and related drugs) are potent central nervous system and heart stimulants. Pets show hyperactivity, panting, dilated pupils, fast heart rate, high blood pressure, tremors, high temperature and seizures. Extended-release capsules prolong the period of risk. Intensive care with sedation, cooling, fluids and heart monitoring is the mainstay, and the signs can persist for many hours.

Sleep aids. Benzodiazepines and 'Z-drugs' such as zolpidem act on the GABA-A receptor. They cause sedation and ataxia in many animals, but in some dogs and cats they cause paradoxical agitation, so you cannot predict the response. Respiratory depression is more likely when taken with alcohol or opioids. Flumazenil

can reverse benzodiazepines in some cases; a clinician decides. Melatonin products are generally considered low risk, but combinations and other ingredients may not be.

Paracetamol

Paracetamol (acetaminophen) is metabolised in the liver by conjugation. A small part is converted into a reactive metabolite which is normally neutralised by glutathione. When too much is taken, glutathione runs out and the metabolite damages cells.

Cats are the most sensitive species because they have poor glucuronidation, so more drug is pushed down the toxic pathway, and their red cells are prone to oxidation. Even a single tablet can be dangerous. The result is **methaemoglobin** (chocolate-brown blood, blue-grey gums, difficulty breathing), Heinz body haemolysis, and swelling of the face and paws. **Dogs** are more tolerant, but higher exposures cause liver injury, and sometimes methaemoglobinaemia and dry eye (keratoconjunctivitis sicca).

The antidote is **N-acetylcysteine**, which replenishes glutathione. It works best when started early. Decontamination, oxygen and supportive care are added. A key exam point: never give paracetamol to a cat, and do not advise it for dogs without veterinary direction. Many combination cold remedies contain paracetamol.

NSAIDs and other human painkillers

Non-steroidal anti-inflammatory drugs such as ibuprofen, naproxen, diclofenac and aspirin inhibit cyclo-oxygenase. Prostaglandins protect the stomach lining and maintain kidney blood flow, so inhibition causes **gastric irritation and ulceration, bleeding and acute kidney injury**. High exposures can also cause neurological signs. Signs include vomiting (sometimes with blood), black stools, abdominal pain, lethargy, poor appetite and later increased thirst or reduced urine output. Signs may be delayed for a day or more.

Species differences are important. Cats clear many NSAIDs slowly, so smaller amounts cause problems. Dogs differ between drugs and individuals. Several drugs are licensed for animals, but human products are not dosed or formulated for them, and an animal NSAID should only be used as prescribed. Never give another NSAID

or a corticosteroid on top of a suspected overdose, because the risk of ulcer and kidney damage adds up.

Management includes decontamination if recent, repeated activated charcoal in some cases because of bile recirculation, stomach protection, fluid therapy to support the kidneys, and monitoring of kidney values for several days. A well-looking animal after an NSAID overdose is not out of danger.

Recognition and response

Think of drug poisoning when a pet suddenly shows odd behaviour: wobbling, unusual sleepiness, agitation, tremors, vomiting, fast or slow heart rate, abnormal pupils or collapse, especially in a household with drugs or a young animal exploring. Match the picture to the class:

- Wobbly, urinating and dilated pupils: think cannabis.
- Slow breathing and small pupils in a dog: think opioid.
- Agitated, hot, tremors, fast heart: think stimulant or antidepressant.
- Blue-grey gums and swollen face in a cat: think paracetamol.
- Vomiting blood and later kidney signs: think NSAID.

Response: remove access to any remaining drug, keep the packaging, note the time, and contact a veterinarian or a poison information centre immediately. Do not give milk, salt water or other home emetics. Human urine drug screening kits are unreliable in animals and should not be used alone to rule drugs in or out. Treat the animal according to its signs even if the history is uncertain.

Seek urgent help for any seizure, collapse, breathing difficulty, severe agitation, or ingestion of extended-release, combination or fentanyl products. Prevention: store medicines high and closed, give pets only medicines prescribed for them, and tell owners that a safe medicine for them may not be safe for their pet.

Concept cleared

Concept cleared: Same drug, different animal

Drug handling is like a factory line. Humans have many workers for paracetamol. Cats have too few glucuronidation workers, so the extra drug goes to the toxic side line. Species, not just weight, sets safety.

Concept cleared: Antidotes versus supportive care

Only some drugs have a true antidote: naloxone for opioids and N-acetylcysteine for paracetamol. For cannabis, stimulants and antidepressants, treatment means keeping the body safe (airway, temperature, seizures, heart) until the drug wears off.

Concept cleared: Short antidote, long drug

Naloxone is like a short-acting shield against a long-acting arrow. When it wears off, the opioid is still there and the animal may become sedated again, so watch after reversal.

Concept cleared: Extended-release products

A slow-release capsule is a time bomb with a long fuse. Signs may start late and last much longer, so monitoring continues beyond the first hours.

Memory aid: Cannabis signs

Cannabis in dogs, think S-A-D-P: Sedation, Ataxia, Dribbling urine, Pupils dilated, with a slow heart rate and low temperature. For cats remember: no paracetamol, no human NSAIDs.

Compare and contrast

Drug class recognition

Drug class	Mechanism	Typical signs	Specific antidote
Cannabis (THC)	CB1 receptor activation	Ataxia, dribbling urine, slow heart, sedation	None; supportive care
Opioids	Mu receptor activation	Sedation, slow breathing, small pupils (dog)	Naloxone
SSRIs and antidepressants	Raised serotonin or heart effects	Agitation, tremor, high temperature, seizures	None; serotonin blocker may be used
ADHD stimulants	Catecholamine release	Hyperactivity, fast heart, high temperature	None; supportive care
Paracetamol	Reactive metabolite, methaemoglobin	Blue-grey gums, face swelling (cat), liver injury (dog)	N-acetylcysteine
NSAIDs	COX inhibition	Vomiting, ulcers, kidney injury	None; gastroprotection and fluids

Cat versus dog

Drug	Cat	Dog
Paracetamol	Highly sensitive: methaemoglobin, haemolysis	Less sensitive: liver injury at higher exposure
NSAIDs	Slow clearance, small exposures can harm	Ulcers and kidney injury, varies by drug
Opioids	May be excited	Usually sedated
Cannabis	Affected but fewer reports	Very sensitive, common

Species notes

Dog

Most exposures are in dogs, which chew packaging. Cannabis, antidepressants, stimulants and

Cat

Highly sensitive to paracetamol and many NSAIDs. Cats may be excited rather than sedated by opioids. Small

NSAIDs are frequent. Extended-release capsules and blister packs can make quantities hard to judge.

exposures are enough to cause harm.

Horse

Medicines given by owners or stored in the barn are a risk. Equine NSAIDs have narrow margins in foals and dehydrated animals, and human drugs should not be used.

Cattle and small ruminants

Rarely affected by recreational drugs, but cannabis plants and discarded medicines can be eaten. NSAIDs and other drugs must be used only in the labelled way.

Birds and small mammals

Small body size makes any exposure serious. Ferrets, rabbits and birds need immediate advice after any ingestion.

Clinical pearls

Self-test: 10 questions

1. THC produces its effects mainly by acting on which receptor?

THC is a CB1 agonist in the brain.

2. Which antidote reverses opioid respiratory depression?

Naloxone is an opioid antagonist.

3. A cat that swallowed paracetamol has blue-grey gums and a swollen face. What has formed?

Methaemoglobin cannot carry oxygen and causes cyanosis.

4. Why are cats sensitive to paracetamol?

Limited conjugation sends more drug through the toxic pathway.

5. Serotonin syndrome includes which combination?

Excess serotonin causes neuromuscular and autonomic hyperactivity.

6. NSAID toxicity mainly affects which organs?

COX inhibition reduces protective prostaglandins in the gut and kidney.

7. Which is a reason to avoid inducing vomiting at home?

Rapid CNS signs make aspiration likely.

8. Why must dogs be watched after naloxone?

Re-sedation can occur.

9. Extended-release stimulant capsules are especially dangerous because

Slow release extends the exposure window.

10. What is the best first response to suspected drug ingestion in a pet?

Early advice allows timely decontamination and the right antidote.

Key points to revise

1. Human drugs poison pets through size and species metabolic differences.
2. THC acts on CB1 receptors; signs are ataxia, sedation and dribbling urine in dogs.
3. Opioids depress breathing; naloxone reverses but is short acting.
4. Antidepressants and stimulants cause tremors, high temperature and seizures.
5. Sleep aids can sedate or cause paradoxical agitation.
6. Paracetamol causes methaemoglobinaemia in cats; N-acetylcysteine is the antidote.
7. NSAIDs cause ulcers and kidney injury, with delayed signs.
8. Do not induce vomiting at home without advice; call a veterinarian or poison centre.

Go deeper on this site

- Ch 13. Venoms, bites and stings (in this book)
- Ch 11. Household and pet toxins (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Overview of Veterinary Toxicology
- ASPCA: People Foods to Avoid Feeding Your Pets
- ASPCA Animal Poison Control

CHAPTER 13 OF 17

Venoms, bites and stings

How venoms from snakes, scorpions, toads, bees and spiders injure animals, which signs point to which toxin family, and the reasoning behind first aid and antivenom use in Indian practice. The focus is on mechanism and decision-making, not on doses.

After this chapter you can

- Distinguish venom, poison and toxin, and name the main Indian venomous snakes

- Contrast neurotoxic, haemotoxic and local tissue-damaging snake venoms and the signs each produces
- Explain the principle of polyvalent antivenom and why it is time-critical and not always sufficient
- Describe the toxic mechanisms and clinical picture of scorpion, toad, bee and spider exposures
- List correct and incorrect first-aid steps and say when urgent veterinary help is needed

Venom, poison and toxin

A **toxin** is any harmful substance made by a living organism. A **venom** is a toxin mixture delivered actively through a bite or sting, by a fang, stinger or spine. A **poison** harms when swallowed, inhaled or absorbed. A toad is therefore poisonous (its skin secretion harms an animal that mouths it), while a cobra is venomous.

Venoms are not single chemicals. They are cocktails of enzymes, peptides and small molecules, and each component targets a different system. This is why one bite can cause nerve paralysis, bleeding and tissue death together, and why the clinical picture depends on the species of the animal that bit.

Indian snakes and their venom types

In India the medically important snakes are traditionally called the **big four**: the spectacled cobra, the common krait, Russell's viper and the saw-scaled viper. Other snakes can be dangerous locally, but the standard antivenom is built around these four.

- **Cobra** (elapid): venom contains post-synaptic neurotoxins that block the acetylcholine receptor at the neuromuscular junction, plus cytotoxins that cause painful local swelling and necrosis.
- **Krait** (elapid): venom acts mainly at the nerve terminal (pre-synaptic) and can cause progressive paralysis with little local swelling, so the bite may be missed. Bites often occur at night.
- **Russell's viper and saw-scaled viper**: venom is haemotoxic. It activates or consumes clotting factors, producing a consumption coagulopathy with

bleeding, along with swelling at the site. Russell's viper envenoming can also injure the kidney.

A common confusion is to think that paralysis always means a neurotoxic snake and bleeding always means a viper. Overlap exists, so treat the whole animal, not only one sign.

Snake envenomation in animals: signs and reasoning

Dogs, cats, cattle, buffalo, horses and small ruminants are bitten, usually on the face, muzzle or limbs while grazing or investigating. Many bites are unwitnessed, so the history may only be sudden swelling, weakness or collapse.

Signs follow the venom type. Neurotoxic bites cause drooling, ptosis, difficulty swallowing, weakness and respiratory failure. Haemotoxic bites cause swelling, bruising, bleeding from the bite and mucosae, and prolonged clotting. A bedside whole-blood clotting test, in which blood left in a clean glass tube fails to clot within a set time, is used in human medicine to show venom-induced coagulopathy and is also a practical clue in animals. Check current clinical guidance for how to use it.

Bite size, species and body size matter. A small animal receives a larger venom load for its weight and may deteriorate faster. A dry bite, in which no venom is injected, also happens, so absence of signs early on does not prove safety. Watch the animal, do not assume.

First aid and antivenom concepts in India

The aims of first aid are to slow venom spread, avoid harm and reach a veterinarian quickly. Sensible steps are to keep the animal calm and as still as possible, limit the movement of the bitten part, and transport without delay.

Harmful practices include cutting or incising the bite, sucking the wound, tight tourniquets, ice, applying herbal or chemical pastes and delaying treatment to consult a healer. They add infection, tissue loss or ischaemia and waste time. Specific bandaging methods such as pressure immobilisation are recommended for some neurotoxic bites in some settings and are debated for others, so follow current guidance and do not improvise.

Antivenom is the only specific treatment. Indian polyvalent antivenom is made by immunising horses and purifying antibody fragments or whole immunoglobulin that

bind venom from the big four. It neutralises venom that is still circulating. It cannot reverse damage already done and is less reliable against venoms of other snakes. Because it is a foreign protein, anaphylactoid reactions can occur, so adrenaline and supportive drugs should be ready. Antivenom supply and its use in animals vary and should be confirmed locally, since shortages and quality problems are widely reported by WHO.

In neurotoxic cases, anticholinesterase drugs are sometimes tried as a supportive measure and ventilatory support may be life-saving. Wound care, fluids, analgesia and monitoring of clotting and renal function complete the plan.

Scorpion, toad, bee and spider exposures

Scorpions. The Indian red scorpion is the best-known dangerous species. Its venom acts on sodium and potassium channels and triggers a massive release of catecholamines, the so-called autonomic storm. Signs include intense pain, salivation, vomiting, sweating, restlessness, rapid or irregular heartbeat, high or low blood pressure and, in severe cases, pulmonary oedema. Treatment is mainly supportive and symptom-directed; specific antivenom exists but availability varies.

Toads. Dogs that mouth or lick toads absorb bufadienolides from skin glands. These compounds inhibit sodium-potassium ATPase in a digoxin-like way. Signs begin quickly: profuse salivation, pawing at the mouth, vomiting, tremor, arrhythmia and seizures. Immediate rinsing of the mouth, with the head held down so that water runs out and is not swallowed, is the key first step, followed by urgent veterinary care.

Bees and wasps. A single sting causes local pain and swelling. Allergic animals may develop anaphylaxis with collapse, vomiting, facial oedema and respiratory distress. Mass stinging, from many stings, behaves like a true venom overdose, with haemolysis, muscle damage and kidney injury. A honeybee sting stays in the skin and should be flicked or scraped off quickly.

Spiders. Clinically significant spider bites are uncommon in Indian veterinary practice. Classic examples elsewhere are widow spiders, whose latrotoxin causes painful muscle rigidity, and recluse spiders, whose venom causes tissue necrosis. Any suspected case should be managed on its clinical signs.

Prevention and when to seek urgent help

Prevention reduces most cases. Keep grass and rubbish short around animal sheds, store feed away from rodents that attract snakes, light walkways at night, and keep dogs on a lead in snake habitats during the monsoon. Control nesting sites of bees near animal housing.

Treat any of the following as an emergency: a bite or sting by a known or suspected snake, rapid swelling of the face, drooling with difficulty breathing, collapse, bleeding that does not stop, or repeated stings. Do not wait to see how the animal looks in an hour. Phone the veterinarian, begin gentle first aid and transport. If a dead snake is brought, handle it carefully, since reflex bites can occur, and use it only to help identification and never to delay care.

Concept cleared

Venom is a cocktail
Each venom contains many components. The mix, not a single chemical, explains why paralysis, bleeding and necrosis can occur together.

Neurotoxic versus haemotoxic
Cobra and krait venoms mainly act at the neuromuscular junction. Russell's and saw-scaled viper venoms mainly disturb clotting and tissue. Overlap is common.

Antivenom neutralises, it does not repair
Antivenom binds free venom. Early use helps most because it cannot undo damage already done.

Poisonous versus venomous
Toads are poisonous because their secretion harms when mouthed. Snakes, scorpions and bees are venomous because they inject toxin.

Memory aid: Bite response: CALM

C: Calm and keep still. A: Avoid cutting, sucking and tourniquets. L: Limit movement of the limb. M: Move to the veterinarian at once.

Compare and contrast

Major Indian snake venoms

Snake	Main venom action	Typical picture	Special concern
Spectacled cobra	Post-synaptic neurotoxin plus cytotoxin	Local swelling, necrosis, paralysis	Respiratory failure
Common krait	Pre-synaptic neurotoxin	Little local change, progressive weakness	Bite may go unnoticed
Russell's viper	Procoagulant and haemotoxic	Swelling, bleeding, clotting failure	Kidney injury
Saw-scaled viper	Procoagulant and haemotoxic	Swelling, bleeding, clotting failure	Small snake, easily missed

Other venomous or poisonous exposures

Source	Toxic mechanism	Key signs	Immediate step
Indian red scorpion	Channel toxins, catecholamine surge	Pain, salivation, arrhythmia, oedema	Urgent supportive care
Toad	Digoxin-like bufadienolides	Salivation, tremor, arrhythmia	Rinse mouth outward
Honeybee	Melittin, allergens	Swelling, anaphylaxis, mass-sting haemolysis	Remove sting, seek help
Widow spider	Latrotoxin	Pain, rigidity	Supportive care

Species notes

Dogs

Most commonly bitten on the head and limbs. Also the usual victims of

Cats

Small body size means a larger venom load per kilogram and faster

toad poisoning because they mouth toads.

deterioration, so early signs deserve urgent attention.

Cattle and buffalo
Usually bitten on the muzzle or lower limbs while grazing. Swelling of the muzzle can obstruct breathing.

Horses
Muzzle and limb bites are common. Antivenom is a foreign horse-derived protein, so sensitisation and reactions should be considered.

Small ruminants
Light body weight makes venom effects rapid, and bites in grazing flocks may be unwitnessed.

Clinical pearls

Self-test: 10 questions

1. Which statement correctly defines a venom?

Venom is delivered actively through a bite, sting or spine. Substances that harm when swallowed or absorbed are poisons.

2. Which snake is part of the Indian big four?

The big four are the spectacled cobra, common krait, Russell's viper and saw-scaled viper.

3. Cobra post-synaptic neurotoxins mainly act by

Post-synaptic neurotoxins occupy the acetylcholine receptor on the muscle end plate, producing flaccid paralysis.

4. Which feature is typical of krait envenomation?

Krait venom acts at the nerve terminal and often leaves little visible local change, so the bite can be missed.

5. Russell's viper envenomation commonly causes

Its venom activates and consumes clotting factors, so bleeding and prolonged clotting are typical, and kidney injury can follow.

6. Which first-aid step is inappropriate after a snake bite?

Cutting and sucking cause tissue damage and infection and do not remove meaningful venom.

7. Polyvalent antivenom in India is best described as

It is a purified antibody preparation raised in horses that binds free venom, but it cannot repair damage that has already occurred.

8. Toad poisoning in dogs resembles which drug effect?

Bufadienolides inhibit sodium-potassium ATPase, giving cardiac glycoside-like arrhythmias along with salivation and tremor.

9. The immediate first step after a dog mouths a toad is to

Rinsing removes secretion from the mucosa. Forced salt is dangerous, and delay allows absorption.

10. Mass bee stinging may cause

A very large venom load acts like an overdose of melittin and other components, causing systemic injury.

Key points to revise

1. Venom is injected, poison is ingested or absorbed, toxin is the general term.
2. The big four Indian snakes are cobra, krait, Russell's viper and saw-scaled viper.
3. Cobra and krait venoms are mainly neurotoxic.
4. Vipers cause coagulopathy, swelling and, in Russell's viper, kidney injury.
5. Keep the animal calm, still and move it quickly to a veterinarian.
6. Avoid cutting, sucking, tourniquets, ice and herbal pastes.
7. Polyvalent antivenom neutralises circulating venom but cannot reverse established damage.
8. Scorpion venom causes an autonomic storm and toad toxin acts like digoxin.

Go deeper on this site

- Ch 14. Drug toxicities and adverse drug events (in this book)
- Ch 12. Recreational drugs and human medicines in pets (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- WHO fact sheet: Snakebite envenoming
- WHO SEARO guidelines for the management of snakebites
- Merck Veterinary Manual: Overview of toxicology

CHAPTER 14 OF 17

Drug toxicities and adverse drug events

Why therapeutic drugs become toxic in veterinary patients, with the characteristic overdose and adverse patterns of NSAIDs, ivermectin, anaesthetics, antibiotics and hormones. The chapter stresses species differences, recognition and the logic of response.

After this chapter you can

- Distinguish dose-related, idiosyncratic and species-specific adverse drug events
- Explain the mechanisms of NSAID toxicity in dogs, cats and vultures
- Describe ivermectin neurotoxicity and the role of MDR1 (ABCB1) in dogs
- Recognise typical adverse effects of anaesthetics, antibiotics and hormones in different species
- Outline a general response to a suspected drug toxicity and the need for reporting

Why drugs become toxins

Almost any drug can poison an animal if the exposure is too high, too prolonged or given to the wrong species or patient. Adverse drug events fall into a few groups. **Dose-related** events are an extension of the normal action (hypoglycaemia from too much insulin). **Idiosyncratic** events are unpredictable and not clearly dose-related. **Species-specific** events arise because enzymes, transporters or physiology differ between animals.

Common causes in practice are calculation or conversion errors, wrong species, wrong route, repeated dosing in an animal with kidney or liver disease, interacting drugs and owner dosing with human medicines. This is why the earlier chapters on pharmacokinetics matter: toxicity is usually the clinical result of a drug accumulating, not being cleared or acting where it should not.

Young, old, pregnant, dehydrated, underweight and sick animals are at higher risk, because drug distribution, metabolism and excretion differ in them. Always match the drug, dose and interval to the individual animal, and recheck the label for species before every use.

NSAIDs

NSAIDs inhibit cyclooxygenase. COX-1 products protect the gastric mucosa and maintain renal blood flow, so excessive or non-selective inhibition causes **gastric ulceration** and, in dehydrated or hypotensive animals, **acute kidney injury**. Signs

include vomiting, black tarry stools, inappetence, abdominal pain, polyuria or oliguria and lethargy. Combining an NSAID with a corticosteroid greatly raises ulcer risk, and switching between NSAIDs without a gap is a classic error.

Cats clear many NSAIDs and paracetamol slowly because they have limited glucuronidation. Paracetamol in cats causes methaemoglobinaemia (chocolate-brown blood, cyanosis, facial oedema) and red-cell damage. Dogs are also affected at higher exposures, with liver injury more prominent. Human NSAID tablets should never be given to pets without veterinary advice.

Vultures are a landmark case. Gyps vultures feeding on carcasses of cattle treated with diclofenac developed renal failure and visceral gout, and populations in South Asia collapsed. Regulatory action against veterinary diclofenac followed in India and neighbouring countries; check the current notification for what is permitted today.

Ivermectin and related macrocyclic lactones

Ivermectin binds glutamate-gated chloride channels in parasites, causing paralysis. In mammals the same drug is normally kept out of the brain by the efflux pump **P-glycoprotein**, encoded by the **MDR1 (ABCB1)** gene. Dogs with the mutant gene, such as Collies, Shelties, Australian Shepherds and related herding breeds, lack functional pump and the drug crosses the blood-brain barrier. It then acts on GABA-gated chloride channels, producing neurotoxicity.

Signs are mydriasis, salivation, tremor, ataxia (the so-called blind staggers), disorientation, blindness, bradycardia, coma and respiratory depression. Overdose in non-mutant dogs can produce the same picture, especially when large-animal formulations are used on small animals. Treatment is supportive and prolonged, as there is no true antidote. Some reports use intravenous lipid emulsion; ask a toxicologist or check current guidance.

Calves, cats and some other species are also susceptible to overdose, and certain reptiles such as tortoises and turtles are sensitive and should not be treated casually. Always check species and breed before using macrocyclic lactones, and check MDR1 status when in doubt.

Anaesthetics, sedatives and local anaesthetics

Most anaesthetic toxicity is dose-related depression of the brain, heart and breathing. Overdose of propofol, thiopentone, inhalants or opioids produces apnoea, hypotension and prolonged recovery. Several species differences are important.

- **Ruminants** are very sensitive to xylazine, showing profound sedation, salivation, bloat and bradycardia. Alpha-2 effects can be reversed with specific antagonists such as atipamezole or yohimbine.
- **Sighthounds** recover slowly from thiobarbiturates because they have little body fat to redistribute drug and metabolise it slowly.
- **Cats** can develop Heinz-body anaemia after repeated propofol, and repeated ketamine can cause prolonged recovery or seizures if overdosed.
- **Local anaesthetics** are safe at the site, but accidental intravenous injection or overdose causes seizures and cardiac toxicity; bupivacaine is especially cardiotoxic. Cats are sensitive to lidocaine at higher exposures.

Opioid overdose is reversed with naloxone, and benzodiazepine overdose with flumazenil, but both reversals wear off sooner than the drug being reversed, so the animal must be watched.

Antibiotics and antimicrobials

Antibiotic toxicity illustrates how a drug that is selectively toxic to microbes can still harm host tissue.

- **Aminoglycosides** (gentamicin, amikacin) are nephrotoxic, ototoxic and can cause neuromuscular blockade. Risk rises with dehydration, long courses and combination with loop diuretics.
- **Fluoroquinolones** can damage cartilage in growing dogs and cause retinal degeneration in cats, particularly with overdose of enrofloxacin.
- **Tetracyclines** bind calcium and can stain developing teeth or bone, and intravenous rapid injection can cause hypotension and collapse.
- **Gut flora disruption.** Some oral antibiotics, such as lincosamides and penicillins, cause fatal enterocolitis in rabbits, guinea pigs, hamsters and horses because they overgrow harmful bacteria.
- **Procaine penicillin** can cause excitement, tremor and collapse in horses if accidentally injected intravascularly.

- **Chloramphenicol** is a risk to humans handling it and is not allowed in food-producing animals in many countries; check the current notification in India.

Residues in milk and meat are an additional kind of toxicity, which is a public-health issue and discussed under withdrawal periods.

Hormones and recognition and response

Hormones are potent and have narrow margins. Excess insulin produces hypoglycaemia with weakness, tremor and seizures. Excess glucocorticoid causes polyuria, polydipsia, immunosuppression, delayed wound healing, ulcers and, in pregnancy, abortion or premature birth in ruminants. Prostaglandin F2 alpha and oxytocin given to the wrong animal can cause abortion or uterine rupture; prostaglandins are also hazardous to handlers, including pregnant women and asthmatics. Oestrogens in dogs can suppress bone marrow, and long-acting progestins risk pyometra and mammary changes. Anabolic steroids and beta-agonists such as clenbuterol are subject to restriction in food animals; check the current notification.

Recognition and response. Suspect a drug event when signs start soon after a new drug, a dose change or an owner-given medicine. First stop the suspected drug. Then support the airway, breathing, circulation and fluids, treat seizures and arrhythmia, give an antidote if one exists, and use decontamination if the exposure was oral and recent. Record the drug, batch, dose given and time. Report serious or unexpected events to the manufacturer and to the competent authority through the channel currently in use; check the latest reporting arrangements in India. Phone a poison information service or toxicologist early.

Concept cleared

Three types of adverse event
Dose-related, idiosyncratic and species-specific events differ in predictability. Species-specific events are the most testable in veterinary exams.

Transporters decide the brain dose

P-glycoprotein keeps drugs like ivermectin out of the brain. A mutation in MDR1 removes this barrier and makes normal doses toxic.

Limited glucuronidation in cats

Cats clear many NSAIDs and paracetamol slowly. The drug persists and metabolites that damage red cells accumulate.

Selective toxicity is relative

An antibiotic harmless to the host in one species can disrupt gut flora or damage kidney, cartilage or retina in another.

Memory aid: Response to suspected drug toxicity: STOP-ABC

S: Stop the drug. T: Take a history and record batch and time. O: Obtain urgent advice. P: Protect the patient and others. A: Airway. B: Breathing. C: Circulation, then antidote and decontamination if suitable.

Compare and contrast

Drug groups and characteristic toxicity

Drug group	Main mechanism of harm	Typical signs	At-risk animals
NSAIDs	COX-1 loss, reduced renal perfusion	Vomiting, melaena, kidney injury	Dehydrated animals, cats, vultures
Ivermectin	GABA channel effect in brain when pump absent	Tremor, ataxia, blindness, coma	MDR1 mutant dogs, young animals
Aminoglycosides	Tubular and inner ear toxicity	Polyuria, azotaemia, deafness	Dehydrated or renal patients
Alpha-2 agonists	Excess adrenergic stimulation	Deep sedation, bradycardia, bloat	Ruminants

Reversal agents for drug overdoses

Drug taken	Reversal agent	Key point
Opioids	Naloxone	Reversal is shorter than opioid effect
Benzodiazepines	Flumazenil	May unmask seizures
Xylazine, medetomidine	Atipamezole or yohimbine	Atipamezole is more selective for alpha-2
Ivermectin	None specific	Supportive care

Species notes

Dogs
Herding breeds with the MDR1 mutation are sensitive to ivermectin and some other drugs. Sighthounds recover slowly from thiobarbiturates.

Cats
Poor glucuronidation makes paracetamol and many NSAIDs dangerous. Enrofloxacin overdose can cause blindness.

Cattle and sheep
Very sensitive to xylazine. Hormonal overdose or wrong timing can cause abortion. Residues are a public-health concern.

Horses
Antibiotic enterocolitis and procaine penicillin reactions are well-known adverse events. NSAID overdose causes right dorsal colitis and ulcers.

Rabbits and rodents
Oral antibiotics that disturb gut flora can be fatal, so choose agents carefully.

Clinical pearls

Self-test: 10 questions

1. A drug effect that is unpredictable and not clearly related to dose is called

Idiosyncratic reactions occur in a few individuals regardless of dose, unlike dose-related events.

2. Why do NSAIDs cause gastric ulcers?

Prostaglandins maintain mucus, bicarbonate and mucosal blood flow, and COX inhibition reduces them.

3. Paracetamol toxicity in cats is characterised by

Limited glucuronidation allows toxic metabolites to oxidise haemoglobin, giving chocolate-coloured blood and cyanosis.

4. Vulture population decline in South Asia was linked to

Vultures developed renal failure and visceral gout after feeding on carcasses of cattle recently treated with diclofenac.

5. MDR1 mutation in Collies increases sensitivity to ivermectin because

Without the efflux pump the drug penetrates the blood-brain barrier and acts on GABA channels.

6. Which animals are especially sensitive to xylazine?

Ruminants show profound sedation, bradycardia, salivation and bloat at amounts that are mild in other species.

7. Aminoglycoside toxicity risk rises with

Dehydration reduces renal perfusion and increases drug accumulation in tubular cells.

8. Oral antibiotics such as lincosamides are dangerous in

Hindgut fermenters can suffer fatal clostridial overgrowth when normal flora are disrupted.

9. What is the first step when a drug toxicity is suspected?

Stopping the cause and stabilising vital functions come before any other measure.

10. Naloxone reversal of an opioid overdose should be followed by

Naloxone has a shorter duration than many opioids, so sedation and respiratory depression can return.

Key points to revise

1. Adverse events are dose-related, idiosyncratic or species-specific.
2. NSAIDs cause gastric ulcer and renal injury by reducing protective prostaglandins.
3. Diclofenac residues caused severe vulture declines in South Asia.
4. Ivermectin neurotoxicity occurs when P-glycoprotein is absent or overwhelmed.
5. Ruminants are very sensitive to xylazine.
6. Aminoglycosides injure kidney, ear and neuromuscular transmission.
7. Some antibiotics cause fatal enterocolitis in rabbits, guinea pigs and horses.
8. Stop the drug, support the patient, give an antidote if available and report serious events.

Go deeper on this site

- Ch 15. Antidotes and emergency decontamination quick reference (in this book)
- Ch 13. Venoms, bites and stings (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Concepts
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Overview of pharmacology
- Merck Veterinary Manual: Overview of toxicology
- Merck Veterinary Manual: Introduction to poisoning (pet owners)

CHAPTER 15 OF 17

Antidotes and emergency decontamination quick reference

A concept-level reference matching common poisons to antidotes, with the mechanism and cautions for each, and the reasoning behind emesis, activated charcoal and lavage. It stresses when decontamination should not be attempted and when to call for urgent help.

After this chapter you can

- Match common poisons to their antidotes and explain each mechanism
- State the main cautions and limits of antidotes
- Explain when emesis is appropriate and when it must not be induced
- Describe how activated charcoal, cathartics and lavage work and where they fail
- Apply a stepwise approach to a poisoned animal, including ruminant and skin or eye exposure

The stepwise approach

The first priority in any poisoning is the patient, not the poison. Secure the airway, breathing and circulation, control seizures and temperature, and only then think about removing or neutralising the poison. The usual order is **stabilise, prevent further exposure, decontaminate, give an antidote if one exists, enhance elimination and give supportive care**.

Most poisons have no antidote. Good supportive care is therefore the commonest treatment. Obtain a history of the agent, the amount, the route and the time of exposure, keep the container or sample, and contact a poison information service or toxicologist early. This chapter is a concept summary; doses and current protocols must come from a current formulary or specialist advice.

How antidotes work

Antidotes work in a handful of ways. Knowing the mechanism helps you remember both the use and the limit.

- **Competitive receptor blockade or reversal:** atropine blocks muscarinic receptors, naloxone blocks opioid receptors, flumazenil blocks benzodiazepine binding and atipamezole blocks alpha-2 receptors.
- **Enzyme reactivation:** pralidoxime reactivates acetylcholinesterase inhibited by organophosphates.
- **Replacing a depleted substance:** acetylcysteine restores glutathione after paracetamol, and vitamin K1 restores clotting factor synthesis after anticoagulant rodenticides.
- **Blocking toxic metabolism:** fomepizole inhibits alcohol dehydrogenase so ethylene glycol is not converted to toxic acids.
- **Chelation:** calcium EDTA, dimercaprol and succimer bind metals such as lead and arsenic so they can be excreted.
- **Binding or neutralising the toxin:** antivenom and digoxin-specific antibody fragments bind their targets, and Prussian blue binds thallium in the gut.
- **Other mechanisms:** methylene blue helps convert methaemoglobin back to haemoglobin, and cyanide antidotes act by forming less toxic complexes.

Antidote quick reference and cautions

The following pairings are commonly taught. Each antidote has limits.

1. **Organophosphate and carbamate:** atropine controls muscarinic signs. Pralidoxime works best early, before the enzyme becomes permanently inhibited (ageing), and is generally not needed for carbamates. Atropine is titrated to drying of airway secretions, not to heart rate alone.
2. **Paracetamol:** acetylcysteine. Cats also need treatment for methaemoglobinaemia.
3. **Methaemoglobin-forming agents:** methylene blue, with caution in cats because it can itself cause Heinz-body anaemia.
4. **Ethylene glycol:** fomepizole in dogs; the timing window is short, and cats need earlier treatment. Ethanol is an older alternative.

5. **Anticoagulant rodenticides:** vitamin K1 for weeks, as some compounds persist; check clotting after stopping.
6. **Opioids and benzodiazepines:** naloxone and flumazenil, which have shorter actions than the poison.
7. **Lead and arsenic:** chelators, with attention to the kidney and to preventing further oral intake.
8. **Cyanide:** nitrite and thiosulfate or hydroxocobalamin are used; hedge by checking current protocols because nitrites form methaemoglobin.
9. **Snakebite:** species-specific antivenom, as covered in the previous chapter.
10. **Isoniazid:** pyridoxine. **Heparin:** protamine.

A frequent confusion is to treat the antidote as a cure for any exposure. It is not: an antidote helps only when it is matched to the agent, given in time and accompanied by supportive care.

Emesis: when and when not

Inducing vomiting removes stomach contents shortly after ingestion. It helps most when the poison was swallowed recently, usually within about one to two hours, is not corrosive or a hydrocarbon, and the animal is alert. In dogs, apomorphine is commonly used; in cats, alpha-2 agonists such as xylazine are commonly used, and cats respond poorly to many dog methods. Hydrogen peroxide and salt are widely advised by laypeople but carry risk, and salt can cause dangerous sodium poisoning, so veterinary guidance should be sought first.

Do not induce vomiting when:

- The animal is already vomiting, seizing, collapsed, depressed or has a poor gag reflex, because of aspiration risk.
- The poison is a **corrosive** (strong acid, alkali), because it burns the oesophagus a second time on the way back.
- The poison is a **hydrocarbon** such as petrol or kerosene, because aspiration causes severe pneumonia.
- The material is sharp, or the animal has a condition likely to worsen with vomiting.
- The species cannot vomit safely: **ruminants, horses, rabbits and rodents** do not vomit effectively.

- The animal has taken a drug that will itself cause rapid sedation or seizures.

Activated charcoal, cathartics and lavage

Activated charcoal has a very large surface area and adsorbs many toxins in the gut, preventing absorption. Repeat doses can also interrupt enterohepatic circulation of drugs excreted in bile and can pull some drugs back from the blood into the gut. It is poor at adsorbing alcohols, ethylene glycol, strong acids and alkalis, and many metals, and it is dangerous if aspirated. Charcoal with sorbitol may cause diarrhoea and fluid shifts; in salt poisoning it can contribute to hypernatraemia, so it should be used under advice.

Cathartics hasten gut transit but have limited proven benefit and can cause dehydration, so they are not routine.

Gastric lavage is used for an anaesthetised animal with a cuffed endotracheal tube in place, to remove stomach contents when emesis is not suitable. It is not suitable for corrosives or sharp objects.

In **ruminants**, activated charcoal and adsorbents are given by stomach tube. Ruminal lavage or rumenotomy to remove toxic plant matter and transfer of rumen fluid from a healthy animal may be used. Because the rumen holds a large volume that is released slowly, exposure may continue for hours after ingestion.

For **skin exposure**, wear gloves and wash with water and mild detergent while preventing hypothermia. For the **eye**, irrigate with copious clean water or saline. Avoid neutralising a corrosive with another chemical, since the reaction generates heat.

Enhancing elimination and when to seek urgent help

Some poisons can be removed faster once absorbed. Fluid diuresis speeds renal excretion of water-soluble agents, and urinary pH manipulation helps for some weak acids. Dialysis can remove agents such as ethylene glycol or some drugs when kidneys fail. Lipid emulsion has been used for lipophilic drugs; consult current guidance.

Seek urgent help at once for: seizures, collapse, difficulty breathing, blue or dark-brown mucosae, persistent vomiting or bloody stools, known ingestion of rodenticide, antifreeze, pesticides, human drugs, or any corrosive, and any

ingestion by a very young or small animal. Delay hurts because time-sensitive antidotes such as fomepizole and pralidoxime lose value as hours pass.

Prevention is the best antidote: store chemicals and drugs out of reach in labelled containers, avoid giving human medicines to animals, read labels on pesticides, and keep animals away from treated fields until the safe interval has passed.

Concept cleared

Match the antidote to the mechanism
Antidotes block, reactivate, replace, chelate or bind. If you know the poison's mechanism, the antidote usually follows.

Most poisons have no antidote
Supportive care is the main treatment in most poisonings. An antidote adds to it and does not replace it.

Timing limits decontamination
Emesis and charcoal help mostly in the first hours. Late attempts add risk without benefit.

Safety of the airway comes first
Many decontamination methods fail because of aspiration. Protect the airway before using them.

Memory aid: No vomiting: CHAOS
C: Corrosives. H: Hydrocarbons. A: Already unconscious or seizing. O: Obstructed or sharp object risk. S: Species that cannot vomit, such as ruminants, horses and rabbits.

Compare and contrast

Poison and antidote pairs

Poison	Antidote	Mechanism	Caution
Organophosphate	Atropine, pralidoxime	Block muscarinic effects, reactivate enzyme	Pralidoxime works best early
Paracetamol	Acetylcysteine	Restores glutathione	Cats also need methaemoglobin care
Ethylene glycol	Fomepizole	Blocks alcohol dehydrogenase	Narrow time window
Anticoagulant rodenticide	Vitamin K1	Restores clotting factors	Long courses may be needed
Lead	Calcium EDTA, succimer	Chelation	Renal monitoring

Decontamination methods

Method	Best used	Main limit or risk
Emesis	Recent ingestion, alert dog or cat	Aspiration, corrosives, hydrocarbons, ruminants
Activated charcoal	Many drugs and plant toxins	Does not bind alcohols, glycols, many metals
Gastric lavage	Anaesthetised animal with cuffed tube	Corrosives, sharp objects
Skin or eye wash	Dermal or ocular exposure	Cold stress, never use chemical neutralisers

Species notes

Dogs

Apomorphine is the usual emetic. Ethylene glycol and chocolate type exposures are classic reasons for early help.

Cats

Emesis uses different drugs from dogs. They are sensitive to methylene blue and paracetamol and respond late to ethylene glycol.

Cattle, buffalo, sheep and goats

Horses

Cannot be made to vomit. Use charcoal by stomach tube, ruminal lavage or rumenotomy as indicated.

Cannot vomit. Gastric reflux and nasogastric tubing with charcoal are possible, with care for aspiration.

Rabbits and rodents
Cannot vomit. Rely on charcoal and supportive care, and watch for hypothermia.

Clinical pearls

Self-test: 10 questions

1. What is the first priority in a poisoned animal?

Life-threatening problems are treated before the poison is addressed.

2. Pralidoxime acts by

It removes the organophosphate from the enzyme, and works best before ageing makes the bond permanent.

3. Acetylcysteine is the antidote for

It restores glutathione, which neutralises the toxic metabolite of paracetamol.

4. Fomepizole prevents toxicity of ethylene glycol by

Blocking the enzyme stops conversion of ethylene glycol to toxic metabolites that injure the kidney.

5. Vitamin K1 is used in poisoning by

These poisons block vitamin K recycling, and giving vitamin K1 restores clotting factor synthesis.

6. Vomiting should NOT be induced after ingestion of

Hydrocarbons are easily aspirated and cause severe pneumonia.

7. Which species cannot vomit effectively?

Ruminants, horses, rabbits and rodents do not vomit effectively, so other decontamination methods are used.

8. Activated charcoal is poor at binding

Small polar molecules such as alcohols and glycols are not adsorbed well.

9. Gastric lavage should be done only when

Without airway protection lavage risks aspiration.

10. For a skin exposure to a chemical you should

Washing removes the agent. Neutralising reactions can produce heat and further injury.

Key points to revise

1. Treat the patient before the poison.
2. Most poisons have no antidote.
3. Atropine and pralidoxime are used for organophosphates.
4. Acetylcysteine is used for paracetamol and fomepizole for ethylene glycol.
5. Vitamin K1 is used for anticoagulant rodenticides.
6. Emesis is useful only soon after ingestion in alert dogs and cats.

7. Do not induce vomiting after corrosives, hydrocarbons, or in seizing animals and species that cannot vomit.
8. Skin and eye exposures need washing, not chemical neutralisation.

Go deeper on this site

- Ch 16. Environmental, poultry and wildlife toxicology (in this book)
- Ch 14. Drug toxicities and adverse drug events (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Concepts
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Overview of toxicology
- Merck Veterinary Manual: Introduction to poisoning (pet owners)
- WHO fact sheet: Snakebite envenoming

CHAPTER 16 OF 17

Environmental, poultry and wildlife toxicology

How poisons move through the environment, feed chain and carcasses to harm animals that were never treated directly. The chapter uses diclofenac and Gyps vultures as the central case, then covers pesticide residues, water and soil contaminants and the common poultry toxicoses.

After this chapter you can

- Explain how diclofenac in livestock carcasses caused vulture declines in South Asia
- Describe bioaccumulation and why persistent pesticide residues matter in food animals
- List common water and soil contaminants and the reasoning behind their toxic effects
- Identify the main poultry-specific toxicoses and their usual sources on farms

- Apply prevention and urgent-help principles to environmental and flock poisonings

Why environmental toxicology is different

In clinical toxicology one animal is exposed and one animal is treated. In environmental toxicology the poison reaches animals indirectly: through water, soil, plants, feed, or the body of another animal. The affected species may never have been given the substance by a veterinarian.

Three ideas link this chapter. First, **exposure route** matters as much as toxicity. Second, a substance that is safe in the species it was meant for can be dangerous to a different species that eats the carcass. Third, many problems appear as a flock or herd event, or as a slow population decline, so the diagnosis depends on pattern recognition and on laboratory support, not on a single sick patient.

Diclofenac and vultures

Diclofenac is a non-steroidal anti-inflammatory drug (NSAID) used in cattle and buffalo for pain and fever. In South Asia, Gyps vultures (white-rumped, long-billed and slender-billed) feed on carcasses of dead livestock. When a treated animal died shortly after dosing, its tissues still held drug residue, and the vultures that fed on it were exposed.

The mechanism is **acute kidney failure**. Affected birds show lethargy, drooping of the neck, and death within days. At post-mortem the typical finding is **visceral gout**: white chalky urate deposits on the liver, heart, air sacs and joints, because failing kidneys cannot excrete uric acid. Vultures are very sensitive to this drug, whereas many other species tolerate it far better. The reason for the sensitivity is not fully settled, so students should state it as a species difference and not claim a single proven mechanism.

Populations of these vultures fell by more than ninety per cent in a short period. Because vultures breed slowly and a small fraction of carcasses carrying residue is enough to kill many birds, the decline was steep. The loss has wider meaning: carcasses were not cleared, scavenging dogs increased, and public health risks such as rabies exposure were raised.

India restricted veterinary diclofenac in 2006. Meloxicam has been promoted as a vulture-safe alternative, and other NSAIDs have raised concern in later work. Please check the current notification from the regulator for the present status of each drug. The lesson for a veterinarian is practical: choose carefully, do not dispense human-formulation vials for animals, and dispose of carcasses of recently treated animals responsibly.

Pesticide residues and bioaccumulation

Pesticides reach animals through sprayed fodder, contaminated water, dips and sprays, and treated seed. Two terms are important. **Bioaccumulation** means a substance builds up in the tissues of one organism over time. **Biomagnification** means concentration rises at each step of the food chain, so predators and fish-eating or carcass-eating birds carry the highest levels.

Persistent organochlorines, such as DDT and related compounds, are fat-soluble and resist breakdown. They collect in body fat and appear in milk and eggs. They act mainly on the nervous system and can also affect reproduction and eggshell quality in birds. Organophosphates and carbamates break down faster, but they act on cholinesterase and cause acute cholinergic signs, which are covered in the earlier pesticide chapters.

For food animals, the concern is **residues** in milk, meat and eggs. Maximum residue limits (MRLs) and withdrawal periods exist to protect consumers. Indian limits are set by the food safety authority and change over time, so check the current notification before quoting any value. Good practice includes using products only as labelled, keeping treated animals from freshly sprayed pasture for the stated interval, and recording treatments.

A common confusion: a low acute toxicity does not mean low residue risk. A fat-soluble, persistent chemical can be safe in a single exposure yet still accumulate.

Water and soil contaminants

Water and soil carry both natural and industrial toxicants. The usual reasoning is to ask what the substance does, where it accumulates, and which animals are most exposed.

- **Fluoride.** Occurs naturally in groundwater in some regions. Long exposure damages teeth and bones (fluorosis), causing mottled teeth, stiffness and lameness. Young animals are affected during tooth and bone development.
- **Arsenic.** Natural or industrial contamination of groundwater. It blocks cellular energy pathways and damages the gut lining, liver and kidney.
- **Lead and cadmium.** From batteries, paints, mining and industrial waste. Lead affects the nervous system and blood formation; cadmium accumulates in kidney and liver.
- **Nitrates and nitrites.** From fertiliser, manure and some plants. Nitrite converts haemoglobin to methaemoglobin, so tissues are starved of oxygen although the animal breathes normally. Ruminants convert nitrate to nitrite in the rumen and are especially at risk.
- **Blue-green algal blooms.** In stagnant, warm ponds. Some species release toxins affecting the liver or nervous system, and sudden death after drinking is typical.
- **Salinity.** Very salty water or sudden access after deprivation can cause nervous signs.

Prevention rests on testing water sources, fencing stagnant ponds, safe disposal of batteries and oil, and providing an alternative clean water supply. If several animals on one source become ill together, think of water early.

Poultry-specific toxicoses

Poultry are kept in large numbers with shared feed and water, so a single error can affect the whole flock. Birds also have fast metabolism and small body size, and they lack some of the safety margins of mammals.

- **Mycotoxins.** Aflatoxin from mouldy grain damages the liver and depresses growth, immunity and egg production. Ochratoxin and trichothecenes such as T-2 toxin cause kidney damage and mouth lesions. Poor storage in humid weather is the main cause.
- **Ionophore coccidiostats.** Monensin, salinomycin and related drugs are safe at the intended level but toxic when mixing errors occur or when given with certain other drugs, such as tiamulin. They damage muscle, so birds show weakness, leg paralysis and reluctance to move. Feed mixing and label checking are the prevention.

- **Salt toxicity.** Excess salt in feed, or water deprivation, causes thirst, wet droppings and nervous signs.
- **Carbon monoxide and gases.** From poorly ventilated brooders. Chicks may be found dead or dull, and the problem is a ventilation fault.
- **Other feed errors.** Wrong premix levels, contaminated feed from equipment shared with other species, and pesticide-treated seed.

The investigation approach is to look at the flock pattern, the timing relative to a new feed batch, and then to submit feed, water and fresh carcasses to a laboratory. Withdraw the suspect feed first and provide clean water; that single step often limits further loss.

Diagnosis, prevention and seeking urgent help

Environmental and flock cases follow a common sequence. Stop the exposure, protect the survivors, collect samples, and treat supportively. Many of these toxicants have no specific antidote, so removing the source is the most valuable action.

Wildlife cases need extra care. Dead wild animals may carry zoonotic disease or poison residues, so handle with gloves, report to the forest or wildlife authority, and do not dispose of carcasses in a place where scavengers will feed. Mass deaths of wild birds should be reported without delay, since the cause may be a poison, an infectious disease or both.

Seek urgent help from a poison laboratory, a toxicology colleague, or the public health and animal husbandry authorities when: several animals die suddenly, a human may have been exposed (for example by eating affected eggs or meat), a protected species is involved, or the source is an industrial discharge. Keep notes and samples, since these may later be needed in a legal investigation, discussed in the next chapter.

Prevention is a matter of habits: use drugs as labelled, store feed dry, test water, avoid human-formulation drugs in livestock, and train farm workers to report unusual deaths early.

Concept cleared

Secondary poisoning

An animal is harmed by eating the tissues of another animal that carries the poison. Vultures and diclofenac are the standard example.

Bioaccumulation and biomagnification

Persistent, fat-soluble substances build up in an organism and become more concentrated at each step of the food chain.

Species differences in sensitivity

A drug safe in cattle can be lethal in vultures. Safety data from one species cannot be assumed for another.

Flock-level thinking

In poultry, think of shared feed and water first. A single mixing or storage error can explain a whole house of sick birds.

Memory aid: Environmental case checklist: SWEEP

Source, Water, Exposure route, Exposed species, Prevention. Run through these five in order when a group of animals falls ill.

Compare and contrast

Persistent and non-persistent pesticides

Feature	Organochlorines	Organophosphates and carbamates
Persistence	Long, resist breakdown	Short, break down faster
Storage	Fat, milk, eggs	Little accumulation
Main concern	Residues and chronic effects	Acute cholinergic signs
Food-chain effect	Biomagnify	Rarely biomagnify

Common poultry toxicoses

Toxicosis	Usual source	Typical clue
Aflatoxicosis	Mouldy grain	Liver damage, poor growth, immunosuppression
Ionophore toxicity	Mixing error or drug interaction	Leg weakness, paralysis
Salt toxicity	Excess salt or water deprivation	Thirst, wet droppings, nervous signs
Carbon monoxide	Faulty brooder ventilation	Dull or dead chicks

Species notes

Vultures
Highly sensitive to diclofenac, with kidney failure and visceral gout after feeding on treated carcasses.

Cattle and buffalo
The treated species; they tolerate the drug but become the source of exposure for scavengers if they die soon after treatment.

Ruminants
Rumen bacteria convert nitrate to the more harmful nitrite, so nitrate-rich fodder and water are higher risk.

Poultry
Sensitive to mycotoxins and ionophores; shared feed means whole-flock outbreaks.

Dogs and wild scavengers
Exposed through carcasses and contaminated water; may act as sentinels of poisoning in the area.

Clinical pearls

Self-test: 10 questions

1. The typical post-mortem finding in vultures poisoned by diclofenac is:

Kidney failure leaves urates unexcreted, which deposit on visceral surfaces as visceral gout.

2. Vultures were exposed to diclofenac mainly by:

This is secondary poisoning through carcass tissue.

3. Biomagnification means:

Persistent substances become more concentrated at higher trophic levels.

4. Which pesticide group is most associated with storage in fat and appearance in milk and eggs?

Organochlorines are persistent and fat-soluble.

5. Nitrite poisoning produces signs mainly because of:

Nitrite oxidises haemoglobin so it cannot carry oxygen.

6. Which of these animals is especially vulnerable to nitrate poisoning from fodder?

Rumen microbes reduce nitrate to nitrite.

7. A flock shows leg weakness after a new feed batch containing coccidiostat. The best suspicion is:

Ionophore overdose or interaction damages muscle.

8. The first step in a suspected feed-borne flock poisoning is to:

Removing the source limits further exposure.

9. Chronic fluoride exposure mainly affects:

Fluorosis causes dental mottling and skeletal changes.

10. Which statement about Indian MRLs is best?

Limits are revised, so rely on the current official notification.

Key points to revise

1. Diclofenac residues in carcasses caused kidney failure and visceral gout in Gyps vultures.
2. India restricted veterinary diclofenac in 2006; check the current notification for NSAID status.
3. Vulture sensitivity is a species difference whose exact mechanism is not fully settled.
4. Bioaccumulation builds up in one organism; biomagnification rises along the food chain.
5. Organochlorines are persistent and stored in fat, milk and eggs.
6. Nitrite causes methaemoglobinaemia and is a particular risk in ruminants.
7. Poultry toxicoses include mycotoxins, ionophores, salt and gas exposure.
8. Removing the source is the first and often the most effective step.

Go deeper on this site

- Ch 17. Medico-legal toxicology in India (in this book)
- Ch 15. Antidotes and emergency decontamination quick reference (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index

- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Toxicology (contents)
- World Organisation for Animal Health (WOAH)
- US FDA Center for Veterinary Medicine

CHAPTER 17 OF 17

Medico-legal toxicology in India

How a veterinarian handles a suspected poisoning that may reach a court: collecting and preserving samples, the outline of laboratory methods, post-mortem findings, chain of custody, reporting and giving evidence. The focus is on reasoning and procedure, not on dosing.

After this chapter you can

- Describe which samples to collect in a suspected poisoning and how to preserve them
- Outline what TLC, GC-MS and ELISA do and where each is useful
- Explain chain of custody and why a break in it weakens evidence
- Recognise post-mortem findings that suggest poisoning and their limits
- Prepare a clear report and understand the basics of court procedure

Why medico-legal work needs a different mindset

A clinical poisoning is treated for the sake of the patient. A **medico-legal** poisoning may also involve a crime, an insurance claim, a dispute between owner and supplier, or a case of cruelty. Examples include malicious poisoning of dogs or cattle, poisoning of racing animals, suspected feed adulteration, and insurance deaths.

The veterinarian is first a clinician and second a witness. Treatment must never be delayed to protect evidence, but every step should be recorded so that the evidence stays reliable. A careful note made at the time is worth more than a long memory later.

Laws and procedure codes in India have been revised recently. Names of sections and acts may differ from older textbooks, so check the current statute and the instructions of the state department before relying on any section number.

Sample collection and preservation

The aim is to obtain the samples most likely to hold the poison and to keep them unchanged until analysis. The reasoning is: collect what the poison reaches first, what stores it, and what removes it.

- **Stomach or rumen contents and vomitus.** The most useful sample when the poison was swallowed, since it may hold the actual material.
- **Liver.** The main site of metabolism and storage; useful for many drugs and metals.
- **Kidney.** Useful for metals and for substances excreted in urine.
- **Blood and urine.** From live animals or fresh carcasses.
- **Brain.** Needed for certain conditions, such as cholinesterase measurement in suspected organophosphate poisoning.
- **Feed, water, bait and suspected container.** Often the most important evidence, since it ties the poison to the source.

Use clean glass or good plastic containers, one for each organ, and never mix samples. Do not use formalin for samples meant for chemical analysis, because it interferes with testing. Cool or freeze samples as advised by the laboratory. Some laboratories in India traditionally ask for visceral samples in a saturated salt solution or in rectified spirit; follow the instructions of the receiving laboratory and state the preservative on the label. Always send a sample of the preservative alone as a control.

Seal each container, label it with case number, animal, organ, date and time, and sign the label. Collect a separate set for histopathology in formalin, as this is a different question from chemistry.

Laboratory methods in outline

The veterinarian does not need to run these tests but should know what each can and cannot answer.

- **Thin-layer chromatography (TLC).** A mixture is spotted on a plate and separated as a solvent moves through it. Spots are compared with known standards. It is simple, cheap and useful for screening, but it is less specific and less sensitive.
- **Gas chromatography-mass spectrometry (GC-MS).** Gas chromatography separates volatile compounds, and mass spectrometry identifies each by its fragment pattern. It is a confirmatory method widely accepted in legal work for many pesticides and drugs. Other forms, such as liquid chromatography with mass spectrometry, cover less volatile compounds.
- **ELISA.** An antibody-based test used for rapid screening of specific toxins or drugs. It is quick, but it can cross-react with related compounds, so a positive result usually needs confirmation by chromatography.

A common error is to treat a screening result as proof. Courts look for a method that identifies the compound with confidence. A second point is that a negative result does not rule out poisoning, since the substance may have degraded, been metabolised, or not been tested for. The veterinarian should give the laboratory a clear history and suspected agents so that the right panel is chosen.

Chain of custody

Chain of custody is the written record showing who held a sample, from collection to the court, and that it was not tampered with. Each transfer is recorded with name, date, time and signature.

The practical steps are: seal samples in front of a witness where possible, write a forwarding note listing the items, hand them directly to the police or the laboratory messenger, and keep a receipt. Keep copies of every document. If a sample sits in an unlocked cupboard or travels without a record, the defence can argue that it was changed, and the evidence may be set aside.

Think of it like a relay baton: any moment where no one can say who held it breaks the chain.

Post-mortem findings in suspected poisoning

A post-mortem should be done early, in a systematic way, with photographs and measured notes. Findings that raise suspicion include sudden death in a previously healthy animal, several deaths together, unusual smell from the stomach contents,

discoloured or ulcerated gut lining, congestion of organs, and visible bait or plant material.

Some patterns point toward groups of poisons. For example, a chemical smell or a bright blue-green colour in stomach contents may suggest a particular pesticide. Pale tissues with bleeding suggest anticoagulant rodenticides. Corrosive injury suggests acids or alkalis. Kidney changes suggest nephrotoxic agents.

The limits are important. Many poisons leave **no specific lesion**. Putrefaction can hide or mimic findings. An infectious disease such as anthrax or clostridial disease can look similar and must be considered. For this reason the post-mortem is a guide to which samples to send, not a final answer. State only what you observed, and avoid declaring a cause of death before laboratory results arrive.

Reporting and court procedure

A good report is plain, factual and dated. It should contain the identity of the animal and owner, history, clinical signs, treatment given, post-mortem findings, samples collected with their preservation, and the chain of custody. Opinions should be separated from observations, and any uncertainty stated honestly.

When the case is a police matter, the report goes to the investigating officer. The laboratory report then arrives separately. The final opinion on cause of death is formed by combining history, lesions and laboratory results.

If called to court, the veterinarian appears as an expert witness. Bring the original notes, and be ready to explain how samples were collected and sealed. Answer only what is asked, in simple language, and do not stretch beyond the evidence. Admit what is unknown. Attendance on the summons date matters, so tell the court in advance if there is a genuine difficulty.

Relevant laws can include provisions on cruelty to animals and on harming animals, and the rules of evidence for experts. Because these Acts have recently been revised, confirm the present provisions with the legal authority before quoting them. Seek advice from a senior colleague or the state veterinary council if unsure how to proceed.

Concept cleared

Evidence, not just diagnosis

In a medico-legal case every step must be documented so that another person could verify it later.

Screening versus confirmation

TLC and ELISA suggest; GC-MS and related methods confirm. A court needs confirmation.

Chain of custody

A signed record of every hand that held the sample, proving it was not changed.

Absence of lesions is not absence of poison

Many poisons leave no specific post-mortem change, so samples must be collected anyway.

Memory aid: Medico-legal steps: SCRIPT

Secure the scene, Collect samples, Record everything, Identify and label, Pass on with chain of custody, Testify honestly.

Compare and contrast

Laboratory methods

Method	Principle	Role
TLC	Separation on a plate, compared with standards	Simple screening
ELISA	Antibody binding to target	Rapid screening, may cross-react
GC-MS	Separation then identification by fragments	Confirmation

Samples and what they show

Sample	Value	Note
Stomach contents	Actual material swallowed	Collect early
Liver	Metabolism and storage	Drugs, metals
Kidney	Excretion	Metals, nephrotoxins
Brain	Specific tests	Cholinesterase in suspected organophosphate case
Feed or bait	Source of poison	Often decisive

Species notes

Dogs

Most common victims of malicious bait poisoning; vomitus and stomach contents are valuable samples.

Cattle and buffalo

Rumen contents are bulky and mixed, so collect from several areas and also sample feed and fodder.

Horses

Poisoning of competition animals involves blood and urine sampling, and strict sealing procedures.

Poultry

Submit several fresh carcasses and feed, since the question is usually about the flock.

Wildlife

Often needs the forest authority; handle carcasses carefully and report promptly.

Clinical pearls

Self-test: 10 questions

1. Which preservative should be avoided for samples meant for chemical analysis?

Formalin interferes with chemical testing; it is kept for histopathology samples.

2. Why is a control sample of the preservative sent?

It rules out contamination from the preservative.

3. Which method is generally regarded as confirmatory?

Mass spectrometry identifies compounds by fragment pattern.

4. ELISA results should be treated as:

Antibody tests may cross-react.

5. Chain of custody refers to:

It shows the sample was handled and not changed.

6. Which sample is often the most valuable in a suspected oral poisoning?

It may contain the actual poison.

7. A post-mortem with no specific lesions:

Many poisons leave no specific lesion.

8. The brain is collected in suspected organophosphate cases for:

Reduced cholinesterase supports exposure to these compounds.

9. In a report, the veterinarian should:

Clear separation protects the credibility of the evidence.

10. Before quoting a section of law in court, one should:

Indian criminal and evidence laws have been revised recently.

Key points to revise

1. Medico-legal cases require documentation at every step.
2. Collect stomach contents, liver, kidney, blood, urine, brain where relevant, and feed or bait.
3. Use separate labelled and sealed containers and follow the laboratory's preservative advice.
4. TLC and ELISA are screening tools; GC-MS confirms.
5. Chain of custody records each person who held the sample.
6. Many poisons leave no specific lesions, and infectious diseases can mimic poisoning.
7. Reports must separate observation from opinion.
8. Check current statutes and notifications before quoting legal provisions.

Go deeper on this site

- Ch 16. Environmental, poultry and wildlife toxicology (in this book)
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Sources

- Merck Veterinary Manual: Toxicology (contents)
- World Organisation for Animal Health (WOAH)

- US FDA Center for Veterinary Medicine

How to use Book 6: a short discussion

Toxicology is the study of how substances harm living animals and what can be done about it. In veterinary practice poisoning is a daily emergency: a dog that has eaten chocolate or a human painkiller, a herd that has grazed a toxic weed after the first rains, a flock exposed to a contaminated feed, a cat that has walked through a freshly treated floor. This book covers seventeen of the most important areas, arranged so that principles come first and detail follows.

Principles before poisons

The first chapter explains how a toxic substance is absorbed, distributed, changed and removed, why dose and timing matter, and how the general approach to a poisoned animal is organised: stabilise, find out what was taken, prevent further absorption, give an antidote when one exists, and support the animal while the body clears the poison. Reading this chapter first makes every later chapter easier, because most poisons follow the same logic with a different target.

Grouped by source

The middle chapters group poisons by where animals meet them: pesticides and rodenticides, herbicides and fungicides, plants, heavy metals, feed contaminants, toxic gases and algae, photosensitising agents, household products, human medicines and venoms. This follows the way a case arrives in clinic, with a history of exposure, so you can move from the history to the likely poison and then to the signs and the response.

Species and Indian conditions

Species differences matter greatly. Cats handle many chemicals poorly, ruminants are vulnerable to plants and feed errors that other species tolerate, and horses react badly to certain feed additives. The book also reflects Indian conditions, including seasonal plant poisoning, pesticide use on farms, snakebite and the fate of vultures

after exposure to a veterinary painkiller. Where Indian rules or availability are mentioned, the text asks you to check the current notification instead of trusting a fixed list.

Antidotes and the law

Chapter 15 gathers antidotes and decontamination methods into a quick reference that explains the mechanism of each and the cautions that apply, without doses. The final chapters deal with environmental, poultry and wildlife toxicology and with medico-legal work: how to collect and preserve samples, how laboratories analyse them, how a chain of custody is kept and what is expected in a report or in court.

Taking a poisoning history

The most valuable tool in toxicology is a careful history. Ask what the animal could have reached, when, in what form and how much, and whether other animals were exposed. Ask about recent feed changes, pesticide use, new plants in the pasture, human medicines in the house and any recent treatment given at home. Keep the packaging or a sample of the suspected material, and take samples early, because some poisons disappear from the body quickly. The chapters repeatedly show how the history points toward the poison, and how the clinical signs then confirm or challenge your first idea.

Using this book safely

This is a study book. It does not contain toxic-dose tables or treatment doses, and it must not be used to manage a real poisoning by itself. In an emergency, contact an animal poison service, a toxicologist or your clinic's senior veterinarian straight away. Use the self-test at the end of each chapter, repeat it after a week, and read the Species notes and Revise points before an examination.

The later chapters link to the drugs and anaesthesia material in Books 2 to 5, because many poisonings are treated with drugs whose mechanisms you have already studied.

BVSC & AH STUDY BOOK 7 OF 7

Therapeutics by Species and Final Revision

Eight chapters that bring the series together: drug choice in dogs and cats, cattle and buffalo, small ruminants, horses, poultry, pigs and rabbits, exotics and wildlife, followed by a mixed practice bank with twenty field cases and a viva set, and a glossary with concept maps. Each chapter ends with a self-test.

8 chapters | **100** practice questions | **No** dose tables

By Dr. Rameez Bloch, BVSc & AH, MVSc

Start here

Pick a chapter from the list on the left (or the top bar on a phone). Chapters 1 to 6 apply the earlier books species by species. Chapter 7 is the practice bank: twenty Indian field cases, a viva question set and thirty mixed questions. Chapter 8 is the glossary and concept maps for last-minute revision. Each chapter has six parts: Learn, Concepts, Compare, Species, Quiz and Revise. Your quiz progress is saved on this device only.

CHAPTER 1 OF 8

Therapeutics in dogs and cats

How to reason from diagnosis to drug choice in common small animal conditions, what not to give to dogs and cats, and how to explain treatment to owners. The chapter links the pharmacology of Books 1 to 6 to everyday clinic decisions.

After this chapter you can

- Apply a stepwise reasoning method to choose a drug for a dog or cat
- Explain why antimicrobials are not the first answer to most acute vomiting and diarrhoea

- Choose between topical and systemic therapy for skin and ear disease using diagnostic findings
- List common drugs and household products that must not be given to dogs and cats and explain why
- Communicate drug use, side effects and follow-up clearly to an owner

From diagnosis to drug: a reasoning method

Good therapeutics begins before the prescription. Ask five questions in order. What is the diagnosis, or the most likely problem list? What is the aim of treatment: cure, control, comfort or prevention? Which drug classes can reach that target? Is this particular patient (species, age, breed, pregnancy, liver, kidney, other drugs) a reason to avoid any of them? And how will you and the owner know it is working?

Many treatment failures come from skipping the first question. Giving an antibiotic, a steroid and a vitamin injection together for 'fever' hides the diagnosis and makes the response impossible to interpret. Revise the principles of Book 1 (pharmacokinetics, adverse reactions) and Book 4 (applied pharmacology) alongside this chapter.

A useful habit is to prefer the narrowest, safest option that fits the aim, and to review the patient after a short interval rather than extend a course blindly.

Dogs and cats are not small people or small dogs

Species differences in drug handling decide many safe-or-harmful choices. **Cats** are deficient in some glucuronidation pathways, so drugs cleared mainly by glucuronide conjugation (paracetamol is the classic example) accumulate and damage red cells and liver. Cats also tolerate many NSAIDs poorly, because the drugs are cleared slowly. **Dogs** of some herding breeds carry the MDR1 (ABCB1) variant, which raises brain exposure to certain drugs such as ivermectin at higher doses (Book 1, Book 6).

Sighthounds recover slowly from some barbiturate anaesthetics because of low body fat and different metabolism (Book 5). Puppies, kittens and old animals have immature or reduced hepatic and renal clearance and less reliable hydration, so they need extra caution and clear monitoring.

A common confusion: 'safe in dogs' does not mean 'safe in cats'. Always check the species on the label and in the reference you use.

Gastrointestinal disease: vomiting and diarrhoea

Most acute vomiting and diarrhoea in dogs and cats is self-limiting or caused by diet, parasites or viruses. The therapeutic priorities are **hydration, electrolyte and acid-base correction, rest of the gut, then re-feeding**. Antibiotics do not treat viral or dietary causes and may worsen dysbiosis; they are reserved for patients with evidence of systemic spread, such as fever with a marked low white cell count, blood in the stool with sepsis signs, or a confirmed bacterial cause.

In parvoviral enteritis, treatment is supportive: fluids, anti-emetics, nutrition, pain control and often an antimicrobial because gut barrier damage allows bacteria to enter blood. The antimicrobial is aimed at that secondary risk, not at the virus. Vaccination and isolation are the real control (Book 2 and Book 4).

Choose anti-emetics by mechanism: central and peripheral agents act at different sites, and an anti-emetic must never be used if an obstruction or foreign body is possible, because it hides a surgical emergency. Be careful with antispasmodics and motility drugs in infectious diarrhoea.

Check for the common Indian causes first: heavy worm burden in puppies and kittens, dietary indiscretion, and tick-borne disease when fever and anaemia coexist.

Skin, ear and infectious disease

Skin disease is the commonest reason for antibiotic use in dogs. Before choosing a drug, find the cause: ectoparasites, allergy, fungal or bacterial infection. Cytology of skin or ear swabs separates bacteria, yeast and mites in minutes and guides the choice.

Where lesions are superficial and localised, **topical therapy** (antiseptic shampoos, topical agents) reduces systemic antibiotic exposure and resistance pressure. Systemic antibiotics are kept for deeper infection, and culture and sensitivity is advised for recurrent or non-responding cases. Treating pyoderma without treating the underlying allergy or parasite means relapse.

In otitis, identify the organism type and check the eardrum before using a topical, because some ear products can be ototoxic if the drum is ruptured (Book 6). Use corticosteroids carefully: they ease itch quickly, but they also suppress immunity, and a steroid given for 'allergy' on a patient with untreated demodicosis can make the disease explode.

For tick-borne disease such as ehrlichiosis or babesiosis, which are common in Indian dogs, diagnosis (smear, serology or PCR) should come first, then a drug active against the specific agent (Book 3). Doxycycline in cats can lodge in the oesophagus and cause stricture unless followed by food or water.

What not to give: safety and drug interactions

Make a short 'never' list that you can recall under pressure.

- **Paracetamol** in cats (and caution in dogs): methaemoglobinaemia and liver injury.
- **Human NSAIDs** (ibuprofen, naproxen, aspirin at human practice) in dogs and cats: gastric ulcers and kidney injury. Use only veterinary-licensed NSAIDs, and avoid them in dehydrated, hypotensive, or renal-compromised patients.
- **NSAID plus corticosteroid together**, or switching between two NSAIDs without the gap stated in the label: serious GI ulceration risk.
- **Permethrin and other pyrethroid products** for dogs applied to cats, or cats licking a treated dog: severe tremors and seizures (Book 6).
- **Xylitol**, chocolate, grapes and onion exposure: not drugs but common owner-introduced toxins.
- **Fluoroquinolones** in cats at high exposure: retinal damage. In growing large-breed puppies they may damage cartilage.
- **Aminoglycosides** in dehydrated or renal patients: nephrotoxicity.
- **Ivermectin-class drugs** in MDR1-affected breeds at doses used for other purposes.

Interaction thinking: loop diuretics plus NSAIDs affect the kidney, and sedatives plus opioids add respiratory depression. Always ask what the owner has already given at home, including Ayurvedic or human medicines from the pharmacy.

Talking to the owner

Drug success depends on the owner as much as on the drug. Explain in plain language: what the drug is for, how it is given, what to expect, what side effects need a phone call, and when to return. Link the instruction to something the owner can see, for example 'if the pet stops eating or vomits blood, stop the tablet and bring the dog in'.

Address the common client pressures honestly. Owners may ask for an antibiotic injection 'to be safe', request human tablets they have used, or stop the course when the pet looks better. Explain that the wrong or half course helps resistant bacteria, that some human drugs are dangerous for pets, and that some conditions (worms, tick fever, skin infection) need the full course or follow-up test.

Discuss cost openly, offer stepwise options, and record the plan. Remind owners that zoonotic risks (hookworm, ringworm, rabies) change how they handle the pet and its excreta. Do not guarantee outcomes. Document consent for off-label use and explain that unlicensed use is a professional decision to be made carefully. Check current Indian regulations for restricted drug classes before dispensing.

Concept cleared

Treat the diagnosis, not the symptom
A drug works only if it targets the cause or a real clinical aim. Antibiotics for viral diarrhoea or steroids for undiagnosed itch give false comfort and hide the true disease.

Species and breed set the safe list
Cats are weak in glucuronidation, some dogs carry MDR1 variants, and young or old animals clear drugs slowly. The same molecule can be safe in one patient and harmful in another.

Topical before systemic when the lesion is local
Local therapy gives high drug at the site with less body exposure and less selection of resistant bacteria. Systemic drugs are for deep or generalised disease.

Stewardship protects future patients

Culture, cytology, correct drug class and a complete course reduce resistance. Reserve higher-tier antimicrobials for cases where first-line drugs have failed or are unsuitable.

Memory aid: DRUG-PET check before prescribing

Diagnosis, Reason for treatment, Unwanted effects, Going home plan; Patient species, Existing drugs, Timing of review.

Compare and contrast

Dog versus cat: key pharmacological cautions

Issue	Dog	Cat
Paracetamol	Caution, liver and red cell injury at overdose	Avoid; very low tolerance
NSAIDs	Use licensed veterinary products with monitoring	Narrower safety; use only labelled products with care
Permethrin spot-ons	Generally tolerated as labelled	Severe neurotoxicity if exposed
Glucuronidation	Adequate	Deficient, drugs accumulate
Doxycycline tablets	Usually well tolerated	Risk of oesophageal stricture without fluid

Topical versus systemic therapy in skin disease

Feature	Topical	Systemic
Best for	Superficial, localised lesions	Deep or generalised infection
Resistance pressure	Lower	Higher
Owner compliance	Needs time and technique	Easy to dose but side effects more likely
Key need	Contact time and correct product	Culture and a full course

Species notes

Dogs

MDR1 variant breeds and sighthounds need special care. Skin and tick-borne disease dominate. Avoid human NSAIDs and chocolate or xylitol exposures.

Cats

Poor glucuronidation. Avoid paracetamol and permethrin. Tablets such as doxycycline should be followed by water or food. Cats hide illness, so earlier review is wise.

Puppies and kittens

Immature liver and kidney, easily dehydrated and hypoglycaemic. Check the label for age limits and worm control schedules.

Geriatric pets

Reduced renal and hepatic reserve. Check kidney function before NSAIDs and review earlier.

Pregnant or lactating animals

Some antimicrobials, antiparasitics and hormones are unsafe. Read the label and check the reference before use.

Clinical pearls

Self-test: 10 questions

1. Which drug is especially dangerous for cats because of deficient glucuronidation?

Cats cannot conjugate paracetamol efficiently, so toxic metabolites accumulate.

2. The main aim of antibiotics in parvoviral enteritis is to:

Antibiotics have no antiviral action; they cover bacteria entering through the damaged gut.

3. First-line therapy for most mild acute vomiting and diarrhoea is:

Most cases are self-limiting; rehydration and diet are the priorities.

4. Before giving an anti-emetic you must exclude:

Stopping vomiting can mask a surgical emergency.

5. Which combination is most likely to cause severe gastric ulceration?

Both reduce gastric mucosal protection and the effects add up.

6. A dog permethrin product applied to a cat is dangerous because:

Cats metabolise pyrethroids poorly and are highly susceptible.

7. Best first step in a dog with recurrent pyoderma is to:

Without treating allergy, parasites or endocrine disease, infection returns.

8. Doxycycline tablets in cats should be followed by:

This helps the tablet pass into the stomach and prevents oesophageal injury.

9. Which is a good reason for topical therapy in superficial skin infection?

Local delivery gives drug at the site and spares the rest of the body.

10. Which owner message improves safety most?

Clear warning signs help early detection of adverse effects.

Key points to revise

1. Ask five questions before every prescription: diagnosis, aim, drug options, patient factors and monitoring.
2. Hydration and electrolyte correction come before antimicrobials in most acute gastroenteritis.
3. Parvoviral enteritis antibiotics target secondary bacterial spread, not the virus.
4. Cytology and culture guide skin and ear therapy.
5. Topical therapy reduces systemic exposure where lesions are local.
6. Cats cannot handle paracetamol and many NSAIDs.
7. Human drugs should not be used in pets unless a veterinarian approves.
8. Good client communication improves compliance and safety.

Go deeper on this site

- Ch 2. Therapeutics in cattle and buffalo (in this book)
- Ch 3. Therapeutics in sheep, goats and camelids (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual
- WSAVA Global Guidelines
- FDA Center for Veterinary Medicine

CHAPTER 2 OF 8

Therapeutics in cattle and buffalo

Drug-choice reasoning for common bovine problems: mastitis, fever, calf diarrhoea, metabolic disease and reproductive disorders. The chapter stresses withdrawal

periods for milk and meat, and how to explain them to dairy farmers.

After this chapter you can

- Explain why every treated dairy animal creates a milk and meat residue question
- Reason through mastitis therapy using type, cause and route of administration
- Distinguish causes of fever in cattle and buffalo before selecting a drug
- Describe supportive priorities in calf diarrhoea and key metabolic emergencies
- Communicate withdrawal and prudent-use advice to farmers

Food animals change the rules

In companion animals the patient is the only concern. In cattle and buffalo the **treated animal also produces food**. Every drug given to a lactating or slaughter-bound animal raises a second question: how long until milk and meat are safe for people? The answer is the **withdrawal period** (milk withdrawal and meat withdrawal are separate), printed on the product label.

Residues matter because they can cause allergy, disturb gut flora, interfere with dairy fermentation and drive antimicrobial resistance. The logic of the maximum residue limit (MRL) was covered in Books 1 and 4. Indian MRLs and permitted or banned substances change; check the current FSSAI and government notifications before advising a farmer.

Practical consequences are simple. Choose, where equal, the drug with the shorter withdrawal. Record the animal, drug, date and withdrawal end. Separate treated milk. Never use a drug listed as prohibited in food animals. Extra-label use should be a considered veterinary decision with an extended and defensible withdrawal, not a guess (Book 6 for toxic residues).

Mastitis

Mastitis is the commonest drug-use reason on dairy farms. Reason in steps. First, is it **clinical** (visible milk or udder change) or **subclinical** (raised somatic cell count,

positive screening test such as the California mastitis test)? Second, is the animal systemically ill? Third, which pathogen group is likely: Gram-positive (Staphylococcus aureus, Streptococcus), Gram-negative coliforms, or others such as Mycoplasma and yeasts?

Mild clinical cases usually need intramammary treatment, frequent stripping out of milk and good hygiene. Systemically ill cows, especially with coliform toxaemia, need **fluid therapy, NSAIDs for toxaemia and pain, and systemic antimicrobials** as clinically indicated. A drug must reach the milk compartment: some agents distribute poorly into milk because of their ionisation and protein binding (Book 1), so route matters.

Culture of milk from non-responding or recurrent cases guides drug choice. Chronic *S. aureus* infection often fails because bacteria hide inside cells and fibrous udder tissue, which is why cure rates are poor and prevention (milking hygiene, teat dipping, culling chronic cases) matters more. Antibiotic dry cow therapy is best used by risk or culture rather than automatically in every animal, subject to local advice.

Buffalo have narrower teat canals and long lactations, so treat any tight, painful udder promptly, and note that subclinical mastitis is silent and common.

Fever and tick-borne disease

Fever in cattle and buffalo is a sign, not a diagnosis. Common causes in India include tick-borne disease (theileriosis, babesiosis, anaplasmosis), bacterial pneumonia, metritis, mastitis, foot and mouth disease and haemorrhagic septicaemia. A systematic exam, blood smear and a look at lymph nodes, udder, uterus and lungs usually narrows the list.

Choose treatment by the diagnosis. Specific antiprotozoal drugs exist for theileriosis and babesiosis (Book 3), and early treatment greatly improves outcome. A broad antibiotic does not treat protozoa, and an NSAID for fever alone can hide the pattern. Viral diseases such as FMD need supportive care and secondary infection control, not antibiotics for the virus.

Antipyretics and NSAIDs reduce fever and pain but also reduce feed intake loss and so can be useful. Keep in mind hydration status and kidney perfusion before using them. Some NSAIDs have long withdrawal periods in food animals, and some drugs

are not permitted in livestock. For example, the diclofenac-vulture issue led to restrictions; check the current notification before using any NSAID.

Vaccination, tick control and quarantine are the long-term answer. Tell farmers that treating a fever without tick control invites repeat illness.

Calf diarrhoea and metabolic disease

Calf diarrhoea (scours) kills mainly through dehydration, acidosis and electrolyte loss, not through the germ itself. The first treatment is therefore **oral or intravenous fluids with electrolytes and an energy source**, and continuing milk feeding when possible. Antimicrobials are needed only when calves show systemic illness (fever, depression, signs of septicaemia) or invasive bacterial infection. Many scours are viral, protozoal (cryptosporidiosis) or nutritional, and antibiotics do not help these. Colostrum intake in the first hours of life is the best prevention.

Hypocalcaemia (milk fever) around calving is treated with slow intravenous calcium and careful heart monitoring because rapid infusion can cause arrhythmia. Relapse is common, so follow-up and correct feeding of dry cows are needed. Do not confuse it with other downer cow causes. **Ketosis** responds to glucose sources and attention to energy intake. Hypomagnesaemia produces tetany and needs magnesium given carefully. In all metabolic disease, treating the cause (feed and management) matters as much as the injection.

These conditions are mostly not antibiotic problems. An antibiotic in a milk fever cow adds only withdrawal burden unless a concurrent infection exists.

Reproductive problems

Retained placenta, metritis and endometritis are linked to difficult calving, hypocalcaemia and poor hygiene. Manual removal of a firmly attached placenta can cause injury and bleeding, so many clinicians prefer supportive measures and monitoring. Systemic antimicrobials are justified for metritis with fever and systemic signs. Intrauterine antibiotics in low-grade endometritis give mixed results and add withdrawal concerns.

Hormones need care. **Prostaglandin F2-alpha** analogues cause luteolysis and can terminate pregnancy, and they are hazardous to pregnant women and asthmatics handling them. **Oxytocin** has valid uses in obstetrics, but misuse to force milk let-

down is a recognised regulatory and welfare concern in India; check the current notification on its sale and use. Hormonal treatment of anoestrus or repeat breeding should follow a proper reproductive examination (Book 2 and Book 4), because in buffalo silent oestrus and poor heat detection are often the real problem and not a lack of hormone.

Always verify pregnancy status before using a drug that can affect gestation.

Prudent use and talking to farmers

Farmers often expect an injection every time. Explain the logic: right diagnosis, right drug, right duration, and time for the body to recover. Antimicrobial resistance moves between animals, farms and people, which is why international bodies such as the WHO promote a One Health approach.

Advise farmers to: complete the prescribed course; keep a treatment record; mark and separate treated animals; discard milk during the whole withdrawal period; avoid selling animals for slaughter before the meat withdrawal ends; and never use leftover or human drugs. Antimicrobials listed as restricted or banned for food animals must not be used; check the current regulatory list.

Encourage prevention: vaccination, deworming, tick control, clean milking, dry-cow management and good transition feeding. Use cost as a teaching point: preventing mastitis or milk fever costs less than treating and discarding milk. Where unsure of a withdrawal time, use the longest labelled value for the drug and consult current guidance rather than risk residues.

Concept cleared

Two withdrawal clocks
Milk and meat withdrawal periods are different and both start after the last dose. The longer applicable one governs what can be sold.

Drug must reach the site
In mastitis, ionisation, protein binding and route decide whether drug reaches milk. Intramammary and systemic therapy suit different situations.

Fluids first in scours

Calf deaths come from dehydration and acidosis, so replacement of fluid and electrolytes is the core treatment.

Prevent more than treat

Hygiene, colostrum, vaccines, tick control and balanced transition feeding reduce disease and drug use together.

Memory aid: TREAT-SAFE for food animals

Test and diagnose, Record the drug, Examine withdrawal, Avoid banned drugs, Tell the farmer; Separate milk, Allow full time, Follow up, Educate.

Compare and contrast

Clinical versus subclinical mastitis

Feature	Clinical	Subclinical
Signs	Visible milk or udder change	None; raised cell count or positive screening test
Detection	Farmer or vet examination	CMT, cell count, culture
Treatment focus	Intramammary, with systemic care if ill	Control by hygiene, dry-period therapy by risk, culling chronic cases
Milk	Discard for withdrawal	Also discard during any treatment withdrawal

Milk fever versus ketosis

Feature	Milk fever	Ketosis
Cause	Low blood calcium	Negative energy balance
Usual timing	Around calving	Early lactation
Treatment idea	Slow calcium with heart monitoring	Glucose source and better energy intake
Prevention	Dry cow mineral management	Good transition feeding

Species notes

Cattle

Most label data and withdrawal times exist for cattle. Check the product label and current Indian guidance. Crossbred dairy cows are prone to tick-borne disease and metabolic disease.

Buffalo

Silent heat, heat stress and narrow teat canals are common issues. Do not assume that cattle label times apply; check the label and use cautious extended times if data are missing.

Calves

Dehydration is the main danger. Immature rumen and liver mean some drugs act differently; check label limits.

Pregnant animals

Prostaglandins and some other drugs can cause abortion. Confirm pregnancy status first.

Lactating animals

Every drug needs a milk decision. Choose products with a clear milk withdrawal and keep records.

Clinical pearls

Self-test: 10 questions

1. A withdrawal period is the time that must pass:

It protects consumers by letting residues fall below safe levels.

2. In a calf with watery diarrhoea and dehydration, the first priority is:

Death is mainly from dehydration and acidosis.

3. Why is chronic Staphylococcus aureus mastitis hard to cure?

Poor drug access and intracellular survival reduce cure rates.

4. A cow with coliform mastitis and toxaemia needs:

Systemic illness needs supportive and systemic care.

5. Which statement about prostaglandin F2-alpha is correct?

It regresses the corpus luteum and hence can end pregnancy.

6. Milk fever treatment should use:

Rapid infusion can cause cardiac arrhythmia.

7. An antibiotic given for fever from theileriosis will:

Theileria is a protozoan; specific drugs are needed.

8. Which is best farmer advice?

Records and discard prevent residues and support traceability.

9. Why is accurate diagnosis important in buffalo reproductive problems?

Poor heat detection is often the real cause of apparent infertility.

10. Which approach supports prudent antimicrobial use on a farm?

Targeted therapy reduces resistance and residue risk.

Key points to revise

1. Treated food animals create residue risk for people.
2. Withdrawal periods must be followed for milk and meat separately.
3. Mastitis therapy depends on clinical state, pathogen and route.
4. Chronic Staphylococcus aureus mastitis cures poorly, so prevention and culling matter.
5. Fever in cattle has many causes; diagnose before choosing a drug.
6. Calf scours are treated first with fluids and electrolytes.
7. Milk fever needs slow intravenous calcium with heart monitoring.
8. Farmers need clear written instructions and records.

Go deeper on this site

- Ch 3. Therapeutics in sheep, goats and camelids (in this book)
- Ch 1. Therapeutics in dogs and cats (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Concepts
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual
- FDA Center for Veterinary Medicine
- WHO antimicrobial resistance fact sheet

CHAPTER 3 OF 8

Therapeutics in sheep, goats and camelids

Small ruminants and camelids are often treated as small cattle, which causes errors. This chapter explains why dosing is constrained, how to control parasites without breeding resistant worms, and which species cautions matter in field practice.

After this chapter you can

- Explain why drugs licensed for cattle cannot be simply scaled down for sheep, goats and camelids
- Describe how anthelmintic resistance arises and how refugia, FAMACHA and targeted selective treatment slow it
- Choose drugs for common small ruminant conditions while respecting withdrawal and residue logic
- List species-specific cautions for goats, sheep and camelids
- Communicate treatment limits and withdrawal periods clearly to farmers

Why small ruminants are therapeutic orphans

Sheep and goats are numerous in India and are kept mostly by small and landless farmers, yet very few products are developed and licensed specifically for them. Most label information comes from cattle. This creates the central problem of this chapter: **extra-label use is common, but it is not safe by default**.

Three ideas explain the constraint. First, species differ in absorption, metabolism and elimination, so a cattle plan may under-treat or over-treat a goat. Second, animals that produce milk or meat for people need a defined **withdrawal period**, and for an extra-label use nobody has measured it. Third, the margin of safety of some drugs is narrow in small bodies, where measuring error is proportionally larger. Revise Book 1 on pharmacokinetics and Book 6 on toxicology alongside this chapter.

Dosing constraints: reasoning, not numbers

Goats are browsers and differ from sheep in how they handle many drugs. In general, goats are often described as clearing several anthelmintics and other drugs faster than sheep or cattle, so an effect that is adequate in one species can fail in another. This is a general teaching point, so always check product literature rather than copying a figure from another species.

Practical constraints you should apply every time:

- **Estimate weight honestly.** Under-dosing is the main driver of resistance, and over-dosing is the main driver of toxicity. Weigh or use a tape, and dose to the

heaviest animal in a small group, not the average, only when the drug has a wide margin.

- **Check the label for the species.** A drug approved in sheep may not be approved in goats, and milk-producing animals have extra limits.
- **Prefer the narrowest suitable route.** Injection sites matter in meat animals because residues persist at the site.
- **Consider the rumen.** Oral drugs meet rumen microbes; some are inactivated, and ruminal flow changes how quickly a drug reaches the abomasum and intestine.

Common confusion: students assume that a drug safe in cattle is safe in a kid or lamb. Young animals have immature metabolism and a much smaller body, so errors are magnified.

Parasite control and anthelmintic resistance

The barber pole worm, *Haemonchus contortus*, is the dominant killer of small ruminants in warm, humid regions. It sucks blood, so heavily infected animals become anaemic, develop bottle jaw and die. Anthelmintic resistance is widespread in small ruminants worldwide, and Indian veterinarians should assume it is present on any farm until shown otherwise by testing.

Resistance develops by selection. Every treatment kills susceptible worms and leaves resistant ones to breed. The worms that survive pass resistance genes on. Under-dosing, treating the whole flock repeatedly and moving treated animals straight to clean pasture all speed this up.

The modern strategy is to **keep susceptible worms alive**:

- **Refugia.** The worms not exposed to a drug, whether in untreated animals or on contaminated pasture, dilute resistant genes. Leaving some animals untreated is therefore a feature of good practice.
- **FAMACHA.** A colour chart for the conjunctiva, used to estimate anaemia from *Haemonchus*. Only animals that are anaemic are treated.
- **Targeted selective treatment (TST).** Treat the animals that show clinical signs, poor production or high faecal egg counts, using tools such as body condition and faecal egg count.

- **Test before trusting.** A faecal egg count reduction test shows whether a drug still works on that farm.
- **Quarantine and treat newcomers** with more than one drug class before mixing them with the flock, so that you do not import resistant worms.

FAMACHA is useful for Haemonchus only; it will not detect other causes of weight loss. Cross-refer to Book 3 for the anthelmintic classes and their mechanisms.

Antibiotics, anti-inflammatories and supportive care

Drug choice should follow diagnosis. Many small ruminant diseases that farmers call fever or pneumonia are parasitic, nutritional or viral, and antibiotics do nothing for them. Before giving an antibacterial, ask three questions: is there evidence of a bacterial cause, is the drug likely to reach the site, and what withdrawal applies in a milk or meat animal?

- **Pneumonia and enteric infection.** Choose by likely organism and by whether a milk or meat withdrawal is documented for that species.
- **Enterotoxaemia.** Prevention by vaccination is far more effective than treatment, because the toxins act within hours.
- **Coccidiosis in young stock.** Treat the group and fix hygiene and stocking density; drugs without management fail.
- **Pregnancy toxaemia and hypocalcaemia.** These are metabolic emergencies where correcting the metabolic problem, not giving antibiotics, is the treatment.
- **Anti-inflammatory drugs.** Use NSAIDs with caution in dehydrated or pregnant animals because of renal and gastric risk, and check the meat and milk status.

Remember the stewardship principle from Book 4: do not use critically important antibiotics as routine first-line drugs in food animals, and check the current notification of the relevant authority about restricted drugs.

Species cautions

These cautions are conceptual reminders. For details, always check the product label and a current reference.

- **Sheep and copper.** Sheep accumulate copper in the liver and are far more sensitive than cattle or goats. Avoid feed or mineral mixes meant for other species. See Book 6.

- **Goats.** Goats are often under-dosed because label doses come from sheep or cattle, and milk-producing goats require special withdrawal care. Do not assume that a sheep or cattle label covers a goat.
- **Ionophores.** Monensin and related feed additives can be toxic to small ruminants, and to horses and camelids, when dosing or mixing is wrong.
- **Camelids.** Camels and other camelids differ from true ruminants in their stomach compartments and in some drug handling, and many ruminant drugs have no camelid label. Seek camelid-specific guidance and be conservative.
- **Urea and non-protein nitrogen** poisoning is a risk in all ruminants fed unmixed supplements.

Common confusion: camelids are not ruminants in the strict sense and are not just small camels; do not extrapolate a cattle dose.

Withdrawal, residues and talking to the farmer

A **withdrawal period** is the minimum time between the last treatment and the sale of milk, meat or eggs, so that residues fall below the legal limit. The limit is called the maximum residue limit (MRL). Indian MRLs and withdrawal rules change, so check the current notification of the relevant authority. Extra-label use has no known withdrawal time, so the safe approach is to consult a source such as a poison and residue information service or the manufacturer, and to document the treatment.

Client communication carries most of the weight:

- Tell the owner in plain language not to sell milk or slaughter the animal until the withdrawal date, and write it down.
- Explain that treating every animal does not protect the flock, and may make worms resistant.
- Explain why you are not prescribing an antibiotic for a viral disease, and what to watch for.
- Record animal identity, drug, date and withdrawal for every treated animal.

A frequent exam error is forgetting that milk goes to children and to traditional dairy products. Residues in cheese and curd, and heat stability of residues, are real public health concerns, so withdrawal must be stated for the product the family actually consumes.

Concept cleared

Extra-label is not label-free
Using a drug outside its label means you carry responsibility for efficacy, safety and withdrawal. It needs a diagnosis, a reason, a source for the withdrawal advice and a record.

Refugia
Worms that escape drug exposure keep susceptible genes in the population. Leaving some animals untreated slows resistance.

Target the animal, not the flock
FAMACHA and targeted selective treatment treat only the animals that need it, using anaemia, condition or egg counts as guides.

Species differences in drug handling
Goats, sheep and camelids absorb, metabolise and eliminate drugs differently from cattle, so a cattle plan cannot be copied across.

Memory aid: Before you dose a small ruminant: SWAP
Species label, Weight estimate, Anthelmintic resistance status, Produce withdrawal (milk and meat). Check all four before you treat.

Compare and contrast

Sheep, goats and camelids at a glance

Feature	Sheep	Goats	Camelids
Main drug issue	Copper sensitivity	Under-dosing from borrowed labels	Few labelled products
Feeding style	Grazers	Browsers	Browsers and grazers with three-compartment stomach
Residue concern	Meat, wool-farm use	Milk and meat	Meat and milk in some regions
Reasoning rule	Check mineral mixes	Do not copy sheep labels	Seek camelid-specific advice

Whole-flock versus targeted treatment

Aspect	Whole-flock treatment	Targeted selective treatment
Drug use	High	Low
Selection for resistance	Strong	Weaker, refugia kept
Effort	Low	Needs FAMACHA or egg counts
Best when	Specific strategic periods advised locally	Routine management

Species notes

Sheep
Sensitive to copper; avoid mineral mixes made for other species. Weigh carefully before dosing.

Goats
Do not assume sheep or cattle labels fit goats; they are often under-dosed. Milk withdrawal needs particular care.

Camelids
Have a different stomach and handle some drugs differently from ruminants; there are few labelled

Young stock
Lambs, kids and crias have immature metabolism and small body size, so dosing errors are magnified.

products, so be conservative and seek specific guidance.

Pregnant and lactating animals
Check each drug for fetal safety and milk residues, and treat metabolic disease as an emergency.

Clinical pearls

Self-test: 10 questions

1. The main reason a cattle label cannot be applied to a goat is that

Species differ in drug handling, and extra-label use has no measured withdrawal.

2. Refugia means

Worms not exposed to drugs dilute resistant genes.

3. FAMACHA is used to

It grades the conjunctival colour so only anaemic animals are treated.

4. Which practice most speeds up anthelmintic resistance?

These practices select strongly for resistant worms.

5. Sheep are especially sensitive to

Sheep accumulate copper in the liver.

6. Targeted selective treatment treats

It keeps refugia and reduces selection.

7. A withdrawal period is

It lets residues fall below the MRL.

8. For a camelid with no labelled product you should

Camelids handle some drugs differently and few are labelled.

9. An owner asks for antibiotics for a viral disease. The best reply is to

Stewardship and client communication.

10. The best test to check whether an anthelmintic works on a farm is

It compares egg counts before and after treatment.

Key points to revise

1. Most small ruminant drug information is extrapolated from cattle, so extra-label use is common and risky.
2. Goats, sheep and camelids differ from cattle and from each other in drug handling.
3. Anthelmintic resistance is widespread in small ruminants and arises by selection.
4. Refugia, FAMACHA and targeted selective treatment slow resistance.
5. Test with a faecal egg count reduction test to see whether a drug still works.
6. Do not give antibiotics for parasitic, nutritional or viral problems.
7. Observe milk and meat withdrawal; check the current notification for Indian limits.
8. Counsel the owner and keep treatment records.

Go deeper on this site

- Ch 4. Therapeutics in horses and donkeys (in this book)
- Ch 2. Therapeutics in cattle and buffalo (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Resistance to Anthelmintics in Animals
- Merck Veterinary Manual: Overview of Gastrointestinal Parasites of Ruminants
- Merck Veterinary Manual: Withholding Periods After Anthelmintic Treatment in Animals

CHAPTER 4 OF 8

Therapeutics in horses and donkeys

The horse is a hindgut fermenter with a fragile gut, high NSAID sensitivity of the colon and strict competition rules. This chapter explains colic analgesia, antibiotic choice and colitis, NSAID reasoning, and how doping and competition rules shape drug use.

After this chapter you can

- Explain why analgesia in colic must not hide the signs needed for diagnosis
- Compare the main colic analgesic groups and their cautions
- Explain why some antibiotics cause colitis in horses and how to choose safely
- Describe NSAID toxicity in horses and how to reduce risk
- Explain doping, withdrawal and competition rules and how to advise owners

The horse as a therapeutic problem

The horse is a hindgut fermenter. Its large colon and caecum contain a huge microbial population that depends on stable conditions. Many drug problems in horses come from disturbing this ecosystem, from the horse's sensitivity to pain

and shock, or from rules that govern competition. A horse also cannot vomit, so gastric distension is dangerous.

Donkeys and mules are often treated like small horses, which is a mistake. Donkeys metabolise some drugs faster and tolerate pain stoically, so signs of colic or laminitis can be subtle. Dose and interval should come from donkey-specific guidance. Revise Book 5 for sedatives and Book 2 for the digestive system.

Analgesia in colic

Colic is a sign, not a diagnosis. Most cases are mild and settle with analgesia, but a few need surgery, and pain is the signal that tells the clinician which is which. The central principle is that **analgesia relieves suffering but can mask the progress of disease**. Examine the horse first when it is safe to do so.

- **NSAIDs (flunixin).** The most commonly used drugs for abdominal pain. They also reduce endotoxin effects. Full doses may hide the signs of a surgical lesion, so many clinicians use a lower dose in cases that might need surgery.
- **Hyoscine butylbromide.** An antispasmodic for mild spasmodic colic. Because it blocks muscarinic receptors, it can raise heart rate, which complicates interpretation.
- **Alpha2-agonists (xylazine, detomidine).** Powerful analgesia and sedation. Xylazine acts quickly but briefly, while detomidine is more potent and longer lasting. They also slow gut motility and reduce cardiac output, so they are not a harmless default.
- **Opioids (butorphanol).** Often combined with an alpha2-agonist. Large amounts can cause excitement and instability.
- **Nasogastric tube.** Not a drug, but relieving gastric reflux is a treatment that prevents rupture.

A frequent mistake is using a strong analgesic repeatedly without re-examining. Rising need for analgesia is itself a reason to refer for surgery. Phenylephrine for nephrosplenic entrapment is used by specialists and is risky in old horses. Never give a laxative such as mineral oil, or any drug by stomach tube, to a horse with gastric reflux.

Antibiotics and colitis

Antibiotics kill bacteria that normally keep pathogens such as *Clostridium* in check. In the horse the result can be acute, severe, life-threatening diarrhoea, called antibiotic-associated colitis. Risk is higher with broad-spectrum agents, oral administration, those excreted in bile into the gut, hospitalisation and stress such as transport, surgery or fasting.

Decisions follow from this:

- **Do not give an antibacterial for an uncomplicated colic, viral respiratory disease or a non-infected wound.** The benefit is zero and the risk is real.
- **When infection is proven or likely**, choose the narrowest effective drug, confirm by culture where possible and stop as soon as you can.
- **Watch for a change in faeces** in any horse on antibiotics, and tell the owner to call at once if diarrhoea starts, because dehydration and endotoxaemia develop fast.
- **Avoid oral lincosamides and some other agents in adult horses.** Details differ between references, so check a current equine source.

Foals handle several antibiotics differently from adults, because their gut flora is still developing and their kidneys are immature. Cross-refer to Book 3 for classes and spectrum.

NSAIDs: benefit and harm

NSAIDs are the most used drugs in horses, for musculoskeletal pain, laminitis, colic and fever. They act by inhibiting cyclooxygenase, which also reduces protective prostaglandins in the gut mucosa and kidney. The horse's right dorsal colon and stomach are especially sensitive, and toxicity can lead to ulcers, protein-losing enteropathy and right dorsal colitis. Renal injury is more likely in dehydrated or hypotensive horses.

Key points:

- Toxicity depends on the drug, **dose and duration**. Giving more than recommended, or giving two NSAIDs together, adds risk without adding benefit.
- Some horses show toxicity at normal doses, so watch for dullness, poor appetite, oedema and low protein.

- Phenylbutazone is generally ranked as more ulcerogenic than flunixin, which is more than ketoprofen. Firocoxib, a COX-2 selective drug, appears safer, but selectivity does not remove all risk.
- Hydrate before and during NSAID use in sick horses.
- Do not give NSAIDs along with corticosteroids without good reason, because the gastric risk adds up.
- Phenylbutazone has important restrictions in horses that may enter the food chain, so check the current notification of the Indian authorities and the horse's passport or history.

Common confusion: flunixin is excellent for visceral pain, while phenylbutazone is often preferred for musculoskeletal pain, but this is a convention, not a rule.

Doping, competition rules and withdrawal

Racing and equestrian sport are governed by rules that treat some substances as forbidden. These rules aim at fair play and horse welfare, because a drug can hide pain and let a lame horse perform. Rules differ between bodies. For international competition, the FEI maintains lists of prohibited substances, including categories such as controlled medication. Indian racing and equestrian authorities have their own rules, so check the current rule book of the relevant body before treating a competition horse.

Concepts to apply:

- **Detection time versus withdrawal time.** A drug may be detectable long after its clinical effect has gone. A competition rule is about the test, not the effect.
- **Threshold substances.** Some compounds are naturally present, so rules set a concentration limit rather than banning them outright.
- **Contamination.** Feed or bedding contaminated by a prohibited plant or drug can cause a positive test; the owner remains responsible.
- **Therapeutic use.** A horse may need treatment for welfare; ask whether a therapeutic use exemption or a rest from competition applies.
- **Food chain status.** Horses are slaughtered for meat in some countries. Some drugs are banned for such horses, so treatment history needs to be recorded.

Never advise an owner to compete a horse within a short interval of treatment on the basis of a guess; recommend checking the rules and, where available, an

official testing laboratory or the authority.

Species cautions and client communication

- **Ionophore feed additives** such as monensin are highly toxic to horses, even in small amounts mixed into feed meant for other species. See Book 6.
- **Ivermectin-type drugs** are widely used in horses but resistance in cyathostomes is common; use faecal egg counts to select animals for deworming.
- **Donkeys** hide pain, may handle drugs differently, and are at risk of hyperlipaemia when they stop eating; do not starve a sick donkey.
- **Foals** are more sensitive to some antibiotics, and their NSAID tolerance differs.
- **Pregnant mares** need drug choices checked for fetal safety.

When talking to owners, explain why you are not giving an antibiotic for an uncomplicated colic, why a horse in pain should not be given repeated painkillers at home without calling the vet, and why a pain-relieved horse still needs observation. Many owners in India give home remedies and injections through unqualified helpers; ask politely about everything the horse has received before you examine it, because those drugs affect your findings and your drug choice.

Concept cleared

Analgesia versus diagnosis
Relieving pain in colic is a duty, but strong or repeated analgesia can hide a surgical lesion. Examine first and re-examine often.

The hindgut ecosystem
Antibiotics, stress and fasting can upset the colonic flora and cause severe colitis, so give antibiotics only for clear indications.

NSAID risk is dose and duration related
Toxicity follows excessive dose, long use, combinations and dehydration; use the lowest effective dose for the shortest time.

Detection is not the same as effect

Competition rules depend on tests, so a drug with no effect can still cause a positive result.

Memory aid: Colic checklist: EXAM

Examine before strong analgesia; eXclude surgical signs; Analgesia in the lowest effective amount; Monitor and re-examine.

Compare and contrast

Colic analgesics

Group	Main use	Main caution
NSAID (flunixin)	Visceral pain, endotoxaemia	Full dose may mask surgical signs; gut and kidney toxicity
Hyoscine butylbromide	Spasmodic colic	Raises heart rate; masks little else
Alpha2-agonists	Strong analgesia and sedation	Slow gut motility, lower cardiac output
Opioid (butorphanol)	Adjunct	Excitement if overdosed; weak alone

Common equine NSAIDs

Drug	Typical use	Relative gut risk
Phenylbutazone	Musculoskeletal pain	Highest of those compared
Flunixin	Colic, endotoxaemia	Intermediate
Ketoprofen	Pain, fever	Lower
Firocoxib (COX-2 selective)	Chronic osteoarthritis	Appears safer

Species notes

Horse

Donkey and mule

Hindgut fermenter; risk of colitis after antibiotics; NSAID-sensitive colon; cannot vomit.

Stoic and may handle drugs differently from horses; hyperlipaemia risk if not eating; use donkey-specific advice.

Foal
Developing gut flora and kidneys; many drugs are handled differently from adults.

Competition horse
Follow the rule book of the relevant authority and think about detection time.

Horse in the food chain
Some drugs are prohibited; keep treatment records and check the current notification.

Clinical pearls

Self-test: 10 questions

1. The main risk of full-dose NSAID in early colic is

Pain relief can hide deterioration.

2. Which drug acts as an antispasmodic in colic?

It blocks muscarinic receptors in gut smooth muscle.

3. A disadvantage of xylazine in colic is that it

Alpha2-agonists reduce motility and cardiac output.

4. Antibiotic-associated colitis in horses is caused by

Antibiotics disrupt the hindgut ecosystem.

5. Which NSAID appears safest for the gut in horses of those listed?

It is COX-2 selective.

6. NSAID toxicity in horses is increased by

Prostaglandin loss matters most in a poorly perfused gut and kidney.

7. Which is the best response to a horse with diarrhoea on antibiotics?

Dehydration and endotoxaemia progress fast.

8. Detection time in doping rules refers to

A drug can be detectable after its effect is gone.

9. Which feed additive is highly toxic to horses?

Ionophores affect the heart muscle of horses.

10. Donkeys differ from horses because they

Do not treat a donkey as a small horse.

Key points to revise

1. Colic is a sign; examine the horse before strong analgesia where safe.
2. Flunixin is the common NSAID for colic, but full doses may mask surgical signs.
3. Alpha2-agonists and opioids are often used together; each has cautions.
4. Antibiotics can cause colitis through disturbing colonic flora.

5. Avoid antibiotics for uncomplicated colic and viral disease.
6. NSAID toxicity depends on drug, dose, duration and hydration.
7. Competition rules depend on detection, not clinical effect; check the current rule book.
8. Donkeys differ from horses and hide pain.

Go deeper on this site

- Ch 5. Therapeutics in poultry, pigs and rabbits (in this book)
- Ch 3. Therapeutics in sheep, goats and camelids (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Merck Veterinary Manual: Overview of Colic in Horses
- Merck Veterinary Manual: NSAID Toxicosis and Right Dorsal Colitis in Horses
- Merck Veterinary Manual: Resistance to Anthelmintics in Animals

CHAPTER 5 OF 8

Therapeutics in poultry, pigs and rabbits

How to think about drug choice when the patient is a flock, a pen of pigs or a rabbit. The chapter covers water and feed medication, why solubility and intake matter, withdrawal logic, and the species-specific toxicities that cause field losses.

After this chapter you can

- Explain why flock and herd medication is a group exercise and what limits it
- Describe how water solubility, stability and water intake affect medicated-water therapy
- Apply the logic of withdrawal periods and egg or meat residues to poultry and pigs
- Name the main species-specific drug hazards in poultry, pigs and rabbits

- Explain how to counsel a farmer or owner about responsible use and residues

Treating a group, not an individual

In a broiler shed or a pig unit the patient is the whole group. Treating one bird at a time is impractical, so the drug usually reaches the animals through **water or feed**. This changes how you think. The questions become: will every animal take in an effective amount, will the drug stay stable in the delivery system, and what happens to the product afterwards?

Individual injection is still used for valuable animals such as breeding boars, sows and pet rabbits, and for vaccines. For commercial poultry, mass medication is the norm.

Group treatment also carries a responsibility. Giving an antimicrobial to healthy in-contact animals is justified only by a clear diagnosis and a reasoned plan. It should not be a substitute for good housing, ventilation, biosecurity and vaccination. See Book 3 on antimicrobial stewardship.

Water medication and solubility

Water is the preferred route for fast flock treatment because sick birds and pigs often keep drinking after they stop eating. Several points decide success.

- **Solubility.** The product must dissolve completely and stay dissolved. Poorly soluble powders settle in tanks, block nipples and filters, and give uneven dosing. Some drugs are available as soluble salts or oral solutions specifically for this reason.
- **Stability.** Some drugs degrade in water, in sunlight, in hard or chlorinated water, or after many hours in a tank. Fresh medicated water must be prepared within the period given on the label.
- **Water intake.** Birds drink more in hot weather and less when ill or when water is too warm or foul. The same concentration therefore delivers different amounts on different days. Concentration is set from expected intake, so check actual consumption.
- **Competing water sources.** Open drinkers, leaks or rain reduce intake of medicated water.

- **Biofilm and lines.** Medicated water can leave residue in pipes. Cleaning and flushing matter for the next batch.

A common confusion is that a higher concentration is always safer for the flock. It is not. Overdosing wastes drug, raises toxicity risk, lengthens withdrawal and promotes resistance.

Feed medication and its limits

Medicated feed suits prevention and long courses, but sick animals eat less, so the sickest receive the least drug. Mixing errors and carry-over into the next feed batch are real hazards. Feed mixing must be even; ionophore coccidiostats and other narrow-margin drugs need very accurate mixing.

Pigs offer all three routes: injection for individuals, water through proportioners, and feed. A practical approach is to treat clinically affected pigs individually where possible and medicate the group only when the diagnosis supports it. Feed and water routes must also meet any rules about permitted medicated feeds. Check the current notification for what is allowed in India.

Withdrawal periods and residue logic

A **withdrawal period** is the time that must pass after the last dose before meat, eggs or milk may enter the food chain. It is set so that tissue residue falls below the maximum residue limit (MRL). It depends on the drug, formulation, route, and the tissue measured. The same drug can need different periods for meat and eggs.

Key reasoning rules:

- Use the label withdrawal for the product and species in front of you. If a drug is used off label, the usual approach is a conservative, documented withdrawal, and the authority's guidance should be consulted.
- Layers are a special problem. Many drugs have no accepted egg withdrawal, and so should not be given to hens producing eggs for human consumption. Treat this as a starting assumption and read the label.
- Kidney, liver and injection-site tissue hold residues longest. Slaughter before the withdrawal ends is a violation even if the animal looks healthy.
- Records are part of the treatment: product, batch, date, group, and expiry of withdrawal.

Residues matter for consumers because of allergy risk, effects on gut flora and resistance selection. Hedged note: MRLs and banned substances in India are set by national authorities and change; check the current FSSAI and Government of India notifications. Some antimicrobials have been restricted or banned for food animals in recent years, so confirm before prescribing.

Species-specific hazards in poultry, pigs and rabbits

Poultry. Ionophore coccidiostats (monensin, salinomycin, narasin and similar) are safe in chickens at label levels but toxic to horses, dogs and some other species, and turkeys are more sensitive than chickens. Feed intended for chickens must never reach horses. Ionophores also interact dangerously with tiamulin, and a few other drugs, causing toxicity in poultry and pigs, so avoid combining them without clear label approval. Heavy-handed sulfonamide use in birds can cause kidney and haematological injury, linking to Book 6.

Pigs. Pigs are sensitive to salt poisoning when water is restricted, and this can be mistaken for an infectious neurological disease. They can be affected by certain feed-borne toxins and by overdose of some injectables. Ivermectin-type drugs are generally safe in pigs at label use. Always match the product to the species on the label, as some pour-on or in-feed products are not intended for pigs.

Rabbits. Rabbits are hindgut fermenters whose caecal flora is delicate. Some antibiotics, particularly lincosamides, many penicillins taken by mouth, and macrolides, can cause a fatal overgrowth of harmful bacteria and enterotoxaemia. Rabbits also reingest caecotrophs, so oral drugs may be recycled. Anorexia is itself an emergency because it leads to gut stasis. Analgesia and nutritional support are part of treatment, and drugs that slow gut movement need thought. Some individual rabbits have enzymes that break down atropine, making response unreliable.

These cautions relate to Book 2 on the gastrointestinal system and Book 6 on toxicology.

Choosing the drug and talking to the client

Reasoning sequence for a flock or herd outbreak:

1. Establish the likely diagnosis from history, necropsy and, if possible, culture or sensitivity (Book 3).

2. Ask whether the problem is infectious, nutritional, toxic or management related. Not every outbreak needs an antimicrobial.
3. Choose a drug with proven activity, an acceptable route for the group, and a withdrawal that fits the production stage (broiler near slaughter, layer, breeder).
4. Use the narrowest effective spectrum and the shortest sensible course.
5. Check for interactions and species-specific toxicity.
6. Record, set a review date and plan prevention.

With farmers, explain in plain terms why a withdrawal must be followed: the meat or egg may look normal but still carry residue. Explain that stopping early, or doubling the dose, creates resistance and loss of the drug for future outbreaks. With rabbit owners, stress that loss of appetite or droppings is urgent, and that medicines licensed for other animals may be harmful. Where the farm sells to export or integrator markets, buyers may have stricter rules than the law.

Cross-references: Book 3 for antimicrobial choice, Book 4 for applied pharmacology and Book 6 for toxicities.

Concept cleared

Group dosing depends on intake
The dose delivered is concentration multiplied by how much the animals actually drink or eat. Heat, illness and poor palatability change intake, so a fixed concentration gives a variable dose.

Solubility and stability are therapeutic properties
A drug that settles out, clogs lines or degrades in the tank cannot treat the flock, however good its spectrum.

Withdrawal is about tissue residue
Withdrawal time protects the consumer by allowing residues to fall under the MRL. It is product, route and tissue specific and is a legal as well as a scientific matter.

Hindgut fermenters are antibiotic-sensitive

In rabbits, upsetting caecal flora can be lethal. Safety is judged by the effect on gut bacteria, not only by the target infection.

Memory aid: SWIM before you medicate a flock

Solubility, Water intake, Interactions, Meat or egg withdrawal. Check all four before mixing the first batch.

Compare and contrast

Routes for group treatment

Route	Strength	Main limitation
Drinking water	Fast start, sick animals keep drinking	Depends on intake, solubility, stability and clean lines
Medicated feed	Convenient for long courses and prevention	Sick animals eat less, mixing errors, carry-over
Individual injection	Precise for each animal	Labour, stress and injection-site residue, impractical for large flocks

Species-specific cautions

Species	Drug or group	Concern
Poultry, pigs	Ionophores with tiamulin	Serious interaction and toxicity
Horses, dogs	Ionophore-contaminated feed	Cardiac and muscle toxicity
Rabbits	Lincosamides, oral penicillins, macrolides	Enterotoxaemia and death
Layer hens	Many antimicrobials	No accepted egg withdrawal, avoid

Species notes

Broiler chickens

Layer hens

Short life cycle means withdrawal often decides whether a drug can be used at all. Ionophore feed is routine for coccidiosis control.

Eggs are a food product, so most drugs should be avoided during lay. Read the label before any use.

Turkeys

More sensitive than chickens to some ionophores. Use only products labelled for turkeys.

Pigs

Group treatment by water or feed is common, but individual treatment of sick pigs is preferred when practical. Watch for salt poisoning after water restriction.

Rabbits

Fragile caecal flora and reingestion of caecotrophs. Antibiotic choice must be made for gut safety and appetite must be supported.

Clinical pearls

Self-test: 10 questions

1. Why is water often preferred for emergency flock medication?

Appetite falls first in sick birds, while drinking usually continues, though intake must still be checked.

2. Which factor can make a fixed drug concentration in water deliver a different dose?

Dose delivered equals concentration times intake, and intake changes with heat and illness.

3. Poor solubility of a water-mixed drug mainly causes

Undissolved drug does not reach birds evenly and can block nipples.

4. A withdrawal period is set so that

It is a consumer-protection measure based on tissue residue depletion.

5. Which statement about laying hens is the safest starting rule?

Egg residues are a separate issue, and many products are not permitted in lay.

6. Ionophore-containing chicken feed is dangerous if eaten by

Horses, and also dogs, are highly susceptible to ionophore toxicity.

7. Which combination is a recognised hazard in poultry and pigs?

This interaction can cause severe toxicity.

8. Why can oral lincosamides be dangerous in rabbits?

Rabbits are hindgut fermenters and are sensitive to antibiotic-induced dysbiosis.

9. Which sign in a rabbit should be treated as urgent?

Anorexia and reduced faeces suggest gut stasis, which can become fatal.

10. For Indian MRLs and banned antimicrobials in food animals, the best advice is to

Rules are revised, so confirm the latest notification before prescribing.

Key points to revise

1. Flock and herd therapy mostly uses water or feed.
2. Intake changes with weather and disease, so dose varies.
3. Poor solubility or stability leads to treatment failure.
4. Overdosing increases toxicity, residues and resistance.
5. Withdrawal periods protect the consumer and depend on product, route and tissue.
6. Many drugs are unsuitable for laying hens.
7. Rabbits can die from antibiotic-induced dysbiosis.
8. Check current Indian notifications for banned drugs and MRLs.

Go deeper on this site

- Ch 6. Therapeutics in exotics and wildlife (in this book)
- Ch 4. Therapeutics in horses and donkeys (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Concepts
- Veterinary Drug Concepts Clearly Explained

Sources

- WHO - Antimicrobial resistance fact sheet
- FAO - Antimicrobial resistance
- WSAVA - Global guidelines

CHAPTER 6 OF 8

Therapeutics in exotics and wildlife

Principles for treating birds, reptiles, small mammals and zoo or wild animals when few drugs are licensed. The chapter focuses on physiology that changes drug behaviour, the reasoning behind cautions, safety of handlers and legal responsibilities.

After this chapter you can

- Explain why few drugs are licensed for exotic and wild species and what that means for prescribing
- Describe how body temperature, metabolism and anatomy alter drug behaviour in reptiles and birds
- Identify antibiotic and drug hazards in small mammals
- Outline the main principles of drug use in zoo and free-ranging wildlife, including handler safety
- Counsel owners and authorities on legal, welfare and public-health aspects

Why exotics are different

Exotic pets and wildlife include hundreds of species, and the diversity is the central problem. Most drugs are tested in a few domestic species. For a parrot, a tortoise or a leopard there is usually little or no approved product, so the clinician must reason from **physiology and published experience**.

Using a drug in a species for which it is not labelled is often called extra-label or off-label use. It must be justified, based on the best available evidence, recorded, and explained to the owner. It must also remember that doses do not scale in a simple linear way with body weight, because metabolic rate does not. Exact dosing information should come from reliable species-specific references, not from memory or from extrapolation. This book gives no numeric doses.

Always begin with husbandry. In exotics, most disease is linked to wrong temperature, diet, light, humidity or crowding, and correcting these is part of therapy. Drugs rarely work in an animal kept in the wrong environment.

Birds

Birds have features that matter to a pharmacologist.

- **High metabolic rate and small size.** Small birds can deteriorate fast, and fasting should be kept short because glucose reserves are small. Stress from handling can itself be dangerous, so plan procedures before restraint.
- **Air sac respiratory system.** Inhalational anaesthetics are taken up and cleared quickly, which gives rapid control but also rapid change. Respiration must be watched closely. Book 5 covers the principles.

- **Renal portal system.** Blood from the lower body partly passes through the kidney before reaching the general circulation. Concern about injecting into the legs for drugs cleared by the kidney has been a classical teaching point. Its practical importance is debated, so use current species references.
- **Uric acid excretion.** Birds are uricotelic, and kidney damage can lead to visceral gout. Nephrotoxic drugs and dehydration are therefore dangerous.
- **NSAID sensitivity in some species.** The best known example is diclofenac, which caused kidney failure and a collapse in vulture populations in South Asia after vultures fed on treated carcasses. India restricted the veterinary use of diclofenac to protect vultures. Check the current notification. This links directly to Book 6 and shows that a drug given to livestock can harm wildlife through the food chain.

For pet birds, delivery is a practical issue. Injections, crop feeding, drinking water medication and food mixing each have limits. Medicated water is unreliable because intake varies and many drugs degrade or taste bitter.

Reptiles

Reptiles are **ectotherms**. Their body temperature depends on the environment, and this controls metabolism, immune response and drug handling. A reptile kept too cold absorbs, distributes and clears drugs slowly and its immune system works poorly. Treatment is usually given while the animal is kept within its preferred optimal temperature range.

Other points:

- Slow metabolism means long intervals between doses for many drugs and long recovery times from anaesthetics.
- A renal portal system exists in reptiles too, and the same discussion about injection sites applies.
- Some drug classes are dangerous in particular groups. Ivermectin is the classic example, being toxic to chelonians (tortoises and turtles). Never extend a product used in other species to a reptile without checking species-specific guidance.
- Many reptile diseases such as shell disease, respiratory disease and metabolic bone disease are due to husbandry or nutrition, so drug choice alone will fail.

- Reptiles can carry Salmonella without signs, which is a public-health issue (see the section on legal and public-health aspects).

Hibernation or brumation also changes metabolism, and treating a cold, inactive reptile needs careful judgement.

Small mammals

Rabbits were covered in the previous chapter. Other small mammals share the same principle: **the gut flora is the weak point**.

- **Guinea pigs, hamsters, gerbils and chinchillas.** Many antibiotics can cause fatal dysbiosis and enterotoxaemia, particularly some penicillins, lincosamides and macrolides when given by mouth. Always check a small-mammal reference before choosing any antimicrobial. Guinea pigs also need vitamin C in the diet, and deficiency affects healing and immunity.
- **Rodents.** Small body size makes volume, injection site and stress limiting. Anorexia is serious, and supportive feeding and warmth are part of the plan.
- **Ferrets.** Carnivores with a short gut and fast transit, they are more tolerant of antibiotics than herbivorous rodents but still need species-specific advice on many drugs.

Small mammals often hide illness, so by the time they are brought in they are dehydrated and hypothermic. Fluids, warmth and feeding come before many drugs.

Zoo animals and wildlife

Treating large or dangerous animals raises problems that are not about drug effect alone.

- **Remote delivery.** Darting and chemical restraint are common, and the animal is often only partly weighed or estimated. The drug choice must have a wide safety margin and, where possible, a reversal agent. Planning of the team, location and recovery site matters as much as the drug.
- **Handler safety.** Some potent opioids used to immobilise large animals can kill a human after accidental exposure. The antagonist and emergency plan must be at hand, and staff must be trained. This is a major clinical meaning of Book 5.
- **Capture stress and capture myopathy.** Exertion, heat and fear can cause muscle damage, acidosis and death some time after a technically successful

procedure. Minimising chase time and stress is part of pharmacology.

- **Species differences in response.** The same drug can have very different effects in a bear, an antelope and a primate. Use species-specific references and experienced colleagues.
- **Residue and food chain.** Drugs used in free-ranging or captive animals that may be eaten, or be eaten by scavengers, can cause harm, as the diclofenac story showed.

Anaesthetic risks such as regurgitation, bloat in ruminants and hyperthermia need monitoring and the right position during recovery.

Legal, public-health and client aspects

Exotics and wildlife are subject to law. In India the Wildlife Protection Act and related rules control possession of many species, and treatment or release may need permission from the forest authorities. Confirm the current legal position before accepting a wild animal for treatment, and involve the authorities.

Many exotic animals carry zoonotic agents, such as Salmonella in reptiles or Chlamydia in birds. WHO describes zoonoses as diseases that spread between animals and humans, and protective hygiene should be taught to owners.

Antimicrobial use in exotics still contributes to resistance, so culture and sensitivity should be used where possible (Book 3).

When talking to owners, be honest: tell them that many treatments are not licensed for the species, that the evidence is limited, that husbandry changes are part of treatment, and that some prognoses are guarded. Ask for informed consent, discuss costs and welfare, and agree on endpoints. Never prescribe a household remedy or a dog or cat product for an exotic pet without checking species safety, since many errors in exotics come from simple extrapolation.

Concept cleared

Physiology drives drug choice

When no label exists, reasoning from temperature, metabolism, anatomy, diet and gut type is the safest guide. Doses must come from species-specific references.

Husbandry is therapy

Wrong temperature, diet or light causes most exotic disease. Drugs given without correcting these often fail.

Gut flora is the weak point in small herbivores

Rabbits, guinea pigs, hamsters and chinchillas can die from antibiotic-induced dysbiosis, so oral antibiotic choice needs special checking.

Drug effects reach beyond the patient

Veterinary diclofenac harmed vultures through carcasses, and potent immobilising opioids can endanger handlers. Consider the environment and the people.

Memory aid: TEMP-GUT-LAW

Temperature, Environment, Metabolism, Physiology; then Gut flora; then Legal permissions and Animal welfare. A quick checklist before treating any exotic or wild patient.

Compare and contrast

Exotic groups and their pharmacological key point

Group	Key feature	Practical consequence
Birds	Air sacs, high metabolism, uric acid	Rapid anaesthetic changes, kidney caution, short fasting
Reptiles	Ectotherms, slow metabolism	Treat at preferred temperature, long dosing intervals
Small herbivorous mammals	Delicate gut flora	Avoid risky oral antibiotics, support appetite
Zoo and wild animals	Remote delivery, large size	Wide safety margin, reversal agent, handler safety

Cautions recap by species

Species	Drug or situation	Concern
Vultures and some raptors	Diclofenac residues	Kidney failure and population collapse
Chelonians	Ivermectin	Toxicity
Guinea pigs and hamsters	Oral lincosamides, some penicillins	Fatal enterotoxaemia
Large wild animals	Potent opioids	Human exposure risk, capture myopathy

Species notes

Pet birds

Fast metabolism and air sacs. Short fasting, careful respiratory monitoring and kidney caution. Medicated water is unreliable.

Reptiles

Keep in preferred temperature during treatment. Be cautious with ivermectin in tortoises and turtles. Remember Salmonella risk.

Guinea pigs, hamsters, chinchillas

Sensitive to antibiotic-induced gut disturbance. Provide warmth, fluids and feeding. Guinea pigs need dietary vitamin C.

Ferrets

Carnivores with fast gut transit and more antibiotic tolerance than herbivorous rodents, but species references are still needed.

Zoo and wild animals

Plan darting, safety margin, reversal agents and recovery. Protect handlers. Watch for capture myopathy and check legal permissions.

Clinical pearls

Self-test: 10 questions

1. What is the best guide when no licensed product exists for an exotic species?

Metabolism differs between species, so evidence and physiology must guide choice.

2. Why must a reptile be kept in its preferred temperature range during therapy?

Reptiles are ectotherms, so temperature affects drug handling and immune response.

3. Which drug is classically hazardous in chelonians?

Ivermectin toxicity in tortoises and turtles is a well-known caution.

4. Why is prolonged fasting avoided in small birds?

Small birds can become hypoglycaemic quickly.

5. The vulture decline in South Asia was linked to

Vultures eating carcasses of treated livestock developed kidney failure.

6. Which problem is a special risk with antibiotics in guinea pigs and hamsters?

These species are sensitive to antibiotic-induced dysbiosis and enterotoxaemia.

7. What does the renal portal system raise a concern about?

Blood from the hind body may pass through the kidney first, so site choice has been questioned.

8. What is the main danger of potent opioids used for large wild animals?

Handlers can be seriously harmed, so antagonist and training are essential.

9. Capture myopathy is best prevented by

Exertion and stress cause muscle injury and metabolic problems.

10. Before treating a wild animal in India you should

Possession and release of many wild species are legally controlled, so confirm current rules.

Key points to revise

1. Few drugs are licensed for exotic and wild species.
2. Off-label use needs justification, records and owner consent.
3. Dose scaling is not linear with body weight.
4. Birds have air sacs and a high metabolic rate.
5. Reptiles depend on environmental temperature.
6. Small herbivorous mammals are sensitive to oral antibiotics.
7. Zoo anaesthesia needs a reversal plan and handler safety.
8. Wildlife treatment may need legal permission; check current rules.

Go deeper on this site

- Ch 7. Practice MCQ bank, case scenarios and viva questions (in this book)
- Ch 5. Therapeutics in poultry, pigs and rabbits (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- WHO - Zoonoses fact sheet
- WHO - Antimicrobial resistance fact sheet
- WSAVA - Global guidelines

CHAPTER 7 OF 8

Practice MCQ bank, case scenarios and viva questions

A revision chapter with twenty Indian field case scenarios worked as reasoning exercises, a viva question set with model answer outlines, exam strategy, and thirty mixed MCQs drawn from Books 1 to 6. Use it to test whether you can apply drugs, not only name them.

> **After this chapter you can**
>
> - Apply drug-choice reasoning to common Indian field presentations in dogs, cats, ruminants, horses, poultry and rabbits
> - Recognise species-specific cautions and the toxicities that follow from them
> - Apply milk, meat and egg withdrawal logic to treatment decisions
> - Answer viva questions in a short, structured way
> - Use a repeatable method to eliminate wrong options in MCQs

How to use this bank

Read the situation, cover the answer and decide *before* reading on. For every case ask four things: what is the likely problem, which drug class fits and why, what must I avoid in this species, and what do I tell the owner. Doses are deliberately absent;

the aim is reasoning. Where a case points to an earlier book, revise that chapter afterwards. Attempt the 30 MCQs in one sitting, then mark the topics you missed.

Field cases 1 to 7

Case 1. A herding-breed dog develops ataxia, salivation and stupor after ivermectin was given for mange. *Think:* why this breed? *Answer:* A MDR1 (ABCB1) mutation leaves P-glycoprotein deficient at the blood-brain barrier, so ivermectin enters the brain. Stop the drug, give supportive care, and consider genotyping; choose another acaricide for the patient.

Case 2. A cat is brought with tremors after the owner applied a dog tick product containing permethrin. *Answer:* Cats are very sensitive to pyrethroids. Wash off the product, control tremors and keep the cat warm. Counsel the owner never to use dog products on cats.

Case 3. A cat given a human paracetamol tablet becomes dull, with brown mucous membranes. *Answer:* Cats have poor glucuronidation, so toxic metabolites cause methaemoglobinaemia and red cell damage. Early decontamination, oxygen and specific antidotal therapy are needed; this is an emergency (Book 6).

Case 4. A buffalo with acute clinical mastitis is treated with an antibiotic and the farmer wants to sell milk the same evening. *Answer:* No. Milk must be discarded for the labelled withdrawal period, which is longer than the treatment course. Explain residues, resistance and consumer risk; check the product label and current notifications.

Case 5. A cow salivates, has diarrhoea and muscle twitching after a pesticide spray around the cattle shed. *Answer:* Organophosphate or carbamate poisoning from cholinesterase inhibition. Decontaminate the skin, give atropine for muscarinic signs, and an oxime only for organophosphates; avoid oximes in carbamate cases as a general rule (Books 1 and 6).

Case 6. A high-yielding cow, down soon after calving, is cold with a dry muzzle. *Answer:* Think hypocalcaemia. Give calcium slowly by vein while listening to the heart, because rapid infusion risks arrhythmia and cardiac arrest. Plan prevention in the dry period.

Case 7. A calf is bloated on lush green fodder, and froth is seen. *Answer:* Frothy bloat traps gas in stable foam. An antifoaming agent lowers surface tension; a stomach tube may not release gas. Pass a trocar if life-threatening, then correct the diet.

Field cases 8 to 14

Case 8. A goat flock with anaemia and bottle jaw has failed repeated deworming. *Answer:* Haemonchus with probable anthelmintic resistance. Confirm with faecal egg counts, treat selectively using anaemia scoring, rotate classes sensibly and avoid underdosing, which selects resistant worms (Book 3).

Case 9. A horse with colic improves dramatically after an NSAID and the owner wants to move it. *Answer:* Analgesia can mask a surgical lesion. Reassess pulse, gut sounds and pain; NSAIDs risk gastric and renal injury, and competition rules on medication also apply.

Case 10. A horse develops severe diarrhoea after an oral lincosamide. *Answer:* Antibiotic-associated colitis from hindgut dysbiosis and Clostridial overgrowth. Avoid lincosamides in horses and manage fluids and shock.

Case 11. A pet rabbit becomes anorexic with bloat after oral broad-spectrum antibiotic therapy. *Answer:* Gut flora disruption in a hindgut fermenter. Choose antibiotics known to be safer in rabbits, avoid lincosamides and some penicillins by mouth, and support feeding.

Case 12. A layer farm treats a respiratory outbreak through drinking water. *Answer:* Check water solubility, uniform intake and egg withdrawal. Layers producing eggs for people need drugs with no egg restriction. Several antimicrobials are restricted in Indian poultry; check the current notification.

Case 13. A horse eating feed made for poultry collapses. *Answer:* Ionophore (monensin) toxicity, which damages heart and skeletal muscle in horses. Stop the feed, give supportive treatment and prevent cross-contamination at the feed mill.

Case 14. A dog bitten by a snake has drooping eyelids and breathing weakness. *Answer:* Likely neurotoxic envenomation. Species-appropriate antivenom is central; supportive ventilation matters. Check current protocols; anticholinesterase adjuncts are used in some cases.

Field cases 15 to 20

Case 15. A dog ate rat bait three days ago and is now bleeding. *Answer:* Anticoagulant rodenticide toxicity; factors II, VII, IX and X are depleted, signs delayed. Vitamin K1 is the antidote and must continue for the long action of second-generation compounds.

Case 16. A cat given an enrofloxacin-containing tablet becomes blind. *Answer:* Fluoroquinolones can cause retinal toxicity in cats, especially with high exposure. Counsel on dose accuracy and choose alternatives when possible.

Case 17. A dog on prednisolone for allergy is also given an NSAID by a neighbour, and passes black stools. *Answer:* Combined corticosteroid and NSAID raises the risk of gastric ulceration. Stop both, protect the mucosa and allow washout before any switch (Book 2).

Case 18. An epileptic dog on phenobarbital has raised liver enzymes after months. *Answer:* Phenobarbital induces enzymes and can be hepatotoxic. Check serum levels and bile acids, and do not stop abruptly because that provokes seizures.

Case 19. A pregnant cow near term was given dexamethasone and aborted. *Answer:* Glucocorticoids can induce parturition in late pregnancy in cattle, so avoid them in pregnant animals unless intended. Prostaglandin F2-alpha is also contraindicated (Book 2).

Case 20. A calf with watery diarrhoea is dull and weak, and the owner demands antibiotics. *Answer:* The main killer is dehydration and acidosis, so give fluids and electrolytes first. Antibiotics are not routine; use them only with systemic illness. Discuss stewardship.

Viva question set

Answer in three parts: define, explain the mechanism, give the clinical point.

1. **Why do collies react badly to ivermectin?** MDR1 mutation, defective P-glycoprotein, drug enters CNS, neurotoxicity, test and avoid.
2. **What is withdrawal period?** Time after the last dose before milk, meat or eggs is safe, so residues fall below the MRL. Check current Indian notifications.
3. **Why is atropine alone not enough in organophosphate poisoning?** It blocks muscarinic effects only; nicotinic effects need oximes (organophosphates) and

supportive care.

4. **Why avoid aminoglycosides in dehydrated animals?** Nephrotoxicity and ototoxicity; renal accumulation worsens with poor perfusion.
5. **Why are cats sensitive to some drugs?** Reduced glucuronidation; examples are paracetamol and some NSAIDs.
6. **Name one rational use of an antifoaming agent.** Frothy bloat in ruminants.
7. **Difference between bacteriostatic and bactericidal?** Inhibit versus kill; in immunocompromised or severe infection, bactericidal is preferred.
8. **Why not use antibiotics routinely for viral diarrhoea?** They do not act on viruses and drive resistance.

Exam strategy

Read the stem twice and predict the answer before looking at options. Eliminate absolutes such as always and never unless the pharmacology demands it. In species-specific questions, ask what is different about this animal: ruminant rumen, equine hindgut, feline glucuronidation, canine MDR1, avian egg. In theory papers use a short definition, a mechanism, one example and one clinical point. In the viva be calm and honest; if you do not know, reason aloud from the drug class, as examiners value reasoning more than recall. Keep a one-page list of antidotes and species cautions for the last night.

Concept cleared

Species decides the drug
Metabolic, digestive and genetic differences between species can turn a safe drug into a toxic one.

Withdrawal logic
Residues in milk, meat and eggs must fall below the MRL before human use; the period is label-specific, check current notifications.

Treat the cause and the complication

Fluids and supportive care often matter more than the headline drug, as in calf diarrhoea and OP poisoning.

Stewardship

Use antimicrobials only when indicated, with the right class and duration, to reduce resistance.

Memory aid: SPEED for case answers

Species, Problem, Evidence, Estimate the drug class, Discuss with the owner (including withdrawal).

Compare and contrast

Antidotes recap across Book 6

Poison	Antidote or key treatment	Key reason
Organophosphate	Atropine plus oxime, decontamination	Muscarinic block and enzyme reactivation
Anticoagulant rodenticide	Vitamin K1	Restores clotting factor synthesis
Paracetamol in cats	Early decontamination and specific antidotal therapy	Methaemoglobin and red cell damage
Snake neurotoxic bite	Antivenom and ventilatory support	Neutralise venom and protect breathing

Species cautions recap

Species	Caution	Reason
Dog (herding breeds)	Ivermectin sensitivity	MDR1 mutation
Cat	Permethrin, paracetamol	Poor detoxification
Horse	Lincosamides, ionophores	Hindgut dysbiosis, cardiotoxicity
Rabbit	Oral broad-spectrum antibiotics	Hindgut flora disruption

Species notes

Dogs

MDR1 breeds react to ivermectin and some other P-glycoprotein substrates; avoid NSAID plus corticosteroid together.

Cats

Poor glucuronidation: avoid paracetamol and permethrin; be careful with fluoroquinolones.

Ruminants

Rumen flora affect oral antibiotics; milk and meat withdrawal apply.

Horses

Avoid lincosamides; monensin is toxic; competition medication rules apply.

Rabbits and poultry

Rabbits are prone to dysbiosis; layers need egg withdrawal and water-medication planning.

Clinical pearls

Self-test: 30 questions

1. Ivermectin neurotoxicity in some collies is due to a mutation in which gene?

MDR1 deficiency removes P-glycoprotein from the blood-brain barrier.

2. Which receptor family acts fastest?

Ion channels open within milliseconds.

3. Cats are sensitive to paracetamol mainly because of poor

Limited glucuronidation leads to toxic metabolites and methaemoglobinaemia.

4. Atropine in organophosphate poisoning mainly reverses

Atropine is a muscarinic antagonist.

5. An oxime acts by

Oximes reactivate phosphorylated cholinesterase if given early.

6. The antidote for anticoagulant rodenticides is

Vitamin K1 restores synthesis of clotting factors.

7. Which is nephrotoxic and ototoxic?

Aminoglycosides accumulate in renal tubular and inner ear cells.

8. A drug that inhibits bacterial cell wall synthesis is

Beta-lactams block peptidoglycan cross-linking.

9. Which is the main reason for a milk withdrawal period?

Residues must be below the MRL before milk is used by people.

10. Frothy bloat is managed with

They break stable foam so gas can escape.

11. Lincosamides in horses carry the risk of

Hindgut flora disruption allows Clostridial overgrowth.

12. Monensin toxicity in horses mainly affects

Ionophores cause myocardial and muscle necrosis.

13. Cats given permethrin dog products show

Pyrethroids cause neurotoxic signs in cats.

14. Which combination raises GI ulcer risk in dogs?

Both reduce protective prostaglandin effects and mucosal defences.

15. Phenobarbital can increase liver enzymes because it

Enzyme induction, and sometimes hepatotoxicity, occur on long-term use.

16. Rapid IV calcium in milk fever may cause

Calcium affects cardiac conduction and contractility.

17. The main priority in calf diarrhoea is

Dehydration and acidosis cause death.

18. Selective deworming with anaemia scoring aims to

Leaving some worms unexposed (refugia) slows resistant populations.

19. Bactericidal therapy is preferred in

Killing the organism matters when host defences are poor.

20. Corticosteroids in late pregnancy in cattle may

Glucocorticoids trigger the parturition cascade.

21. Drug dose in obese animals is best calculated by

Hydrophilic drugs distribute mainly in lean tissue.

22. First-pass effect refers to

Portal blood passes through the liver before reaching the circulation.

23. Which route avoids first-pass metabolism?

IV drug enters the systemic circulation directly.

24. Ruminants given oral antibiotics risk

Antibiotics kill rumen microbes needed for digestion.

25. A drug that blocks beta-1 receptors would

Beta-1 blockade reduces cardiac stimulation.

26. Heinz bodies and methaemoglobin are associated with

Oxidants denature haemoglobin.

27. The main purpose of antimicrobial stewardship is

Prudent use preserves drug effectiveness.

28. Neurotoxic snake bite is managed chiefly with

Antivenom neutralises venom and respiratory support prevents death.

29. Which sign suggests organophosphate toxicity?

Excess acetylcholine causes muscarinic signs.

30. Enrofloxacin carries a retinal risk in

Retinal degeneration is reported in cats, particularly with high exposure.

Key points to revise

1. Case reasoning combines species, pathology and pharmacology.
2. MDR1 mutation explains ivermectin neurotoxicity in some dogs.
3. Cats are sensitive to permethrin and paracetamol.
4. Withdrawal periods protect consumers from residues.

5. Atropine does not treat nicotinic signs of OP poisoning.
6. Antibiotic-associated colitis is a serious risk in horses and rabbits.
7. Corticosteroids can induce abortion in late pregnancy in cattle.
8. Structured viva answers earn more marks than lists.

Go deeper on this site

- Ch 8. Glossary and exam-day concept maps (in this book)
- Ch 6. Therapeutics in exotics and wildlife (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- Cornell University College of Veterinary Medicine: Drug sensitivity (MDR1)
- University of Minnesota Libraries: Pharmacology, G protein-coupled receptors
- FDA Center for Veterinary Medicine: Antimicrobial resistance

CHAPTER 8 OF 8

Glossary and exam-day concept maps

A plain-language glossary of about 80 key terms from Books 1 to 6, linked to the earlier chapters, with one-page concept maps for each part. Use it for fast revision before the exam.

> **After this chapter you can**
>
> - Recognise and define about 80 core pharmacology terms
> - Link terms to the chapters where they are explained
> - Use concept maps to connect mechanism, clinical use and cautions
> - Distinguish commonly confused term pairs
> - Plan last-minute revision using ADME-R and species cautions

How to use this glossary

This chapter is for the last week before the exam. Read the glossary once for recognition, then cover the definition and test yourself. Each entry gives a short plain meaning; for mechanism, doses in the field and cautions, go back to the chapter on that topic in Books 1 to 6.

The concept maps at the end show how the ideas connect. In a viva, examiners reward links: for example, why a lipid-soluble drug has a large volume of distribution, and why that matters for withdrawal. Draw each map from memory, then compare it with the printed one.

Glossary: pharmacokinetics and pharmacodynamics (Book 1)

Bioavailability: fraction of a dose that reaches the systemic circulation unchanged; low after poor absorption or heavy first-pass loss.

First-pass effect: removal of oral drug by gut wall and liver before it reaches the general circulation.

Volume of distribution: an apparent space that links the amount of drug in the body to its plasma concentration; large for lipid-soluble drugs.

Clearance: the volume of plasma cleared of drug per unit time; it sets the maintenance requirement.

Half-life: time for the plasma concentration to fall by half; guides dosing interval and time to steady state.

Steady state: the balance reached when input equals elimination, usually after several half-lives.

Loading dose: an initial larger exposure to reach effective levels quickly, used when half-life is long.

Protein binding: reversible attachment to plasma proteins; only the free drug is active, filtered or metabolised.

Biotransformation: enzymatic conversion of a drug to metabolites, mainly in the liver (phase I and phase II).

Glucuronidation: a phase II conjugation step that is deficient in cats, so some drugs linger and become toxic.

Enterohepatic recycling: biliary excretion followed by gut reabsorption, which prolongs drug action.

Ion trapping: accumulation of a weak acid or base on the side of a membrane where it is ionised.

P-glycoprotein: an efflux pump (MDR1/ABCB1) that limits entry of drugs into brain and gut; defective in some collie-type dogs.

Therapeutic index: the margin between a toxic and an effective dose; narrow means little room for error.

Agonist: a drug that binds a receptor and produces a response.

Antagonist: a drug that binds a receptor but produces no response and blocks the agonist.

Partial agonist: gives a submaximal response even at full occupancy.

Potency and efficacy: potency is how much drug is needed; efficacy is the maximum effect possible.

Tolerance and tachyphylaxis: reduced response on repeated use, slowly or rapidly.

Second messenger: an intracellular signal such as cAMP, IP3 or calcium that relays receptor activation.

Glossary: autonomic, CNS and inflammation (Book 2)

Cholinergic: acting through acetylcholine, as with muscarinic and nicotinic receptors.

Anticholinergic: blocks muscarinic receptors, causing dry mucosa, tachycardia and reduced gut motility.

Adrenergic: acting through noradrenaline or adrenaline on alpha and beta receptors.

Alpha-2 agonist: sedative-analgesic that also slows the heart and raises early blood pressure; reversed by specific antagonists.

Neuromuscular blocker: stops transmission at the motor end plate; the animal is paralysed but not anaesthetised.

Anticonvulsant: a drug that raises seizure threshold or limits seizure spread.

Sedative: calms an animal while it can still be roused.

Analeptic: a stimulant of respiration or the CNS, now little used.

Euthanasia: a death that is painless and humane, with unconsciousness first.

Histamine: autacoid in allergy and gastric acid secretion, acting on H1 and H2 receptors.

Eicosanoid: lipid mediator such as prostaglandin or leukotriene made from arachidonic acid.

Cyclooxygenase: enzyme making prostaglandins; blocked by NSAIDs.

NSAID: non-steroidal anti-inflammatory drug that is analgesic, antipyretic and anti-inflammatory; watch kidney, gut and platelet effects.

Antipyretic: a drug that lowers fever by acting on the hypothalamic set point.

Glucocorticoid: adrenal steroid or analogue with anti-inflammatory and immunosuppressive action.

HPA suppression: shutdown of the pituitary-adrenal axis after prolonged steroid use; stop gradually.

Disease-modifying drug: one that slows the structural course of a disease such as osteoarthritis.

Autacoid: a local hormone acting near where it is released.

Pharmacological antagonism: blockade at the same receptor; contrast with physiological antagonism through opposite effects.

Adverse drug reaction: any harmful, unintended response at normal doses.

Glossary: cardiovascular, renal, respiratory, digestive and endocrine (Book 2)

Inotrope: a drug that changes the force of cardiac contraction.

Chronotrope: a drug that changes heart rate.

Antiarrhythmic: a drug that restores or controls rhythm; may itself be proarrhythmic.

Vasodilator: widens vessels, lowering preload, afterload or both.

Preload and afterload: filling load before and resistance after contraction.

Diuretic: increases urine output by reducing tubular sodium and water reabsorption.

Loop diuretic: acts on the thick ascending limb; strong and fast, can cause potassium loss.

Azotaemia: raised urea and creatinine; check before choosing renally cleared drugs.

Anticoagulant: blocks clotting factors or thrombin.

Haematinic: supplies iron, copper, B12 or folate to build red cells.

Bronchodilator: relaxes airway smooth muscle.

Mucolytic and expectorant: drugs that thin or help clear airway secretions.

Antiemetic: drug that controls vomiting through the chemoreceptor trigger zone or vomiting centre.

Prokinetic: drug that improves coordinated gut propulsion.

Proton pump inhibitor: strongly reduces gastric acid by blocking the H+/K+ ATPase.

Rumen microflora: the microbe community that digests feed; harmed by sudden diet or antibiotic change.

Negative feedback: a hormone limiting its own release, central to endocrine drug action.

Hyperadrenocorticism: excess cortisol, treated by blocking synthesis rather than adding steroid.

Anabolic steroid: a synthetic androgen that builds tissue; banned as a growth promoter in food animals under many rules, check the current notification.

Oxytocic: a drug that causes uterine contraction; used only when the birth canal is clear.

Glossary: chemotherapy, anaesthesia and toxicology (Books 3, 5 and 6)

Bactericidal and bacteriostatic: killing versus inhibiting bacteria; the label matters less than host defences.

MIC: minimum inhibitory concentration, the lowest level that stops visible growth.

Time-dependent killing: effect depends on time above MIC, as with beta-lactams.

Concentration-dependent killing: effect depends on peak level relative to MIC, as with aminoglycosides and fluoroquinolones.

Antimicrobial resistance: loss of bacterial susceptibility, driven by selection pressure from use.

Stewardship: using antimicrobials only when needed, choosing narrow agents and correct duration.

Withdrawal period: the interval after last treatment before milk, meat or eggs are safe for food.

MRL: maximum residue limit, the legal ceiling of a residue in food; check the current notification for Indian values.

Intramammary therapy: drug put directly into the udder; milk withdrawal applies.

Anthelmintic: drug against parasitic worms; resistance is a major problem in small ruminants.

Ectoparasiticide: drug against ticks, mites, lice and flies.

Antiprotozoal: drug against protozoa such as Babesia, Trypanosoma and coccidia.

Cytotoxic: drug that kills dividing cells; bone marrow and gut are common targets.

Premedication: drugs given before anaesthesia to calm, reduce drug need and add analgesia.

Balanced anaesthesia: combining several agents in small amounts to reduce side effects of each.

MAC: minimum alveolar concentration; a measure of inhaled agent potency.

Local anaesthetic: blocks sodium channels in nerves; intravenous error can cause toxicity.

Antidote: an agent that counters a poison, by blocking, binding or reversing it.

LD50: dose expected to kill half of test animals; an index of acute toxicity, not a safe dose.

Decontamination: removing poison from skin, gut or eyes before it is absorbed.

One-page concept maps by part

Map 1. General pharmacology (Book 1)

- Drug enters the body
  - Route and formulation decide absorption
  - Bioavailability, first-pass loss
- Drug moves
  - Protein binding and volume of distribution
  - P-glycoprotein and barriers
- Drug acts
  - Receptor, agonist or antagonist, second messenger
  - Potency, efficacy, therapeutic index
- Drug leaves
  - Biotransformation and clearance
  - Half-life sets interval and withdrawal
  - Species and age change every step

Map 2. Systemic pharmacology (Book 2)

- Nervous system
  - Cholinergic versus anticholinergic; adrenergic and alpha-2 agents
  - Anticonvulsants and sedatives
- Inflammation
  - Arachidonic acid, cyclooxygenase, NSAIDs
  - Glucocorticoids and HPA suppression
- Organ systems
  - Heart: inotropes, antiarrhythmics, vasodilators
  - Kidney: diuretics, renal caution

    - Gut: acid, vomiting, motility, rumen
- Endocrine
    - Feedback loops guide drug choice
    - Sex hormones and growth promoters are regulated

Map 3. Chemotherapy (Book 3)

- Diagnose, then choose
    - Likely bug, site, culture and MIC
- Pattern of killing
    - Time-dependent versus concentration-dependent
- Consequences
    - Resistance, stewardship
    - Residues, withdrawal, MRL
- Parasites, fungi, viruses, cancer follow the same rule: selective toxicity

Map 4. Applied, anaesthesia and toxicology (Books 4 to 6)

- Applied
    - Fluids, acid-base, vitamins, feed additives
- Anaesthesia
    - Assess patient, premedicate, induce, maintain, monitor, recover
- Toxicology
    - Stop exposure, decontaminate, antidote, support
    - Record and report for medico-legal cases

Map 5. Species therapeutics (Book 7)

- Species cautions
    - Cats: glucuronidation; dogs: MDR1; ruminants: rumen; horses: colitis
- Food animals: withdrawal first, then drug choice

Concept cleared

Think in loops

Absorption, distribution, metabolism and excretion decide how much drug is at the receptor, and the receptor decides the effect. Most exam questions test one link in this chain.

Species changes the rule

Many drug rules are really species rules. Cat glucuronidation, canine MDR1 and the ruminant rumen are the standard examples.

Food animals add a second question

After asking whether a drug works, ask whether milk, meat or eggs will be safe. Withdrawal follows elimination.

Antidote logic

Match the antidote to the mechanism, not the poison name: block, bind, reverse or support.

Memory aid: ADME-R

Absorption, Distribution, Metabolism, Excretion, Receptor: say it in order when explaining any drug in a viva.

Compare and contrast

Terms students confuse

Pair	Difference
Potency vs efficacy	Amount needed vs maximum effect
Tolerance vs tachyphylaxis	Slow vs rapid loss of response
Bactericidal vs bacteriostatic	Kills vs inhibits growth
MIC vs MRL	Bacterial inhibitory level vs legal residue ceiling
LD50 vs therapeutic index	Acute lethality marker vs safety margin

Where each part sits

Book	Core idea
1 General	Handling and action of drugs
2 Systemic	Organ-system drugs
3 Chemotherapy	Selective toxicity, resistance, residues
4 Applied	Fluids, nutrition, additives
5 Anaesthesia	Safe loss of consciousness and pain
6 Toxicology	Poisons and antidotes

Species notes

Cats
Weak glucuronidation, so extra caution with many analgesics and phenolics.

Dogs
MDR1 mutation in some herding breeds raises risk with certain drugs.

Ruminants
Oral antibiotics can upset the rumen; withdrawal times apply to milk and meat.

Horses
Colitis risk with some antibiotics; competition rules restrict many drugs.

Poultry and pigs
Flock water medication and egg or meat withdrawal need planning.

Clinical pearls

Self-test: 10 questions

1. Fraction of a dose reaching the systemic circulation is called:

Bioavailability is the fraction reaching the systemic circulation.

2. Which pair describes a reduced response on repeated use, rapid in onset?

Tachyphylaxis is rapid; tolerance develops more slowly.

3. Cats are especially sensitive to some drugs because of weak:

Cats have limited glucuronyl transferase activity.

4. P-glycoprotein deficiency in some dogs is linked to which gene?

MDR1 (ABCB1) encodes P-glycoprotein.

5. NSAIDs act mainly by blocking:

They block prostaglandin synthesis via COX.

6. The lowest antibiotic concentration that stops visible bacterial growth is the:

MIC is the minimum inhibitory concentration.

7. A legal ceiling for a drug residue in food is the:

MRL is the maximum residue limit.

8. MAC measures:

MAC is minimum alveolar concentration.

9. A loop diuretic acts mainly on the:

Loop diuretics act on the thick ascending limb.

10. Withdrawal period is the time:

It protects consumers from residues.

Key points to revise

1. A glossary is for recognition; maps are for linking.
2. Bioavailability, clearance and half-life drive dosing.
3. Agonist and antagonist differ in intrinsic activity.
4. NSAIDs block cyclooxygenase.
5. Resistance grows with selection pressure; stewardship slows it.
6. Withdrawal periods protect consumers; check current Indian notifications.
7. MIC is a laboratory measure of susceptibility.
8. Antidotes act by block, bind, reverse or support.

Go deeper on this site

- Ch 7. Practice MCQ bank, case scenarios and viva questions (in this book)
- Ch 6. Therapeutics in exotics and wildlife (in this book)
- Veterinary drugs list: classes, uses and cautions
- Veterinary Drug Index
- Veterinary Drug Concepts Clearly Explained

Sources

- MSD Veterinary Manual: Overview of Pharmacology
- MSD Veterinary Manual: Overview of Veterinary Toxicology
- US FDA: Antimicrobial Resistance (animal and veterinary)

How to use Book 7: a short discussion

The first six books built a complete picture of veterinary pharmacology, toxicology, chemotherapy and anaesthesia, topic by topic. Book 7 turns that picture upside down. Instead of starting with a drug and asking what it does, it starts with a species and asks which drugs help, which are risky and which should simply be avoided. That is how the knowledge is used in practice and how clinical examinations often test it.

Species chapters

The first six chapters cover dogs and cats, cattle and buffalo, sheep, goats and camelids, horses and donkeys, poultry, pigs and rabbits, and finally exotics and wildlife. Each one lists common conditions, explains the reasoning behind drug choice, names the cautions that are specific to the species and points back to the relevant chapters in the earlier books. In food animals the chapters give special attention to withdrawal periods and residues, and in companion animals they stress client communication and the safety of human medicines in the home.

Why species matter so much

The same drug can be a routine treatment in one species and a poison in another. Cats cannot handle some painkillers, horses react badly to certain feed additives, rabbits can develop a fatal gut disorder after the wrong antibiotic, and ruminants alter drugs in the rumen. The Species sections throughout the series gather these facts, and this book groups them by animal so that they can be revised together.

The practice bank

Chapter 7 is a revision tool. It contains twenty field cases drawn from Indian practice, each with a short situation, guiding questions and a reasoning outline, together with a set of viva questions and thirty mixed multiple-choice questions covering all the books. Work through the cases before reading the reasoning, and speak the viva answers aloud, because explaining an idea in your own words is the best test of whether you understand it.

Glossary and concept maps

Chapter 8 provides plain-language definitions of about eighty terms and text concept maps that show how ideas link within each part of the series. Use it on the last day before an examination, and use the search box above the chapter list to find a term quickly.

Reasoning through a case

When you read a case in this book, follow the same four steps every time. First identify the species, age and physiological state of the animal, including pregnancy, lactation and any food-chain status. Second, decide what the problem is and whether a drug is needed at all, because rest, fluids, nursing and management often matter more. Third, choose a drug by mechanism and by the cautions for that species, and think about what it will do to the gut, kidney, liver and nervous system. Fourth, plan the follow-up: what to monitor, what to tell the owner, when to review, and how long any milk, meat or eggs must be withheld. This habit is more useful in an examination and in practice than any list of drug names.

A final reminder

As throughout the series, the book does not contain dose tables and does not replace a product label, a current formulary or the judgement of a registered veterinarian. Indian regulatory points are marked for checking against the current notification, because rules on drugs, residues and controlled substances change. Treat the series as a framework for understanding, keep revising with the self-tests, and return to the earlier books whenever a species chapter points you there.

Good luck with your studies, and if a chapter helped you, share the site with classmates so that more students can learn the same material.