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.

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