Chapter 1

Introduction to pharmacology

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Aim

The aim of this chapter is to provide an introductory overview of the aspects of pharmacology that are important for paramedic practice.

Learning outcomes

After reading this chapter, the reader will:

1. Be aware of the potential for error in every stage of drug administration, and strategies to avoid medication error.
2. Be able to distinguish the generic and trade names of drugs, and know the conventions for generic names of drugs in the same class.
3. Know the range of sites at which the majority of drugs act to produce their effects.
4. Understand the importance of correct choice, dosing and administration of a drug.

Test your knowledge

1. Which medicines are considered to be completely safe?
2. How can the risk of accidental harm from medicines be reduced?
3. When taking a medication history, what should you prompt a patient to include?
4. What is the generic name and what is the trade name of a medication and where is each name located on the packaging?

Pharmacology is the study of medications. It includes the study of how and when to use them safely and effectively, as well as the search for and the development of new and more effective medications. Although in paramedicine, the term 'medication' is often used in reference to therapeutic agents and the term 'drug' in reference to illicit agents, in this chapter we will use the term

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'drug' with the broader meaning of 'any substance that produces a change in physiological function' when discussing the pharmacology of the active substances rather than formulated preparations.

Health practitioners have at their disposal a formidable armoury of powerful pharmacological agents which have the ability to save lives and relieve suffering. These same agents, used incorrectly, are equally capable of causing death, suffering and irreparable damage. The use of these powerful tools comes with a responsibility to know how to use them safely, and to have a deep understanding of what they can do. Paramedics, often called on to select and correctly use medications in uncontrolled environments with the additional pressures of time and stress, have an even greater need to be experts in the medicines they will administer, performing, as they do, the roles of physician, pharmacist and nurse in the field. Add to this a constantly evolving scope of practice in paramedicine, and it can be seen that the expectations placed on paramedics in the practice of pharmacotherapeutics are very high.

Medication errors in healthcare generally are a significant problem, accounting for a large number of hospitalisations and deaths per year. In prehospital care in particular, medication errors are thought to be significantly under-reported (Batt, 2016; Hobgood et al. 2006; Lammers et al. 2014; Nguyen, 2008). Data from a number of studies on medication errors in Australian hospitals suggested that between 5% and 10% of administrations may be made in error (Roughead et al., 2013), and in England alone, more than 237 million medication errors are made every year (Elliott et al., 2018). Medication errors made in all areas of healthcare are a similar concern in the United States, the European Union, and in most countries of the world. In recognition of the problem, in 2017 the World Health Organization launched a global initiative to reduce severe, avoidable medication-associated harm worldwide by 50% over 5 years.

Medication errors in paramedicine can include the general misuse of a medicine, such as administering the wrong dose, using the wrong administration route, or failing to identify contraindications. But, because the paramedic is responsible for all phases of the administration of the medication, including the selection of the appropriate medication and the decision about whether and when to use it, two other types of error can also occur: under- or overuse of medicines. The failure to use a medication that could be of benefit to a patient, such as failing to give aspirin for acute coronary syndrome, would be considered an error of underuse, while using an unnecessary medication, or using a second medication to treat a side-effect produced by the first medication, could be considered errors of overuse (Batt, 2016).

The Institute of Safe Medication Practices (ISMP) Canada, in its 2020 safety bulletin, reported on a multi-incident analysis of medication incidents involving paramedicine. This analysis identified the following five main themes in medication errors in paramedicine:

1. The clinical assessment and management of patients, including taking a complete medical and medication history.
2. Therapeutic product use, including misreading of labelling or mistaking products with similar packaging.
3. Intravenous dosing and administration, including calculating dose and setting up pumps.
4. Handover communications, including communication to hospital personnel.
5. Inventory management, including correct restocking of the ambulance with medication and correct positioning of drugs.

These themes serve to reinforce the multiple responsibilities of paramedics when it comes to administering medicines – paramedics are responsible for taking a complete patient history, calculating a correct dose and administering the medication correctly, right through to ensuring the medication is in the ambulance in the correct place before going out on the road. The scope for medication error increases with each layer of responsibility.

A number of authors have suggested standard methodologies to ensure that the correct approach to medicines use is followed every time, especially under high-stress conditions. The following mnemonic for the assessment of patients was developed by ISMP Canada:

SAMPLE
Signs
Allergies
Medication
Past pertinent history
Last oral intake
Events leading to injury

Students of paramedicine are usually familiar with the golden rules of safe administration of medicines, published as 10 golden rules (McGovern, 1992) but also appearing in shortened forms. These rules stipulate that when giving any medication:

1. Give the right drug
2. To the right patient
3. In the right dose
4. Via the right route
5. At the right time
6. Explain about the medication to your patient
7. Take a complete medication history
8. Find out about any allergies
9. Know about potential drug interactions
10. Document each medication administration.

These rules serve as a guide for safe administration of medicines in the field, but they can also be a useful guide to learning pharmacology. Learning what drugs do and how they do it; who they can be given to and when caution should be exercised; what dose ranges they should be used in; by what routes they can be administered and the correct timing of their administration via these routes; what drugs they cannot be combined with and why, are all part of the pharmacology every student of paramedicine must learn and continue to add to as they gain professional experience and as new medicines become available. The need to be a lifelong learner is never more pressing than in the field of clinical pharmacology.

Companies selling medicines are required by law to provide basic information about the medicine for patients before it is made available to them. In the UK, this information is known as the Patient Information Leaflet (PIL), and in Australia it is the Consumer Medicines Information (CMI). The aim of this information is to educate patients about their medicines so that they can ensure they are taking them safely and effectively.

This information includes:

- What the medicine is used to treat (the **indications** of the medicine)
- Warnings about when the medicine should not be taken (the **contraindications** of the medicine)
- Warnings about when the medicine should be taken with caution
- Other medicines that should not be combined with the medicine (known as **interactions**)
- Possible side-effects (known as **adverse effects**)
- The dose to take and any special instructions regarding how to take the medicine
- What to do in the case of an overdose of the medicine
- How to store the medicine.

The language used in these documents has been chosen to make the information accessible to any patient, hence the avoidance of too much technical language, but it is nonetheless the same information that health professionals need in order to ensure the safe and effective administration of medicines to their patients.

Skills in practice

The decision about whether to administer or withhold a medication requires a process of clinical reasoning, based on your assessment of the patient, their medical and medication history and the indications and contraindications of the medication.

An indication for a medication is a particular symptom or sign reported or displayed by a patient. An indication should not be confused with a definitive diagnosis. In paramedicine, a primary assessment and history taking should be carried out if possible, prior to establishing an indication. Administering an indicated medication should only occur if the potential benefit of the medication is judged to outweigh the risk to the patient, such as in the following examples:

- An unconscious child who is hypoglycaemic is indicated for glucose 10% administration. The signs used here as indications for the medication are both the finding of hypoglycaemia and the child's level of consciousness.
- A 50-year-old male patient who is experiencing crushing left-sided chest pain has an indication for aspirin administration, provided you have established that he has no abnormal bleeding tendencies.

Sometimes, despite there being an indication for a medication, you will not be able to administer it because of a contraindication. A contraindication is a reason to withhold medication because it might cause harm to the patient, as in the following examples:

- Aspirin is contraindicated for analgesia and fever in paediatric patients who are under 16 years of age because of the risk of Reye's syndrome. The syndrome is quite rare and only occurs in children, but is very serious.
- Ipratropium, a bronchodilator commonly used with salbutamol for the treatment of bronchospasm, is usually contraindicated in patients who have glaucoma, as a known side-effect is an increase in intraocular pressure.
- Amiodarone is an antiarrhythmic indicated for tachyarrhythmias (cardiac arrhythmias which involve an increased heart rate), but contraindicated in torsades de pointes, a potentially fatal tachyarrhythmia which can result from long QT syndrome, because amiodarone will result in further protraction of the QT interval.

As data about medications are gathered, indications and contraindications may change, so it is important to remain abreast of these changes in your practice as a paramedic.

Episode of care

You attend a 49-year-old male patient complaining of left-sided central chest pain. He is diaphoretic, pale and short of breath.

You ask him about his medical history. He reports he has a 'high blood pressure problem'. You glance at his medication list and do not recognise any common antihypertensive medications.

Your check his observations and gain a detailed history, while preparing him for a 12-lead ECG. The ECG suggests a lateral myocardial infarct. Your provisional diagnosis is acute coronary syndrome and you proceed with administering aspirin and a vasodilator.

En route he rapidly becomes hypotensive with a decreased level of consciousness. At hospital, you discover he has recently commenced on a vasodilator for aggressive management of his pulmonary hypertension. This medication was not on his medication list.

You may see medications that patients are taking for indications other than the listed indications. Vasodilators such as sildenafil (Viagra®) and vardenafil (Levitra®) are often prescribed to males for erectile dysfunction, but can also be used to treat pulmonary hypertension.

Patients may be unsure what they are taking medications for and it is imperative to gain a detailed history prior to administration of any medication to ensure contraindications are not encountered. Medications can be used for purposes other than their primary indication.

Naming and classifying drugs

Every drug will have a number of names. Knowing the correct name of a drug is vital in the prevention of medication errors, and becomes even more important when drugs can be identified by several different names. All drugs will have an individual chemical name which conveys very accurately (at least to a chemist!) the drug's molecular structure. These names are usually long, difficult to say and impossible to remember, and they are usually left to research chemists. Many drugs can also be known by the name of the chemical class they belong to, such as opioids or benzodiazepines. But it is the generic, or official, name of the drug that health practitioners should always recognise a drug by. This name should be sufficiently different from any other drug name to minimise the risk of any drug being mistaken for another. With a few exceptions, generic names are usually the same regardless of where in the world you are, and they often derive in some way from the name of the chemical class of the drug, which is often convenient as it makes it easy to identify the class a drug belongs to by its generic name. The generic names of drugs belonging to the statin class of drugs, for example, end in -statin, with agents such as atorvastatin, rosuvastatin, fluvastatin and simvastatin. Generic names of drugs belonging to the beta-blocker class end in -olol and include propranolol, atenolol, pindolol and nebivolol.

Many drug formulations will also have a trade name given to the particular drug formulation by the company that produced it. These names may relate to the generic name or they may relate more closely to their therapeutic use, but because of the multiple formulations available and multiple companies producing them, the trade names of drugs will vary widely depending on where the drug is sold and what it is sold for. Needless to say, these names are not a reliable way to identify the drugs but unfortunately, they are often the most prominent and eye-catching name on the packaging, which will mean that patients will usually refer to drugs by the trade name, unless they are receiving a generic version of the drug. To try and reduce confusion, the Australian government, for example, passed a law, effective February 1, 2021, that requires prescribers to write the generic name of the medication first on any prescription, either without a trade name or with the trade name in brackets after it. Combined with requirements for drug manufacturers to make the generic name of the active drug in the medication more prominent on the packaging than the trade name, the aim is to increase awareness of the active ingredients in medications and to reduce confusion.

With the huge range of drugs currently licensed for use, there are often multiple individual drugs available for any particular indication, so it is important that we also classify our drugs to make talking about them easier. We can classify drugs based on their chemical structures, mechanism of action or broader area of therapeutic use. The functional classifications (those relating to what the drugs do or what they are used for) are the most widely used, as they reflect the clinical uses of the drugs, but we often refer to certain groups of drugs by their chemical classification, as usually all agents belonging to a certain chemical class also have a predictable effect on function. Table 1.1 gives some examples of the ways in which drugs are named and categorised.

Look-alikes and sound-alikes

Mistaking one medication for another because the two names (either generic or trade names) sound alike or the packages look alike is a common cause of medication error. Errors due to look-alike sound-alike (LASA) medications have become so widespread that the World Health Organization launched a worldwide effort to reduce medication errors that come about in this way (WHO, 2007), and many governments have made changes to their medication labelling and naming The addition of 'tall man' writing in the name of a drug has been introduced in the UK, Canada, Australia and the US to make the differences between drug names clearer. This technique involves capitalising the parts of the name that are most likely to be misread, for example:

AmiloRIDE, AmlodiPINE, BuPROPion, BupreNORphine.

The mix of capitalised lettering in the name disrupts rapid reading and forces a more careful observation of the name.

The main element in reducing medication errors, however, continues to be careful cross-checking of LASA medications prior to administration, and ensuring that look-alike medications are not stored in close proximity to each other. Because the packaging and appearance of medications can change, the generic name of the medication should always be checked, and the identity of a medication should never be assumed from its appearance without checking the label. For example, a 500 mL or 1000 mL bag of clear fluid could be Hartmann solution, sodium chloride or glucose 10%.

Table 1.1 Categorisation of drugs based on clinical usage, general action or specific mechanism of action.

Generic name	Trade names	Chemical class	Therapeutic use	General action	Specific mechanism of action
Diazepam	Valium® Valpam® Antenex®	Benzodiazepines	Anxiolytics	Central nervous system depressants	GABA agonists
Atorvastatin	Lipitor® Torvastat®	Statins	Cholesterol synthesis inhibition	Lipid-lowering agents	HMG Co-A reductase inhibitors
Candesartan	Candesan® Adesan® Atacand®	-	Antihypertensives	Blood pressure-lowering agents	Angiotensin receptor antagonists
Salmeterol	Serevent®	-	Acute asthma control	Bronchodilators	Long-acting beta-2 agonists
Diclofenac	Voltaren® Voltarol® Difenac® Clonac®		Analgesic, anti-inflammatory	Non-steroidal anti-inflammatories	Cyclo-oxygenase inhibitors

GABA, gamma-aminobutyric acid; HMG-CoA, 3-hydroxy-3-methylglutaryl coenzyme A.

How drugs bring about their actions

With only one or two exceptions (such as drugs which absorb other substances, e.g. charcoal or resins), drugs act by binding chemically to specific binding sites. It is this fact which explains the various observed characteristics of a drug, for example, the relationship between the shape of a drug molecule and its actions; the relationship between how readily it binds to its site of action and the concentration of drug needed at the site of action to bring about a therapeutic effect; the relationship between the number of different binding sites the drug can bind to and the number of different effects it produces; the strength with which it binds to the site and length of time for which it exerts its effects, and so on.

The site at which a drug binds to have its effects is known as the receptor for that drug, and it may be a receptor normally used by endogenous signalling molecules, such as hormones or neurotransmitters, or a binding site on an enzyme, ion channel or transport molecule. A substance binding at any of these sites would be able to alter physiological function when the structure to which the drug is binding is itself responsible for producing various physiological changes.

How are we able to manipulate physiological function using drugs?

Physiological systems make use of hundreds of specific signalling chemicals to carry out their own signalling function and this provides an opportunity to use drugs to mimic or block the effects that those endogenous signalling chemicals would produce. By employing drugs with chemical structures

similar to those of endogenous chemicals, we gain an opportunity to 'operate the levers' of the human machine. Not surprisingly, therefore, the vast majority of the drugs used act by altering the function of one of these key pieces of signalling and transport machinery:

- Receptors
- Enzymes
- Ion channels
- Transport molecules

Drugs used as therapeutic agents act by manipulating physiological mechanisms, which reinforces the importance of having an understanding of human physiological responses as the basis for understanding pharmacology. Without a sound knowledge and understanding of how physiological systems respond, it is impossible to make sense of how drugs will interact with those systems.

Receptors as sites of drug action

An opioid drug such as morphine acts by binding to the receptors for endogenous opioids and, by activation of those receptors, produces similar actions to those generated by the endogenous opioids, including analgesia and a range of other effects. Similarly, bronchodilator drugs such as terbutaline and salbutamol, used during an episode of acute asthma, produce their bronchodilator effect by activating adrenergic beta receptors on the airways. These receptors would be activated physiologically by adrenaline and noradrenaline secreted during the fight or flight response, and the binding of adrenaline or noradrenaline to the beta receptors in the airways would produce a dilation of the airways, allowing a more rapid ventilation of the lungs. A drug which is able to produce this effect without producing the rest of the fight or flight response is a very useful therapeutic agent during an episode of acute asthma (Figure 1.1).

Enzymes as sites of drug action

Enzymes are the large proteins that catalyse the thousands of biochemical reactions that maintain physiological function. An enzyme carries out the catalysis (speeding up) of a particular reaction by binding the reacting molecules and making it 'easier' for the reaction to occur (Figure 1.2). Drugs which have enzymes as their targets tend to be inhibitors of those enzymes, preventing the normal reacting substances from binding with the enzyme for catalysis.

Drugs such as non-steroidal anti-inflammatory drugs (NSAIDs), the prototype of which is aspirin, act by inhibiting the enzyme cyclo-oxygenase, which is responsible for speeding up the reaction producing a range of important signalling molecules known as prostaglandins. It is the reduced level of prostaglandins as a result of blockade of cyclo-oxygenase that produces the range of effects associated with NSAIDs. Another example of a widely used class of drugs which act by blocking an enzyme is the statin class, including atorvastatin and fluvastatin. These drugs lower cholesterol levels by inhibiting the enzyme HMG-CoA reductase, responsible for the production of cholesterol in living cells.

Ion channels

Ion channels represent the only means for ions to cross cell membranes, and all cells contain multiple species of ion channel in their membranes. These channels can be gated in a number of ways, and drugs which can bind to specific channels can alter cellular activity profoundly by altering the passage of ions across the membrane, thereby altering the cell's membrane potential. Most drugs that act in this way block ion channels rather than open them.

The local anaesthetic lidocaine, for example, acts by binding to and inhibiting voltage-gated sodium channels in neuronal cell membranes, preventing the generation of action potentials by the affected neurons. Sensory neurons detecting touch, pressure and pain stimuli therefore become less responsive to those stimuli, resulting in anaesthesia.

The benzodiazepine class of drugs, including agents such as midazolam and diazepam, act by binding to a chloride ion channel in neuronal membranes.

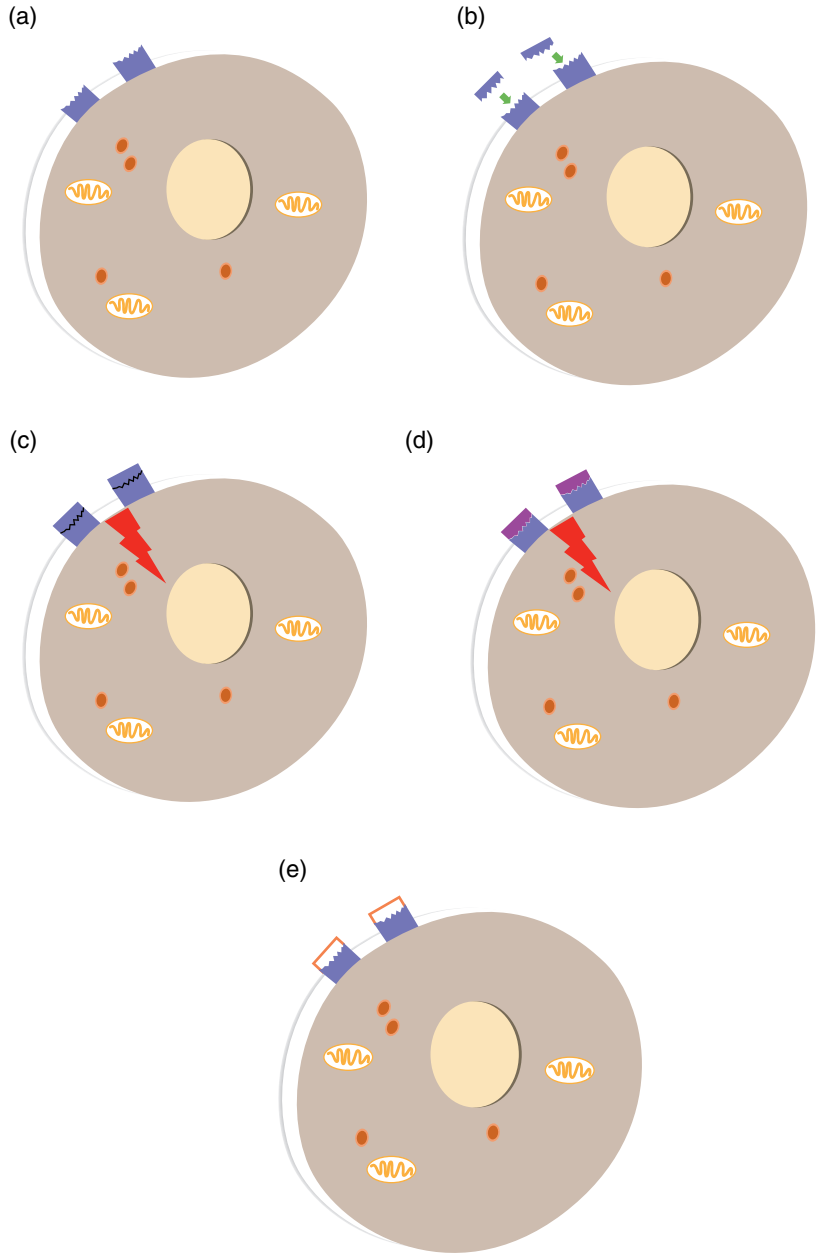

Figure 1.1 Drugs which act at receptors. (a) A cell has receptors for a specific signalling compound (e.g. a neurotransmitter or hormone) located on the cell membrane. (b) The endogenous signalling molecule binds to its receptors, fitting the receptor perfectly. (c) The binding triggers a series of actions inside the cell. These actions would be the normal response to that signalling compound. (d) If the molecular structure of a drug is sufficiently similar to that of the endogenous signalling compound, the drug will also be able to bind to the receptor and produce the same actions in the cell. This drug would be known as an agonist at this receptor. (e) If a drug has a molecular structure vaguely similar to that of the endogenous signalling compound, it may still be able to bind to the receptor, but not fit it perfectly enough to produce the same actions in the cell. This drug could prevent the endogenous signalling compound (and the agonist) getting to the receptor, thereby blocking their actions. This drug would be known as an antagonist at the receptor.

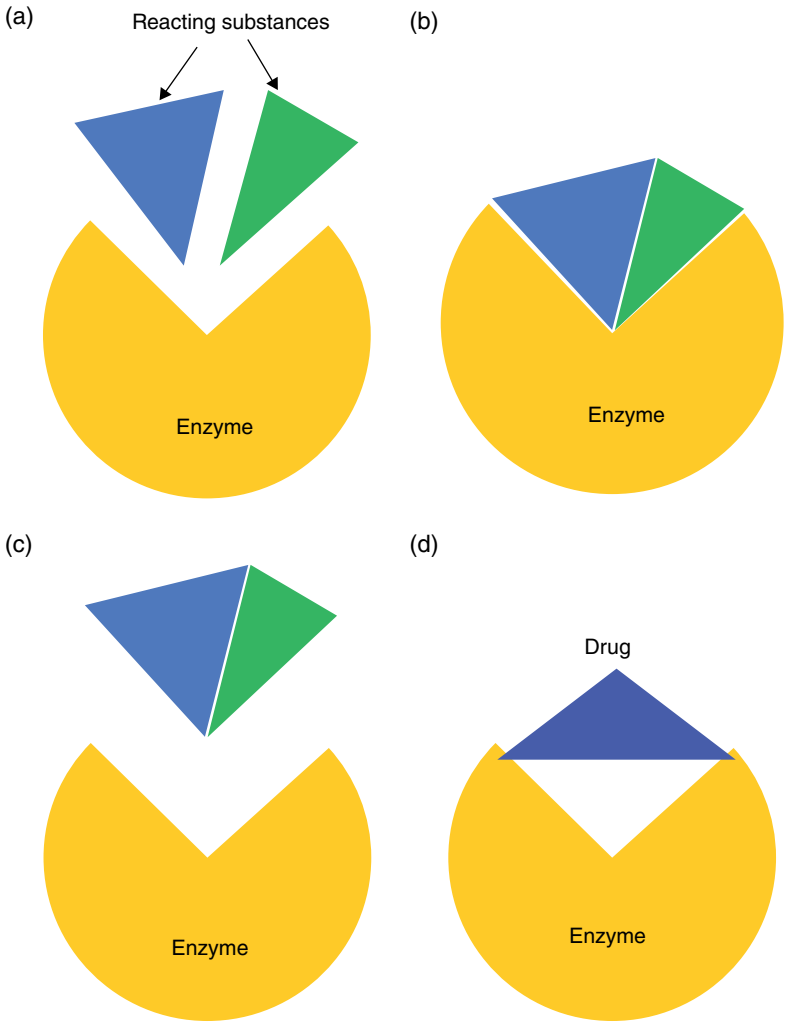

Figure 1.2 Enzymes operate by binding reacting substances (a) and accelerating their reaction – in this case the reaction is a combination of two molecules (b), then releasing the product from the enzyme's binding site (c). A drug which can also bind to this site can prevent the catalytic function of the enzyme, thereby reducing the level of product (d).

This channel is opened normally by the inhibitory neurotransmitter GABA (gamma-aminobutyric acid). Opening a chloride channel in the membrane allows the influx of negatively charged chloride ions to the cell, which hyperpolarises the cell, making it less likely to produce action potentials. The benzodiazepine class of drugs also act at this ion channel, albeit at a different site to GABA, but when they bind, they enhance the inhibitory actions of GABA, and add to the hyperpolarisation of neurons and the resulting nervous system depressant effect (Figure 1.3).

Transport molecules

The large, complex proteins responsible for active transport of substances across cell membranes represent another valuable drug target for manipulation of physiological function.

There are active transporters or pumps in all cell membranes for sodium, potassium and calcium ions, and these are activated when those ions have to be transported across the cell membrane against their concentration gradient, i.e. from a lower to a higher concentration of ions. Ions can

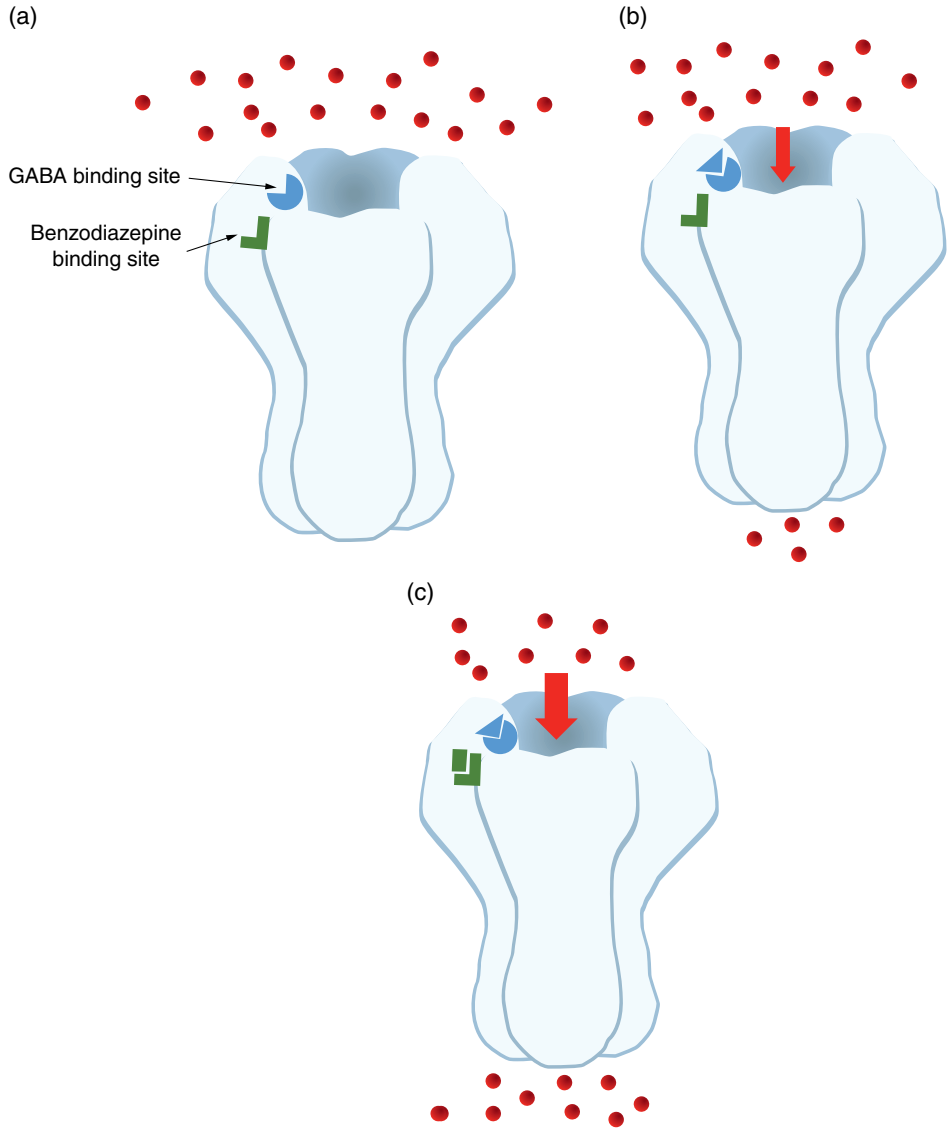

Figure 1.3 Benzodiazepines act by binding to a chloride channel. (a) The inhibitory neurotransmitter GABA has its receptor on the ligand-gated chloride ion channel in neurons. The channel also has a binding site for drugs of the benzodiazepine class. (b) Binding of GABA to its receptor opens the channel, allowing chloride ions to flow into the neuron and hyperpolarise the membrane, inhibiting further neuronal activity. (c) Binding of a benzodiazepine to its site will, in the presence of GABA, further increase the flow of chloride ions into the cell by keeping the channel open for longer, thereby further inhibiting neuronal activity.

move through open ion channels if they are travelling down their concentration gradient, but will need active 'pumping' if they are to move the other way.

As with enzymes and ion channels, the drugs that bind transport molecules tend to inhibit the transport when they bind. This alters cell function by interfering with the distribution of ions across the cell membrane, thereby altering membrane potential. The cardiac glycoside drug digoxin, used to treat cardiac failure, acts by binding to a transport molecule – the sodium/potassium ATP-ase or sodium/potassium pumps on the cell membranes of cardiac muscle cells. Digoxin inhibits the function of the sodium/potassium pumps, leading to an accumulation of sodium ions inside cardiac muscle

cells, which in turn results in an accumulation of calcium ions in the cells (the additional intracellular sodium ions stimulate another transporter, which pumps sodium ions out of the cell in exchange for calcium ions). The increased level of calcium ions inside the cardiac muscle cells results in stronger contractions, which translates to a stronger, more forceful heartbeat.

Selectivity of binding and its effect

Some drugs are very selective in their binding sites, and can bind to a very limited number of sites, or only one site, but most drugs will be able to bind to more than one site. For example, a bronchodilator medication that acts as an agonist at adrenergic beta receptors may bind at only beta-2 receptor subtypes, in which case it would be a selective beta-2 agonist, but is more likely to bind to both beta-1 and beta-2 receptors, because of the degree of chemical similarity between the two receptor subtypes. The more selective a drug is for a single receptor, the fewer effects it is likely to bring about, so a more selective drug is likely to be one with fewer side-effects. On the other hand, a less selective drug which activates two or three related receptors may have more therapeutic uses, but it will also have more side-effects. The selectivity of a drug will tend to decrease as the dose increases, because binding to other receptor types will become more likely as the concentration of the drug increases. This helps to explain the dose dependency of many side-effects of medications.

Clinical considerations

Salbutamol, also known as albuterol, is a beta-2 receptor agonist and is frequently administered in the out-of-hospital setting for management of bronchospasm. It can also be used in the management of hyperkalaemia because it stimulates the transport of potassium ions from the blood into skeletal muscle cells. This effect is also mediated by the action of salbutamol on beta-2 receptors.

Many patients who have been prescribed salbutamol may have already self-administered their own 'puffer' prior to your arrival and may be tachycardic as a result. This is due to binding to beta-2 receptors in cardiac muscle after absorption of salbutamol into the bloodstream. Tachycardia may predispose the patient to arrhythmias, so regarding these patients as high risk for a cardiac event is warranted.

Muscle tremors may also occur in these patients, due to binding of the drug to beta-2 receptors in skeletal muscle. Although the drug is quite selective for beta-2 receptors, it will also bind to beta-1 receptors at high doses, so if the patient has used their puffer very extensively prior to your treatment, there may be additional tachycardia due to an action on beta-1 receptors in the heart, increasing cardiac risk.

The drug–body interaction is a dynamic process

The interaction between any administered drug and the person it is administered to is dynamic. From the moment it is administered, the drug will be moving from its administration point to other compartments of the body, being absorbed into the bloodstream, and leaving the blood to enter other tissues or other body compartments, so the concentration of the drug in the blood and in various tissues and body compartments will be changing. As the drug passes through the liver, it will be acted on by metabolic enzymes which will convert it to a different form, which may be more or less pharmacologically active, but certainly more water soluble. The drug travelling in the blood will also be filtered by the kidneys, and the water-soluble form of the drug will be trapped there and excreted in the urine.

As the drug is being carried around the body, some of it will arrive at and bind to its sites of action, producing its effects. Even the binding of the drug to its receptors is a dynamic process, akin to molecules playing musical chairs with the receptors – molecules of the drug will bind and detach and bind again rather than simply binding and remaining in place. Each time the molecule detaches from its binding site, it may be whipped away and metabolised, and its place on the receptors may be taken by another, competing molecule. This constantly changing relationship between the drug and

the living system it has been introduced into explains a great deal about how drugs have their effects. The delay between administration and action of a drug, the duration of action of the drug, and the ability to reverse or overcome the actions of one drug by giving another drug are all the result of this dynamic interaction between drug and living system.

For the paramedic administering drugs into a system which may be free of other drugs but more likely already contains some pharmacological agents, this constantly changing effect of the drug on the patient will require you to have a good enough grasp on what these agents can do, either alone or in combination, to be able to predict and maintain some control over their actions.

One challenge we are always faced with is getting enough of a drug from its site of administration to its site of action for it to have a therapeutic effect. The drug is effectively in a race to reach its site of action and have its effect before it is chemically degraded and removed from the body. A drug which has a highly desirable therapeutic action may turn out to be useless from a clinical point of view if it cannot be delivered to its site of action. So, a drug that is going to stand a chance of being useful would usually possess characteristics which allow it to be easily absorbed into the bloodstream, preferably after oral administration, which in turn would mean that the drug would not be destroyed by the acid of the stomach or digestive enzymes. And although it would probably be subject to metabolism by the liver, the metabolism should not be so rapid that it is almost completely gone after a single pass through the liver (a phenomenon known as first-pass metabolism), as this would mean that very little of the active drug remained in the bloodstream to circulate after absorption. Other routes of administration might avoid the problem of first-pass metabolism, but each administration route will have its own advantages and disadvantages.

Clinical considerations

Administration of medications in the out-of-hospital setting can be challenging due to poor lighting, uncontrolled environment or a chaotic scene. Practising all steps of safe medication administration is key to reducing the risk of error (Chapter 4 discusses medicines management and the role of the paramedic). Ensuring the same routine is exercised every single time you administer any medications will embed safe practice so you do not overlook a crucial step during a high-acuity incident.

Hand hygiene is important to prevent introduction of harmful pathogens in the out-of-hospital environment. Access to running water may not be practical in the out-of-hospital setting, so utilisation of alcohol-based hand rub is the gold standard in this setting. Healthcare-associated infections generate significant comorbidity and burden for the patient, the community and the healthcare system. Healthcare-associated infections are avoidable and simple hygienic practice and aseptic technique are crucial in breaking the chain of transmission from community, to patient and into care settings such as hospitals.

Intravenous cannulation is a key source for bloodstream infections and risk mitigation efforts, such as use of alcohol-based hand rub and not touching the area between cleaning the skin and immediately prior to cannulation, should be exercised.

Other routes of administration which are common in the out-of-hospital setting include intravenous, intramuscular, topical, intranasal, endotracheal and intraosseous. See Chapter 6 for further discussion.

Once absorbed into the bloodstream, a drug needs to be able to penetrate to its sites of action relatively quickly. If the drug was an antimicrobial being used to treat an infection of the blood, then getting enough drug into the bloodstream for long enough would be all that was required. However, if the drug were required to penetrate the central nervous system, for example, or get into joint spaces or some other protected body compartment, then it would also have to be able to move out of the bloodstream and travel through the cellular walls that form those body compartments. This presents another challenge to a molecule; in order to get through cell membranes, a drug molecule either needs to be soluble in lipids (lipophilic) or, if it is more water soluble (hydrophilic), then it would have to be a very small molecule. Drugs that are highly lipid soluble are generally able to move readily through cellular compartments without difficulty, and will therefore leave the bloodstream

and enter the tissues, often concentrating there. Drugs that readily cross the blood–brain barrier, such as those used in general anaesthesia, are highly lipid soluble, allowing them to pass very rapidly into the protected environment of the brain, which explains their ability to produce general anaesthesia in a matter of seconds after being introduced into a vein.

The dose, route and timing of administration will all play key roles in the effectiveness of the drug. This is discussed in greater detail in Chapter 5.

Episode of care

You are treating 94-year-old Nelida, who has fallen in her residential aged care facility while going to the bathroom. She has a large bruise on the side of her head (temporal region) and a shortened and rotated left leg, as well as a deep laceration to her left upper thigh caused by the shard of a mirror that broke during the fall. Staff report that the patient has dementia but can still converse appropriately most days. The patient is in extreme pain but her heart rate is not elevated. You realise this is probably due to her being on a beta-blocker for hypertension. You administer intranasal fentanyl repeatedly en route to hospital to treat her pain. On arrival, her level of consciousness has decreased. Reflecting on what might have caused this, you consider that the combination of blood loss and a blunted compensatory response due to the beta-blockers, along with a reduced renal capacity due to her age, and the fact that the repeated fentanyl doses have not been cleared as rapidly as expected has resulted in an accumulation of medication, leading to adverse effects.

While this is not a contraindication of fentanyl, it is important to remember that older patients often clear medications much more slowly than younger patients, and dosing may need to be adjusted to account for this, to avoid adverse effects.

Skills in practice

Medications can come in varying concentrations and formulations for different modes of delivery. Adrenaline is a naturally occurring catecholamine hormone produced by the adrenal glands and is often also administered in the management of life-threatening presentations such as cardiac arrest, anaphylaxis and croup.

The concentration of adrenaline can be expressed as 1:1000 or 1:10 000. This is expressed verbally as 'one in one thousand' and 'one in ten thousand' respectively. This ratio refers to the medication mass per volume of solution:

$$1:1000 = 1\,\text{gram of adrenaline per } 1000\,\text{mL}$$

$$1:10\,000 = 1\,\text{gram of adrenaline per } 10000\,\text{mL}$$

Adrenaline concentrations can and do vary, but the following is a guide to concentrations and routes of administration for various indications:

Concentration	Route of administration	Indication
Adrenaline 1:1000	Intramuscular Nebulised	Anaphylaxis Croup Asthma
Adrenaline 1:10 000	Intravenous	Cardiac arrest Cardiogenic shock

Administering medication to children

Historically, children were considered small adults, with the same physiology and metabolic requirements as an adult, but on a smaller scale. This is now known not to be the case, but many medications are still not tested on children, so safe doses in this patient group are not established empirically. A basic understanding of the differences between adult and child anatomy and physiology will ensure safer administration of medication to children. For example, the child's heart does not have the same capacity to raise cardiac output by increasing its force of contraction and relies on increasing the heart rate to compensate for increased demand. As a result, peripheral vasoconstriction usually occurs more readily, in order to maintain blood pressure.

Medications which cause peripheral vasoconstriction need to be used with extra caution in children because of this. Adrenaline will cause peripheral vasoconstriction when used to treat anaphylaxis or asthma, and the beta-2 agonist salbutamol (albuterol) is also often contraindicated in children because of the possibility of tachycardia. Using medications that cause tachycardia will place further demands on a child's heart, possibly at a time when it is already working hard to compensate. These medications have to be dosed and administered with extreme care in children, and some may be contraindicated.

Reflection

How is dosing calculated for children? If you don't know the weight of the patient and there is no one to give you the weight, how would you estimate it, to ensure you give a safe and effective dose?

What special considerations need to be borne in mind when giving medications intranasally to children?

When administering medications to a child, ensure consent is gained from the parent, caregiver or a response given by the child is appropriate for their age and presentation. Ensure your approach to treating a child extends to providing oversight to the parent/caregiver as well.

Conclusion

The out-of-hospital setting is not the same as the controlled environment of the hospital and the unpredictable and uncontrolled nature of paramedicine requires that the practising paramedic performs the work that would be done by three different health professionals in a hospital. This places a great responsibility on the paramedic when it comes to the safe and effective use of medicines. The paramedic must be an expert in both the correct choice and administration of medications. In addition, because the environment in which the paramedic is operating is particularly conducive to making errors, the paramedic must also be constantly vigilant and ensure the stringent and consistent checking of medication route, dose, time, expiration date and patient. As the scope of paramedic practice increases and more medications are administered in the prehospital setting, the need for paramedics to have a mastery of medicines becomes even greater.

Glossary

Agonist	A drug that binds to a receptor and produces the same response as the endogenous substance. For example, morphine is an agonist at opioid receptors because it produces the same response as the endorphins produce.
Antagonist	A drug that binds to a receptor and prevents the endogenous substance or an agonist from binding and having its effect. Also known as a blocker, because it blocks the activation of the receptor.
Contraindication	A characteristic or condition which would prevent a patient from being able to receive a certain medication.
First-pass metabolism	The metabolism of a large proportion of an administered dose of a drug by the liver almost immediately after absorption.
Indication	A condition or symptom which a medication is approved to treat.

Pharmacodynamics	The actions of a drug on the body.
Pharmacokinetics	The actions of the body on the drug.
Receptor	The site at which a drug molecule binds to have its action.

References

Batt, A. *Enhancing patient safety education for paramedics with the IHI Open School*. http://prehospitalresearch.eu/?p=6171

Elliott, R.A., Camacho, E., Campbell, F. et al. (2018). *Prevalence and Economic Burden of Medication Errors in the NHS in England*. Sheffield: Policy Research Unit in Economic Evaluation of Health and Care Interventions (EEPRU).

Hobgood, C., Bowen, J.B., Brice, J.H., Overby, B. and Tamayo-Sarver, J.H. (2006). Do EMS personnel identify, report and disclose medical errors? *Prehospital Emergency Care* **10**(1): 21–27.

Institute for Safe Medication Practices Canada. (2020). Multi-incident analysis of incidents involving paramedicine. *ISMP Canada Safety Bulletin* **20**(1): 1–4.

Lammers, R., Willoughby-Byrwa, M. and Fales, W. (2014). Medication errors in prehospital management of simulated pediatric anaphylaxis. *Prehospital Emergency Care* **18**(2): 295–304.

McGovern, K. (1992). 10 Golden rules for administering drugs safely. *Nursing* **22**(3): 49–56.

Nguyen, A. (2008). Bad medicine: preventing drug errors in the prehospital setting. *Journal of Emergency Medical Services* **33**(10): 94–100.

Roughead, L., Semple, S. and Rosenfeld, E. (2013). *Literature Review: Medication Safety in Australia*. Canberra: Australian Commission on Safety and Quality in Health Care.

WHO Collaborating Centre for Patient Safety Solutions. (2007). *Look-Alike Sound-Alike Medication Names. Patient Safety Solutions: Solution 1*. https://cdn.who.int/media/docs/default-source/integrated-health-services-(ihs)/psf/patient-safety-solutions/ps-solution1-look-alike-sound-alike-medication-names.pdf?sfvrsn=d4fb860b_6&ua=1

Further reading

Australian Medicines Handbook (AMH). 2020 print edition or online: https://amhonline.amh.net.au

British National Formulary (BNF). 2020 print edition or online: www.bnf.org

Multiple-choice questions

1. A medication error occurs when:
   - **(a)** The wrong dose is administered
   - **(b)** A drug that would benefit a patient is not given
   - **(c)** A drug that it not necessary is given
   - **(d)** All of the above.
2. The purposes for which a medication can be used are the:
   - **(a)** Mechanism of action
   - **(b)** Contraindications
   - **(c)** Indications
   - **(d)** None of these.
3. The conditions in which a drug cannot be used are the:
   - **(a)** Mechanism of action
   - **(b)** Indications
   - **(c)** None of these.
4. When drugs such as alprazolam are referred to as benzodiazepines, they are being classified according to their:
   - **(a)** Mechanism of action
   - **(b)** Indications
   - **(c)** Chemical class
   - **(d)** Original trade name.

5. When drugs such as reboxetine are referred to as antidepressants, they are being classified according to their:
   (a) Mechanism of action
   (b) Indications
   (c) Chemical class
   (d) Original trade name.
6. A medication which is prescribed for an indication other than its listed indications is being used:
   (a) Illegally
   (b) Off-label
   (c) Even though it is contraindicated
   (d) None of the above.
7. The drugs known as specific serotonin reuptake inhibitors, which include fluoxetine (Prozac®), would act by binding to:
   (a) A receptor for a neurotransmitter
   (b) An ion channel
   (c) An enzyme
   (d) A transport molecule.
8. In general, the more selective a drug is in its binding sites:
   (a) The fewer side effects it will have
   (b) The more easily it will reach its site of action
   (c) The more potent it will be
   (d) The more it will interact with other drugs.
9. When administering adrenaline intravenously, which dilution is most appropriate?
   (a) 1:100
   (b) 1:1000
   (c) 1:10 000
   (d) 1:100 000
10. A drug that is an antagonist or blocker of a receptor is likely to 'fit' the receptor chemically better than a drug that is an agonist.
   (a) True
   (b) False
11. A drug, such as a general anaesthetic, that can penetrate the blood–brain barrier very rapidly after intravenous administration is likely to be:
   (a) Highly water soluble
   (b) A protein
   (c) Highly lipid soluble
   (d) No drugs can penetrate an intact blood–brain barrier.
12. A medication dose may need to be adjusted down in which of these situations?
   (a) Renal failure
   (b) High first-pass metabolism
   (c) Diarrhoea
   (d) Vomiting
13. The NSAID aspirin has its effects due to action at:
   (a) An ion channel
   (b) A neurotransmitter receptor
   (c) A transport molecule
   (d) An enzyme.

14. You are attending a patient who has suffered trauma and lost a lot of blood. The patient's heart rate is normal, even though their blood pressure is low. Which of the following medications being taken is most likely to be responsible for this?
(a) Ibuprofen
(b) Metformin
(c) Atenolol
(d) Tetracycline

15. If a drug undergoes extensive first-pass metabolism, which of these routes should be avoided as administration routes for this drug?
(a) Intramuscular
(b) Intravenous
(c) Oral
(d) Intranasal