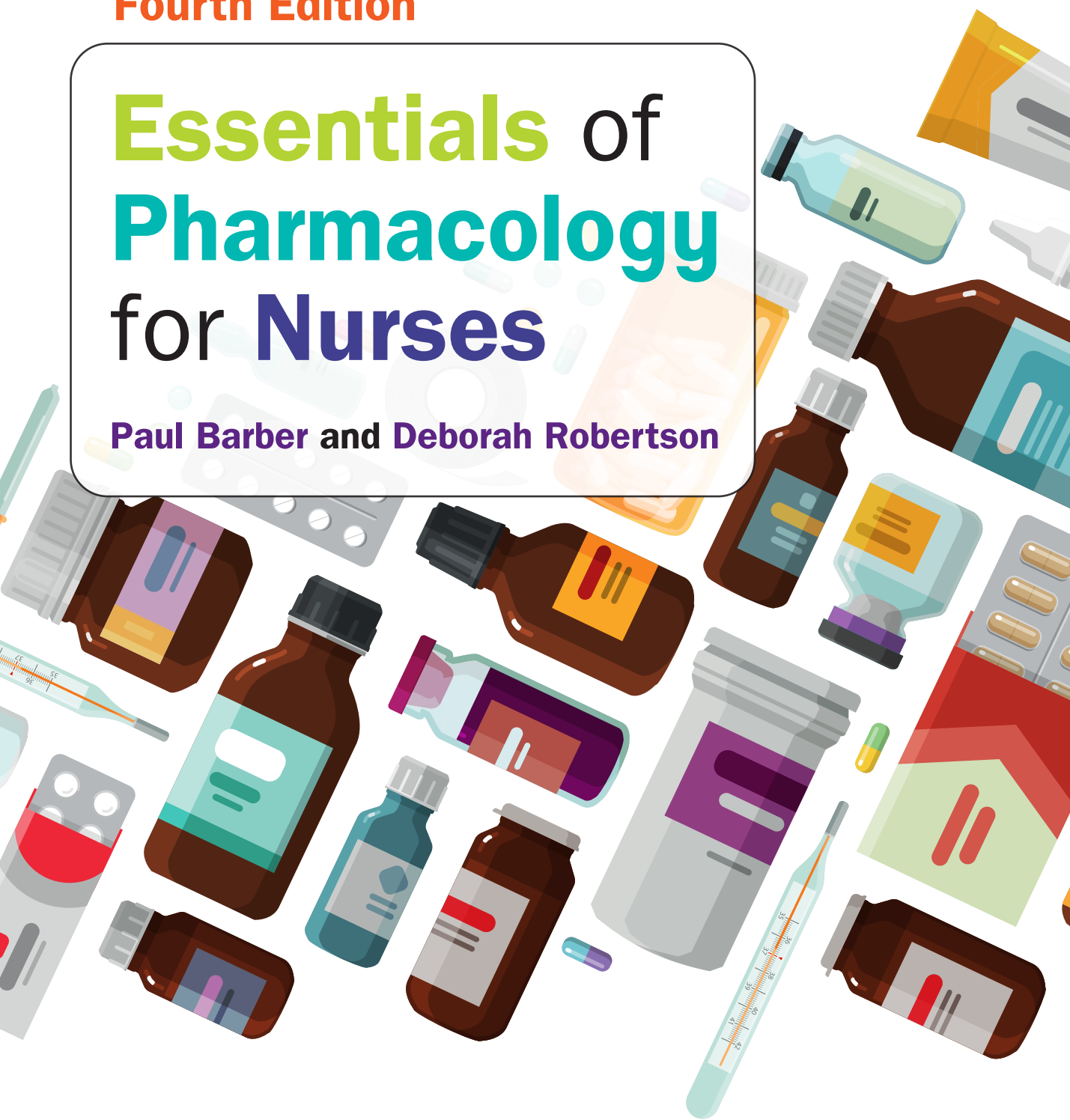
Includes 120 calculation tests and 130 MCQs!

Fourth Edition

Essentials of Pharmacology for Nurses

Paul Barber and Deborah Robertson



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Praise for this book

Overall, this book is an excellent resource for healthcare students that will support their learning throughout their training and beyond. It covers fundamental concepts of how the major classes of medications exert their therapeutic effect, but also how side effects and adverse reactions can occur. Chapters on legal aspects of medication administration and drug calculations enhance this usefulness of this book – all of which are supported by example questions, calculations and clinical 'tips'. This book has been fully updated to reflect the 2018 NMC standards and as such provides a one-stop shop for any students studying safe administration of medications.

Dr Andy Powell, Physiology Lead for Nursing, Birmingham City University

The outlay of the chapters is easily navigated and the level of the knowledge that the book starts at is at a basic level enough for any student nurse from year 1-3 to start with and builds in complexity. They are in lovely bite-size chunks that are easy to read and easily understood. The 10 MCQ's at the end of a chapter are a very useful method of chapter consolidation and the case studies further reinforce learning.

Georgina Cox, Senior Lecturer in Adult Health, Middlesex University

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About the authors

Paul Barber (MSc Practitioner Research, BSc (Hons) Nursing, Dip N (Lond), Cert Ed, RNT, SRN, RMN) commenced his nursing career in 1974 as a cadet nurse. He completed both his Registered Mental Nurse and State Registered Nurse training. Paul spent his early career in surgery, high dependency, and accident and emergency, and then progressed to become manager of a small surgical unit. Paul commenced a teaching career in October 1988 and has held a variety of positions in education from senior lecturer to head of an educational centre. Paul has now retired from full-time teaching as a senior lecturer.

Deborah Robertson joined the School of Health & Society at the University of Salford in March 2018. Prior to that she was in nurse education in the Faculty of Health and Social Care at the University of Chester (starting in 2004). Deborah is an RGN but also holds a BSc (Hons) and PhD in Pharmacology. She teaches on the Non-Medical Prescribing Course where she uses her expertise in pharmacology. Deborah also inputs heavily into the pre-registration nursing curriculum and teaching around anatomy, physiology, pharmacology and medicines management as well as being involved in postgraduate research and education.

Acknowledgements

The authors would like to acknowledge the contributions of Dr. Alexander Robertson, General Practitioner, to some of the clinical therapeutic aspects of Chapters 4–13.

List of abbreviations

5-HT	5-hydroxytryptamine
AAA	abdominal aortic aneurysm
ABCDE	airway, breathing, circulation, disability, exposure
ACE	angiotensin-converting enzyme
ACS	acute coronary syndromes
ADE	adverse drug event
ADHD	attention deficit hyperactivity disorder
ADR	adverse drug reaction
AED	anti-epileptic drug
AF	atrial fibrillation
AIDS	acquired immunodeficiency syndrome
ARB	angiotensin II receptor blocker
BBB	blood–brain barrier
BHF	British Heart Foundation
BNF	British National Formulary
BP	blood pressure
BZD	benzodiazepine
CCB	calcium channel blocker
CDAO	controlled drug accountable officer
CD/LD	carbidopa/levodopa
CHD	coronary heart disease
CMP	clinical management plan
COPD	chronic obstructive pulmonary disease
COX	cyclo-oxygenase
CR	controlled release
CSF	cerebrospinal fluid
CSM	Committee on Safety of Medicines
CTZ	chemoreceptor trigger zone
DA	dopamine
DH	Department of Health
DKA	diabetic ketoacidosis
DM	diabetes mellitus
DMARD	disease-modifying anti-rheumatoid drug
DNA	deoxyribonucleic acid
DOAC	direct acting anticoagulant
DVT	deep vein thrombosis
EMLA	eutectic mixture of local anaesthetics
EPSE	extra-pyramidal side-effect
g	gram
GABA	gamma-aminobutyric acid
$GABA_A$	GABA receptor subtype A
GI	gastrointestinal
GP	general practitioner
GTN	glyceryl trinitrate
HIV	human immunodeficiency virus
H-receptor	histamine receptor
IDDM	insulin-dependent diabetes mellitus
IM	intramuscular
INR	international normalized ratio
IV	intravenous
kg	kilogram
LABA	long-acting beta 2 agonist
LAMA	long-acting muscarinic antagonist
LD	learning disability
MAO-B	monoamine oxidase B
MAOI	monoamine oxidase inhibitor
mcg	microgram
MDI	metered dose inhaler
mg	milligram
mg/kg/day	milligrams per kilogram per day
MHRA	Medicines and Healthcare Products Regulatory Agency
MI	Myocardial infarction
mL	millilitre
NA	noradrenaline
NARI	noradrenaline reuptake inhibitor
NG	nasogastric
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIDDM	non-insulin-dependent diabetes mellitus
NMC	Nursing and Midwifery Council
NPSA	National Patient Safety Agency

NRM	nucleus raphe magnus
NSAID	non-steroidal anti-inflammatory drug
NSTEMI	non-ST-segment elevation myocardial infarction
OCD	obsessive-compulsive disorder
OTC	over the counter
PABA	para-amino benzoate/para-aminobenzoic acid
PAG	periaqueductal grey
PDE	phosphodiesterase
PEG	percutaneous endoscopic gastrostomy
PEP	post-exposure prophylaxis
PGD	Patient Group Direction
PPI	proton pump inhibitor
PrEP	pre-exposure prophylaxis
prn	*pro re nata*
PTSD	post-traumatic stress disorder
RIMA	reversible inhibitor of monoamine oxidase-A
RNA	ribonucleic acid
SC	subcutaneous
SI	International System of Units
SNRI	serotonin–norepinephrine re-uptake inhibitor
SSRI	selective serotonin re-uptake inhibitor
STI	sexually transmitted infection
STEMI	ST-segment elevation myocardial infarction
TB	tuberculosis
TCA	tricyclic antidepressant
TTR	time in the therapeutic range
TXA	thromboxane
VTE	venous thromboembolism
WHO	World Health Organization

Introduction

This book is aimed largely at nurses in training, but given the level of detail in many areas, qualified nurses will find it useful throughout their careers. It is important to understand that nurses need pharmacology education. This has been clearly outlined in the Pre-Registration Nursing Education Standards set out by the Nursing and Midwifery Council (NMC) in 2018. Nurses require pharmacology education so that they can inform patients about any medications prescribed, the need for those medications and the consequences of both taking and not taking them. The relevant sections of the Standards are outlined in the introductory chapters of the book, but it is important to remember that pharmacological knowledge standards apply throughout this text. Where there are specific standards relating to specific areas of education, these are introduced in the relevant chapters. You should remember that as a student or as a qualified nurse, your adherence to the Code (NMC 2015) includes medicines management.

Learning about medicines is a fundamental part of the nurse's role, whatever the field of nursing you decide to choose as a career pathway. This book is written to engage you in the subjects of pharmacology and calculation of drugs and for you to be able to apply these principles in your practice. First, you will notice that not all drugs are listed. This book is an essentials text and its aim is to introduce you to the most common areas of nursing practice regarding medications. It will focus on some of the major drug groups to outline the importance of your pharmacological knowledge without overwhelming you. Each of the chapters that discusses major drug groups has been enhanced by the inclusion of relevant aspects of physiology to help you understand drug action.

There is some application of drug calculation in all relevant chapters. Some calculations are simple (as they would be in practice) and some are more complicated due to the nature of the drugs. We wanted the calculations to reflect each of the chapter's contents and give you a sense of what might be expected in practice. Very detailed and complex calculations are not included here, as these are covered in other texts, some of which you will find in the recommended reading section at the end of each chapter.

A further feature of the book is the inclusion of case studies. At the end of each chapter there are a number of scenarios, covering relevant fields of practice.

Where possible we have also tried to focus the pharmacology on nursing practice. You will notice that in each chapter there are several boxes entitled 'Clinical tip'. These are designed to increase your understanding of the importance of pharmacology within nursing. They should also assist you in reflecting on your everyday practice in medicines management.

Finally, we have included 10 multiple-choice questions at the end of most chapters. All the questions are based on information included in the chapter, so there are no trick questions. We thought the idea of evaluating what you have gained in knowledge from reading each chapter was important and we hope you enjoy getting them all right! We know how important it is to students to evaluate their learning as they proceed.

References

Nursing and Midwifery Council (NMC) (2015) *The Code: Professional Standards of Practice and Behaviour for Nurses, Midwives and Nursing Associates*. London: NMC. Updated 2018.

Nursing and Midwifery Council (NMC) (2018) *Standards of Proficiency for Registered Nurses*. London: NMC.

Pharmacodynamics and pharmacokinetics

1

Chapter contents

Learning objectives

After studying this chapter, you should be able to:

- Understand what is meant by pharmacokinetics and pharmacodynamics.
- Describe aspects of absorption, distribution, metabolism and excretion of a drug.
- List the principal routes of drug administration.
- Name the phases in hepatic metabolism.
- Describe what is meant by the term ‘cell receptor’.
- Understand the concept of receptor occupancy.
- Outline how drugs affect the body.
- Give three examples of different cell receptors.
- Outline what is meant by ‘ion channel’.
- Describe the term ‘first pass metabolism’.
- Understand at a basic level the term ‘affinity’.

Introduction

Part of the nurse's role, alongside the pharmacist, is to ensure that medicines are administered appropriately. The Nursing and Midwifery Council's Standards for Pre- Registration Nursing Programmes published in May 2018 state that education must

> *ensure that field-specific content in relation to the law, safeguarding, consent, pharmacology and medicines administration and optimisation is included for entry to the register in one or more fields of nursing practice*

This is backed up by the Standards of Proficiency for Registered Nurses:

> Platform 3: Assessing needs and planning care
> *3.2 demonstrate and apply knowledge of body systems and homeostasis, human anatomy and physiology, biology, genomics, pharmacology and social and behavioural sciences when undertaking full and accurate person-centred nursing assessments and developing appropriate care plans*
> *3.3 demonstrate and apply knowledge of all commonly encountered mental, physical, behavioural and cognitive health conditions, medication usage and treatments when undertaking full and accurate assessments of nursing care needs and when developing, prioritising and reviewing person-centred care plans*

and

> Platform 4: Providing and evaluating care
> *4.5 demonstrate the knowledge and skills required to support people with commonly encountered physical health conditions, their medication usage and treatments, and act as a role model for others in providing high quality nursing interventions when meeting people's needs*
> *4.14 understand the principles of safe and effective administration and optimisation of medicines in accordance with local and national policies and demonstrate proficiency and accuracy when calculating dosages of prescribed medicines*
> *4.15 demonstrate knowledge of pharmacology and the ability to recognise the effects of medicines, allergies, drug sensitivities, side effects, contraindications, incompatibilities, adverse reactions, prescribing errors and the impact of polypharmacy and over the counter medication usage*
> *4.16 demonstrate knowledge of how prescriptions can be generated, the role of generic, unlicensed, and off-label prescribing and an understanding of the potential risks associated with these approaches to prescribing*
> *4.17 apply knowledge of pharmacology to the care of people, demonstrating the ability to progress to a prescribing qualification following registration*

That is why it is essential that the nurse has a good knowledge and understanding of pharmacology and the relevant calculations in terms of patient care. Pharmacology is the study of drugs (chemicals) and their interactions with the body. The term is derived from the Greek *pharmakon*, which can mean both 'remedy' and 'poison'. In modern medical practice, drugs are being used more and more to treat and manage disease, so it is vital that nurses understand the basic mechanisms of drug action and reaction.

The aim of this chapter is to introduce the basic principles of pharmacology in relation to nursing practice. The chapter will give you an appreciation of *pharmacodynamics* and *pharmacokinetics*. It will identify the main targets for drug action and allow you to develop an understanding of drug absorption, distribution, metabolism and excretion.

Put quite simply:

- *pharmacodynamics* is the effect that drugs have on the body; while
- *pharmacokinetics* is the study of the way in which drugs move through the body during absorption, distribution, metabolism and excretion.

For drugs to produce their effects, they must interact with the body. This can happen in many ways and depends on the properties of the drug and will be discussed later in this chapter. Pharmacokinetics influences decisions over the route of administration. The processes that occur after drug administration can be broken down into four distinct areas (known as ADME):

- **A** Absorption of the drug
- **D** Distribution of the drug molecules
- **M** Metabolism of the parent drug
- **E** Excretion or elimination of the drug and its metabolites

Absorption

Before a drug can begin to exert any effect on the body, it has to be absorbed into the body systems. Of the many factors that can affect the absorption process, the most important is the route of administration (see Box 1.1). Many patients require the administration of their medication to be tailored to their particular medical condition or the medication that they have been prescribed. It is thus important that nurses understand the implications attached to choosing the route of administration of drugs based on their absorption, as it can impact on the patient's ability or desire to take their medication.

Box 1.1 Principal routes of drug administration

Route	Advantages	Disadvantages
Enteral routes		
Oral	Convenient, non-sterile, good absorption for most drugs	Gastrointestinal (GI) irritation, potential for interactions, first pass destruction, inactivated by acids, variable absorption
Sublingual/buccal	Avoids first pass (see p. 8), avoids gastric acid	Few preparations suitable
Rectal	Avoids first pass, avoids gastric acid	Less dignified for the patient
Parenteral (refers to IV, IM and SC) routes		
Intravenous (IV)	Rapid action, complete availability	Increased drug levels to heart, must be sterile, risk of sepsis and embolism
Intramuscular (IM)	Rapid absorption	Painful, risk of tissue damage
Subcutaneous (SC)	Good for slower absorption	Absorption variable
Inhaled (lungs)	Large absorption area, good for topical use	Few disadvantages
Other routes include intra-arterial, intrasternal, intrathecal, intra-articular, intraperitoneal, intraventricular, nasal, bronchial, vaginal, skin and conjunctiva		

The other factors that can affect the rate and reliability of drug absorption fall into two categories: physiological and physico-chemical. *Physiological* factors relate to human physiological functions:

- **Blood flow to absorbing site.** The better the blood supply to the area, the greater the rate of absorption. Therefore, if a person has a good circulation they will have the ability to absorb the drug well.
- **Total surface area for absorption.** The greater the surface area, the greater the rate of absorption. The intestine has a very large surface area, making it an ideal target for drug absorption. This is why most drugs are given orally when possible.
- **Time of arrival and contact time at absorption site.** The longer the drug is in contact with the absorbing surface, the greater the rate of absorption. Therefore, if a person is suffering from diarrhoea, the chances of a drug given orally being absorbed completely are lowered and other means of administration must be considered.

Physico-chemical factors relate to the chemical make-up of the drug in relation to human physiological functions:

- **Solubility.** How soluble is the drug in body fluids? As the body consists of a large amount of water, drugs can dissolve readily. However, certain drugs do not dissolve into small enough particles to ensure their rapid absorption.
- **Chemical stability.** Will it break down readily?
- **Lipid to water partition coefficient.** Is the drug more fat soluble than water soluble? This is an important thing to consider. As our cells are made up of a phospho-lipid layer, any drug that can dissolve well in lipids will pass through the tissues far more rapidly. Examples of drugs that are highly lipid soluble are anaesthetic agents and benzodiazepines.
- **Degree of ionization.** Some drugs are both weak acids and weak bases (alkalis). These drugs tend to disassociate when administered. This means that some of the drug remains active and some is inactive. Often this depends on the pH of the solution (i.e. its acidity or alkalinity) in which the drug is being dissolved. For example, a weak acid does not disassociate as much if dissolved in an acid environment. This means that the drug can cross membranes in a more active form than if it had been dissolved in a neutral or base solution.

Clinical tip

It is very important that the patient takes the medicine as directed by the prescriber to obtain the best therapeutic value from it. As a nurse, therefore, you need to understand the mechanics of absorption so that you can explain to the patient why it is important that a drug is taken in the correct way.

Distribution

Once a drug has been administered and absorbed, it must be distributed to its site of action. For some drugs that site is known, and such drugs are available to give locally or topically. All other drugs need to be distributed throughout the body.

There are four main elements to this:

1. **Distribution into body fluids.** These are mainly plasma, interstitial fluid and intracellular fluid. Molecular targets for drugs are found in these areas.
2. **Uptake into body tissues/organs.** Specific tissues take up some drugs – for example, iodine and thyroid gland.
3. **Extent of plasma protein binding.** Plasma proteins such as albumin can bind drug molecules. This varies widely among drugs. Drugs bound to plasma proteins are pharmacologically inert; only free drugs are active.

Some drugs do not bind (e.g. caffeine) whereas others are highly bound (e.g. warfarin, which is 99% bound to plasma proteins). Some drugs can displace others from their binding sites on the plasma proteins – for example, phenylbutazone can displace warfarin from plasma proteins. This is an important consideration for drugs that have this effect.

4 **Passage through barriers.** The two main examples are the placenta and the blood–brain barrier (BBB). Drugs must be highly lipid soluble to pass across these barriers. If not, they may not be able to reach their site of action.

Clinical tip

As a nurse in practice it is important you have knowledge about drugs such as warfarin so that you can be aware of the symptoms which the patient may display if they become toxic with the drug.

The factors that affect drug distribution are taken into consideration by drug companies when developing and formulating medications. While these factors are of interest, the nurse's main role in monitoring drug distribution is to monitor the onset of the effect of, or the response to, the medication. If analgesia is given and the patient reports reduced or relieved pain, the drug has been distributed to its target site.

Biotransformation

The biotransformation of drugs, which is the process of turning the parent drug into different compounds called metabolites, occurs mainly in the liver (hence the term *hepatic metabolism*). Drug metabolites may have greater, lesser or similar pharmacological activity compared with the parent drug. It may also have a different activity. Some drugs are called *pro-drugs* – that is, the drug itself is pharmacologically inactive until it is metabolized by the liver to its active form. A good example is codeine, which is metabolized to morphine by the body. The metabolite is more polar (i.e. chemically charged) than the parent drug and therefore is more readily excreted by the kidney. Drug metabolism can influence strength of dose and frequency of dosing. Drugs that are metabolized quickly have a short duration of action and need to be administered more often (two to four times daily). Drugs that are metabolized slowly have a longer duration of action and may only need to be given on a once-daily basis.

Phase	Process
Phase I metabolism	Oxidation
	Reduction
	Hydrolysis
Phase II metabolism	Conjugation

Table 1.1 Metabolic phases and processes

Hepatic metabolism

The terms shown in Table 1.1 are different chemical reactions that change the properties of drugs to facilitate their removal from the body by excretion. Most drugs undergo phase I oxidation followed by phase II conjugation.

Clinical tip

It is important as a nurse to recognize that babies, particularly those less than 6 months old, do not have a mature liver and therefore drugs must be given with great caution. Exercise caution also when giving drugs to patients who have diseases that have an impact on liver function – for example, congestive heart failure – as their ability to metabolize a given drug will be greatly impaired.

Excretion

Once a drug has had its desired effect, it needs to be excreted by the body. The principles of excretion include renal elimination and clearance, secretion into bile for faecal elimination and entero-hepatic recirculation. As previously outlined, some drug metabolites can also have pharmacological effects. If these compounds were not to be eliminated, they would accumulate in the bloodstream and could cause toxic and unwanted effects.

The main means of renal elimination is by active glomerular filtration. This is where ionized drugs are actively secreted into the proximal tubule. These ionized compounds are actively excreted by the kidney and are 'pushed' out into urine. A more passive form of drug compound movement occurs in the distal tubule of the kidney. Here there is passive reabsorption and excretion of drug molecules and metabolites according to a concentration gradient. Molecules move from a high concentration to a lower concentration by diffusion. This applies to un-ionized compounds (drugs without charge) and prevents the entire dose of a drug being excreted at once. This helps to maintain circulating plasma levels to allow the drug effect to continue until the next dose is taken.

Clinical tip

People who have renal impairment may require alterations in dose to achieve a therapeutic level. Older patients also need special consideration, as kidney performance declines in the elderly, resulting in a lower glomerular filtration rate.

Excretion into bile is another way of eliminating drug molecules and metabolites. The liver produces bile, which is secreted into the bowel (and some is stored in the gall bladder) and can contain drug metabolites. These are secreted from the liver into bile and into the gut for faecal elimination. As in renal excretion, not all of the drug and its metabolites are eliminated at once. Some drugs undergo entero-hepatic recirculation. This is where some of the drug is reabsorbed from the gut, back into the bloodstream and presented to the liver for further metabolism. This can help to maintain circulating levels of active molecules to prolong a drug's effect until the next dose. One example of a drug that undergoes this form of elimination is the combined oral contraceptive pill.

General and molecular aspects of pharmacodynamics

It is important that nurses involved in medicines management are aware of the sites of action for many commonly used drugs. Drugs exert their effects at molecular (chemical) targets, of which there are many. Some of the most common are detailed below.

Receptors

The plasma membrane of a human cell is selectively permeable, in that it helps control what moves in and out of the cell. The cell membrane consists of a thin structured bilayer of phospholipids and protein molecules. The surfaces of plasma membranes are generally studded with proteins that perform different functions, such as the reception of nutrients. In biochemistry, these protein molecules are referred to as *receptors*. Molecules that bind to these receptors are called *ligands*. Examples of ligands are neurotransmitters, hormones and drugs.

Many drugs exert their effect through interaction with receptors. Examples include:

- ligand-gated ion channels (ionotropic receptors) such as the $GABA_A$ receptor and the $5\text{-}HT_3$ receptor;
- G-protein coupled receptors such as adrenoceptors and prostaglandin receptors;
- kinase-linked receptors such as the insulin receptor and the receptor for growth hormone;
- nuclear receptors such as the thyroid receptor and oestrogens.

In 1. we see a drug blocking the permeation of the actual ion channel itself.

In 2. we see a drug binding to the channel but not sitting within the channel itself.

Figure 1.1 Drug binding at ion channels

Ion channels

Ion channels, such as those for sodium, calcium and potassium, provide receptors which drugs can interact with. Drug actions at ion channels can take two forms (see Figure 1.1). The first form are known as *channel blockers*, whereby the drug blocks permeation of the channel; the second form are *channel modulators*, whereby the drug binds to a receptor site within the ion channel and modulates permeation of the channel. This can happen by the drug altering the channel's response to its normal mediator.

Enzymes

Enzymes are biological catalysts that increase the rate of chemical reactions in the body. They are integral to many normal physiological functions. Many drugs target enzymes to prevent them from carrying out their normal function – for example, ibuprofen acts on cyclooxygenase enzymes, acting to reduce inflammation. In this example, the substrate arachidonic acid is acted upon by the cyclooxygenase enzyme to produce prostaglandins. Targeting this enzyme with a drug such as ibuprofen reduces the production of the inflammatory agent.

Transport systems

These are also known as carrier molecule interactions. In some transmitter systems, there is normal physiological recycling of the transmitters, such as serotonin. After the release of serotonin from a neurone, it is taken back up by that same neurone using a serotonin-selective re-uptake system. The drug fluoxetine blocks the uptake transporter for serotonin as its mode of action. This results in an increased level of serotonin in the neuronal synapse. This mechanism has an onward effect that facilitates an increase in mood and makes fluoxetine and drugs like it good antidepressants.

Drug action

The time to the onset of drug action involves delivery of the drug to its site of action. This is largely controlled by the:

- route of administration;
- rate of absorption;
- manner of distribution.

These are important considerations, as often we want the drug to have its effect within a certain time frame. We can speed up the time to the onset of drug action in many ways. If the drug is administered orally, we can use liquid or dispersible formulations instead of regular tablets. If drug action is needed more quickly, we can use the intramuscular (IM) or intravenous (IV) route as necessary. For example, if a patient requires pain relief following myocardial infarction, they would be given intravenous morphine rather than an oral preparation.

It is also possible to delay drug onset or prolong the effect by using enteric-coated or slow release preparations orally, or by using the transdermal or subcutaneous (SC) route. For example, people suffering with chronic pain from conditions such as rheumatoid arthritis may be given analgesia in the form of a transdermal patch. This is much preferred by the patient, as it decreases the amount of oral analgesia required.

The duration of drug effect relates to the time it takes for the drug to be removed from its site of action. This is largely controlled by the:

- rate of hepatic metabolism;
- rate of renal excretion.

It is important to know how long a drug will remain effective. Drug companies undertake extensive studies to determine this information. They use the data they obtain to decide upon

dosing schedules. It is vital that nurses know the normal dosing schedules for the drugs they are administering (this can easily be found in the British National Formulary, or BNF) so that the correct regimen is implemented. Drugs need to be given more than once to have continued effect. Some drugs need to be given daily, while others need to be given two, three or four times per day to maintain their effective action.

First pass metabolism

Some drugs undergo destruction by *first pass metabolism*. When absorbed through the stomach after oral administration, a drug enters blood vessels that lead directly to the liver. We call this the *portal circulation*. This means that drugs which are largely destroyed by liver enzyme systems will not enter the general systemic circulation. An example of such a drug is glyceryl trinitrate (GTN), which is metabolized completely by the liver at this stage. Therefore, you will find GTN being given via routes other than orally.

The concept of affinity

Drugs have what is termed an *affinity* for their receptors, or chemical targets. This is a measure of how well a drug can bind to its chemical target. The tighter the bond, the better the drug action. Some drugs have a higher affinity for their chemical targets than others. Those with a higher affinity will bind first, in preference to any other drug molecule present. Some drugs have a higher affinity for their targets than even the normal physiological molecule. This can be very useful in drug action, especially where the normal molecule is abundant and is the cause of the problem or symptom the patient is experiencing. Higher affinity means that even small amounts of the drug will bind preferentially.

Agonistic and antagonistic drug action

Drugs can either be *agonists* or *antagonists* at their target sites. This is best explained using receptors as an example (see Figure 1.2). When agonists or antagonists bind to receptors, they are said to *occupy* the receptor site. The amount of drug occupying the receptor site relates to the magnitude of response to the drug itself. In simple terms, the more of an agonist drug occupying a receptor, the greater the response.

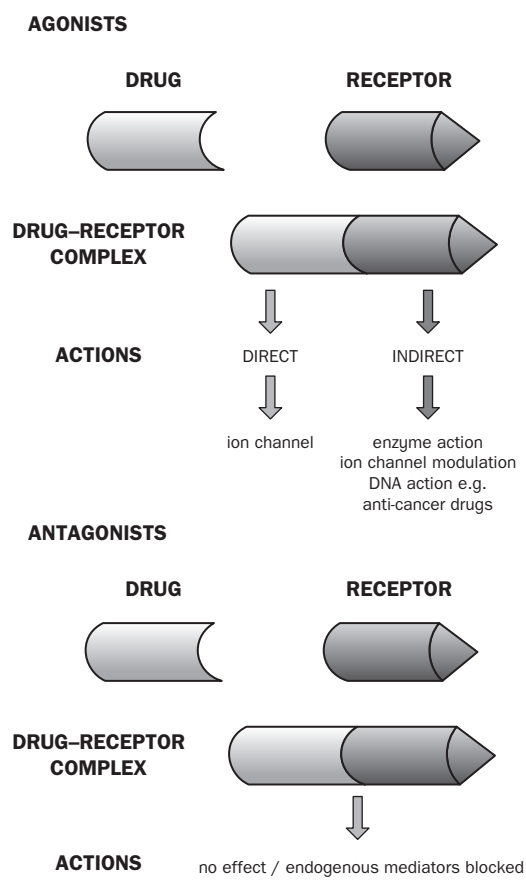

Figure 1.2 Basic receptor theory

Agonists are drugs that bind to their targets and form a drug–receptor complex. Agonists activate the receptors to produce a response (known as *full agonists)* and have what is termed *positive efficacy*. Antagonists are drugs that bind to their targets and form a drug–receptor complex, but without causing activation or response. They can block the receptor to its endogenous activator, thereby blocking normal function. They have what is termed *zero efficacy*. Receptor occupancy by antagonists is important if the drug is a competitive antagonist, i.e. it competes for occupancy with another drug or with the receptor's normal mediator. The amount of drug occupying will determine any response.