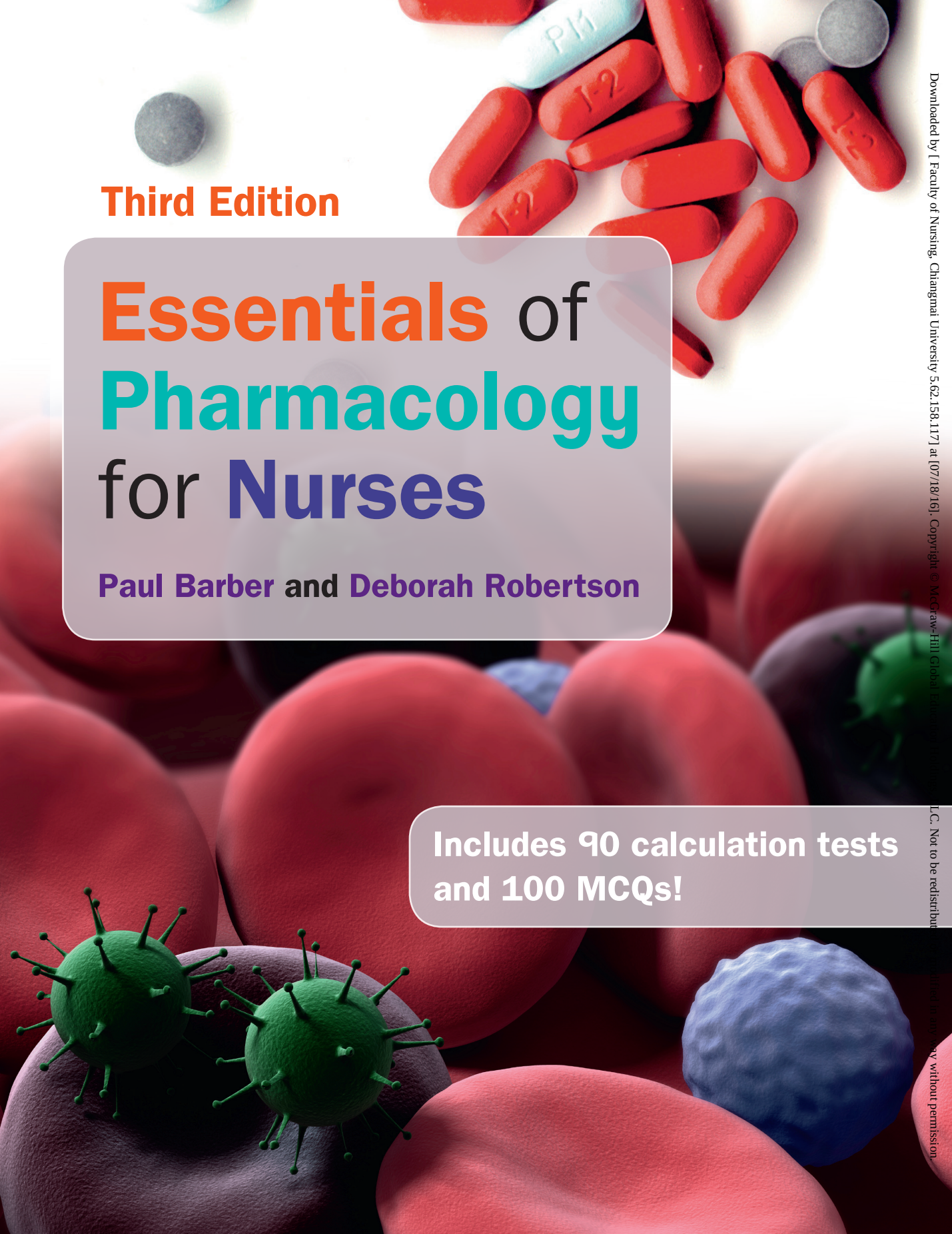


Third Edition

Essentials of Pharmacology for Nurses

Paul Barber and Deborah Robertson

Includes 90 calculation tests and 100 MCQs!

Essentials of Pharmacology for Nurses

Essentials of Pharmacology for Nurses

Third Edition

Paul Barber and Deborah Robertson

Mc Graw Hill Education
Open University Press

Open University Press
McGraw-Hill Education
McGraw-Hill House
Shoppenhangers Road
Maidenhead
Berkshire
England
SL6 2QL

email: enquiries@openup.co.uk
world wide web: www.openup.co.uk

and Two Penn Plaza, New York, NY 10121-2289, USA

First published 2009
Second edition published 2012
First published in this third edition 2015

A catalogue record of this book is available from the British Library

ISBN-13: 978-0-33-526196-3
ISBN-10: 0-33-526196-5
eISBN: 978-0-33-526197-0

Library of Congress Cataloging-in-Publication Data
CIP data applied for

Typeset by Aptara, Inc.

Praise for this book

"This latest edition of a key textbook on pharmacology for nurses has moved forward from previous editions by becoming stronger by the inclusion of a greater scope of material so maintaining its place as an essential pharmacology book for current and forthcoming nursing students in all clinical practice fields to give them a strong evidence base for their studies and clinical practice. The addition of a chapter on drug calculations is an essential step forward in this edition for all students as this is a key component within all current nursing degree programmes. The continued use of case studies and clinical tips makes learning fun both as an individual but also in small learning groups of students.

It follows a clear pathway for learning: it is easy to read, is clearly written and shows the importance of aspects of pharmacology within the work of a nurse."

Keith Booles, Senior Nurse Lecturer/Module Leader, Faculty of Health Sciences, Staffordshire University, UK

Brief table of contents

Detailed table of contents

About the authors

Paul Barber

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's current role is that of senior lecturer and he teaches both pre- and post-registration nurses.

Dr Deborah Robertson

Debbie Robertson joined the faculty of Health and Social Care at University of Chester in 2004, where she is currently employed as a senior lecturer. Debbie is an RGN but also holds a BSc (Hons) and PhD in Pharmacology. She is programme leader for the Non-Medical Prescribing Course where she uses her expertise in pharmacology. Debbie also contributes to other modules within the faculty including Research in Clinical Practice, Contemporary Aspects of Healthcare Provision and inputs into the pre-registration nursing curriculum. Her publications to date are derived from her time as a research scientist where she investigated the effects of stress in depression. Her current research interests involve e-learning and the delivery of the Non-Medical Prescribing course.

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
ADR	adverse drug reaction
AIDS	acquired immuno-deficiency syndrome
BBB	blood-brain barrier
BNF	British National Formulary
BSE	bovine spongiform encephalopathy
BZD	benzodiazepine
CD/LD	carbidopa/levodopa
CMP	clinical management plan
COAD	chronic obstructive airways disease
COPD	chronic obstructive pulmonary disease
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 mg/kg/day (milligrams per kilogram per day)
DMARD	disease-modifying antirheumatoid drug
DNA	deoxyribonucleic acid
EMLA	eutectic mixture of local anaesthetics
EPSE	extra-pyramidal side-effect
g	gram
GABA	gamma-aminobutyric acid
GABA-A	GABA receptor sub type 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
iu	international unit
IV	intravenous
kg	kilogram
LABA	long-acting beta 2 agonist
LAMA	long-acting muscarinic antagonist
MAO	monoamine oxidase
MAOI	monoamine oxidase inhibitor
mcg	microgram
MDI	metered dose inhaler
mg	milligram
mg/kg/day	milligrams per kilogram per day
MHRA	Medicines & Healthcare Products Regulatory Agency
ml	millilitre
NA	noradrenaline
NARI	noradrenaline reuptake inhibitor
NG	nasogastric
NHS	National Health Service
NICE	National Institute for Health and Clinical 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-aminobenzioc acid
PAG	periaqueductal grey
PDE	phosphodiesterase
PEG	percutaneous endoscopic gastrostomy

PGD	Patient Group Direction
PPI	proton pump inhibitor
prn	*pro re nata*
PTSD	post-traumatic stress disorder
RIMA	reversible inhibitor of monamine oxidase-A
RNA	ribonucleic acid
SC	subcutaneous
SI	International System of Units
SNRI	serotonin–norepinephrine reuptake inhibitor
SSRI	selective serotonin re-uptake inhibitor
STD	sexually transmitted disease
STEMI	ST-segment elevation myocardial infarction
TB	tuberculosis
TCA	tricyclic antidepressant
TTR	time in the therapeutic range
VTE	venous thromboembolism
WHO	World Health Organization

Introduction

As this book is primarily for undergraduate nursing students it seems fitting that we let them begin the introduction.

> 'Nurses need pharmacology education so they can inform the patient of what they're giving, why they're giving it and what it's going to do to them, and what to look out for.'
>
> 'The patient needs to know what they're taking, why they're taking it and when to take it, they need to know what it's for precisely, and its precise function in their life so that they take it seriously.'
>
> 'Pharmacology education will be important in the future because the nurse's role is expanding, taking more away from junior doctors. Nurse prescribing is expanding in the community, and is probably going to happen more in hospitals.'
>
> 'I think I had about two separate sessions that lasted about an hour. It was definitely not enough, we complained about it several times actually, that we should have had more pharmacology sessions. I'm sure they could have fitted a few more pharmacology sessions in.'

Where then do we start with the process of education? It is our belief that the key to education is through a process of motivation. We both remember, as students, sitting and trying to come to terms with scientific language and almost falling asleep in an attempt to unravel the intricacies of mathematical formulae and biochemical presentations of molecular function.

Learning about medicines is a fundamental part of the nurse's role, whichever field of nursing you decide to choose as a career pathway. This book is written in an attempt to bring to life and engage you in the subjects of pharmacology and calculation of drugs. First, you will notice that not all drugs are listed. Indeed, we have tried to focus on some of the major drug groups so as to give you a taste of how interesting the subject can be, without initially overwhelming you. Each of the chapters that discusses major drug groups has been enhanced by the inclusion of relevant aspects of physiology.

When putting the initial idea for the book together, we decided that it should include both aspects of pharmacology and drug calculations. However, the book does not contain detailed types of formulae – rather it gives you a basic structure on which to build. We wanted the calculations to reflect each of the chapter's contents and give you a sense of what might be expected in practice. You will not find many examples of the giving of intravenous fluids, because we felt this to be well covered in other texts, some of which you will find in the recommended reading section at the end of each chapter. These sections deliberately repeat the key texts in this field for your ease of reference, and in addition include works specific to the chapter's topic.

A further feature of the book is the inclusion of case studies. At the end of each chapter you will find two, three or four scenarios (although the chapters on chronic conditions are treated differently). Unlike most other books, we have included examples of some of the issues that you should consider in analysing each case.

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 for each of the chapters in the book;

those questions relating to Chapters 8–10 are in Chapter 10. 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!

Well dear student, it is now time to embark on what we hope will be a fascinating journey. We hope this journey will assist you with your initial learning needs, inspire you to ask more questions, and also motivate you to move on to more detailed texts. As we said earlier, motivation is the key to education. You are now our judge and jury. Enjoy!

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 the need to ensure that medicines are administered appropriately. 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 we use drugs 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 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. This absorption process can be affected by many things but the main factor relating to absorption is the route of administration (see Box 1.1).

It is important that nurses understand the implications attached to choosing routes of administration of drugs based on their absorption. Many patients may need to have their medication administration tailored to their particular medical condition or the medication which they are prescribed, and this is an important factor to consider as it can impact on the patient's ability or desire to take their medication.

Other factors controlling the rate and reliability of drug absorption can be said to be *physiological* or *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 you will find that most drugs are given orally where 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. This is why 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 function:

- **Solubility.** How soluble is the drug in body fluids? As the body is made up of a large amount

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. 9), 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		

of water, drugs can dissolve readily. However, certain drugs do not dissolve into small enough particles to ensure rapid absorption.

- **Chemical stability.** Will it break down readily?
- **Lipid to water partition coefficient.** Is it more fat soluble than water soluble? This is an important area to consider. As your cells are made up of a phospho-lipid layer, any drug that can dissolve well in lipids will pass through your tissues far more rapidly. Examples of drugs that are highly lipid soluble are anaesthetic agents and benzodiazepines.
- **Degree of ionization.** Some drugs are weak acids and weak bases (alkalis). These drugs tend to disassociate when given to a person.

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 in order to obtain the best therapeutic value from it. Therefore as a nurse it is important that you understand the mechanics of absorption so that you can explain to the patient the reason for the drug being taken in the correct way.

Distribution

Once drugs have been administered and absorbed, they have to be distributed to their 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) and some are highly bound (e.g. warfarin which is 99 per cent 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 which 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 which affect drug distribution are taken into consideration by drug companies when developing and formulating medications. While these factors are of interest, the nurse's role in monitoring drug distribution is mainly in monitoring 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

Biotransformation of drugs is the process of metabolizing the parent drug compound and occurs mainly in the liver (hence the term *hepatic metabolism*) to different compounds called metabolites. The drug metabolite may have decreased, increased or undergone no change in pharmacological activity compared to the parent drug. It may also have a different activity. Some drugs are what are termed *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 dose and frequency of dosing. Drugs which are metabolized quickly have a short duration of action and need to be administered more often (two, three or four times daily). Drugs which are metabolized slowly

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

Table 1.1 Metabolic phases and processes

can have a longer duration of action and may only need to be given on a once-daily basis.

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 may not have a mature liver and therefore drugs are given with great caution. Also, patients who have diseases which have an impact on liver function – for example, congestive heart failure – should be given drugs cautiously as their ability to metabolize a given drug will be greatly impaired.

Excretion

Once drugs have had their desired effect they need to be excreted by the body. 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 eliminated, they would accumulate in the bloodstream and could cause toxic and unwanted effects.

The main method 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 unionized 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 dosage alterations to achieve a therapeutic level. Older patients also need special consideration, as the kidney does not perform as well as we get older, resulting in a lower glomerular filtration rate.

Excretion into bile is another method of eliminating drug molecules and 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 entirely at once. Some drugs undergo enterohepatic recirculation. This is where some of the drug is reabsorbed from the gut, back into the bloodstream and represented to the liver for further metabolism. This can help to maintain circulating levels of active molecules to prolong drug effect until the next dose. An important example of a drug that undergoes this is the combined oral contraceptive pill.

General and molecular aspects

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. Below are some of the commonest.

Receptors

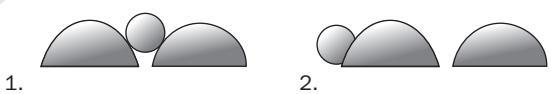
The plasma membrane of a human cell is selectively permeable in that it helps control what moves in and out of the cell. The cell membrane consists of a thin structured bilayer of phospholipids and protein molecules. The surfaces of plasma membranes are generally studded with proteins that perform different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

A large number of drugs, which are clinically effective, exert their action by interaction with receptors. Examples include:

- ligand-gated ion channels (ionotropic receptors) such as the $GABA_A$ receptor, which binds benzodiazepines;
- G-protein coupled receptors such as adrenoceptors;
- kinase-linked receptors such as the insulin receptor;
- nuclear receptors such as the thyroid receptor.

Ion channels

Ion channels 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, and the second 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.



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

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, Enalopril acts on angiotensin converting enzymes, thereby preventing an increase in blood pressure.

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 which facilitates an increase in mood and makes fluoxetine and drugs similar to 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:

- 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 given 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 transdermal or

subcutaneous (SC) routes. 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:

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

It is important to be aware of the duration a drug will have its effect for. Drug companies do 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 – 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 effective action.

First pass metabolism

Some drugs undergo destruction by *first pass metabolism*. When absorbed through the stomach after oral administration, the drugs enter blood vessels which go 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. This is why 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 causing 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

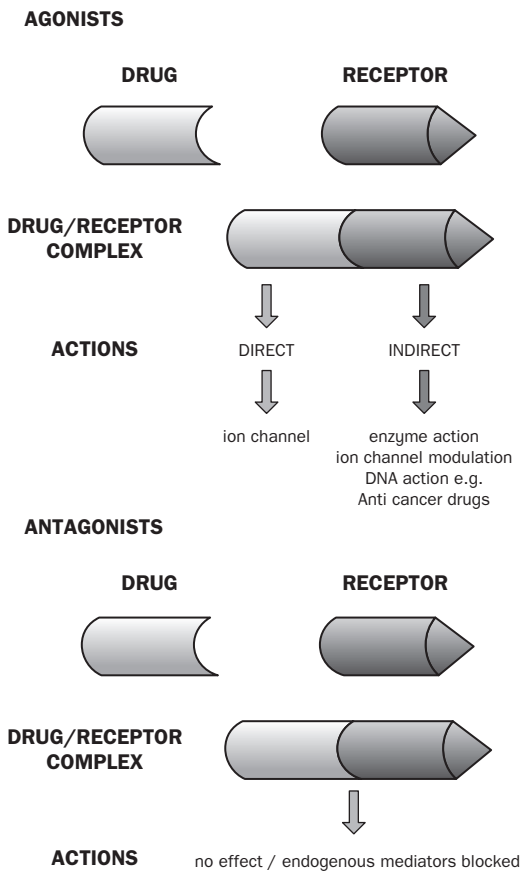


Figure 1.2 Basic receptor theory