Disease Management

A guide to clinical pharmacology

Third edition

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Pharmaceutical Press

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THIRD EDITION

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Preface

Our aim is to put pharmacology, which is being learnt or was learnt some time ago, into the context of clinical practice. We believe that this book will be of use to later-year pharmacy students who are encountering clinical pharmacy and pharmacology for the first time, and to pre-registration pharmacists who are putting their training into practice, and will be of general interest to pharmacists in practice. However, the prescribing role of other healthcare professions is likely to expand and we believe that *Disease Management* will also prove a useful resource for introducing and dealing with important issues associated with medicines management.

Disease Management has grown from a course in clinical pharmacy and pharmacology (Disease and the Goals of Treatment), with which we have been involved in the Master of Pharmacy course at the University of Nottingham. In that course, we have used a case-study based approach, coupled to summary lectures, to introduce important therapeutic areas. In doing this we have become aware of the value of a disease-based approach to learning. In *Disease Management* we have sought to build on the course by taking common diseases such as diabetes, hypertension, asthma, depression and peptic ulceration, and dealing with the therapeutic issues. The structure that we have adopted is to provide a brief outline of the disease characteristics and clinical features. We have generally worked on the basis that diagnosis is beyond the scope of this book but have provided clinical features, particularly in the context of alerting symptoms for referral. These are followed by brief accounts of the pharmacology of the agents used to manage the conditions. Where guidelines exist and are in widespread use, we have incorporated brief summaries. The reader is of course referred to the more detailed guidance available and should also recognise that there is currently a wealth of resources that provide clinical guidance, such as the National Institute for Health and Care Excellence (NICE).

We have focused on drug choice and taken a holistic approach to recognise that a patient may have several related or unrelated conditions, e.g. rational drug choice in hypertension should be based on managing the hypertension without affecting other concurrent conditions such as asthma. Similarly, drug interactions represent an important therapeutic challenge and here we have attempted to highlight important examples of interactions and how they may be dealt with. Given the plethora of information on drug interactions we have largely drawn on *Stockley's Drug Interactions* (Baxter 2013) for information, because this provides an evidence-based approach with considered advice.

The topics of drug choice are intended to enable the reader to appreciate the rationale behind logical prescribing and advice in medicines management. We have also considered the patient rather than the disease, and here we have produced some points in which patients should be counselled about their disease and their drug treatment.

Our initial concept was to produce a short textbook focused on primary care but we now believe that we have produced an introduction to the management of diseases that are commonly encountered in, but not exclusive to, primary care. As such, we believe that *Disease Management* will provide a useful generalist introduction to medicines management.

Since the first edition of *Disease Management* there have been many changes in therapeutics and this is reflected in the third edition. In this new edition the revisions to clinical guidelines have been

incorporated to reflect some substantial changes, notably in the management of hypertension, the use of statins and chronic heart failure. Key to therapeutics is the rational choice of medicines, and this is reflected in a new chapter focused on the considerations of drug choice in prescribing, taking account of prescribing in special cases. Although *Disease Management* is a generalist introduction, a new chapter on anticancer chemotherapy has been included, and this also deals with some of the newer, more targeted therapies introduced recently.

Michael D Randall, Karen E Neil

Reference

Baxter K, ed. (2013). *Stockley's Drug Interactions,* 10th edn. London: Pharmaceutical Press.

General reading

In producing this book we have used an extensive range of excellent standard textbooks and reference sources. These are listed here both as acknowledgement and to enable the reader to carry out further reading. More specific references, further reading and resources are provided in each chapter.

General medicine

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Basic and clinical pharmacology

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Clinical pharmacy

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Rutter P (2013). *Community Pharmacy*, 3rd edn. Edinburgh: Churchill Livingstone.

Walker R, Whittlesea C (2011). *Clinical Pharmacy and Therapeutics*, 5th edn. Edinburgh: Churchill Livingstone.

Wills S (2005). *Drugs of Abuse*, 2nd edn. London: Pharmaceutical Press.

Dietary supplements and clinical nutrition

Barnes J, Anderson LA, Phillipson JD (2007). *Herbal Medicines*, 3rd edn. London: Pharmaceutical Press.

Mason P (2000). *Nutrition and Dietary Advice in the Pharmacy*, 2nd edn. Oxford: Blackwell Science.

Mason P (2011). *Dietary Supplements*, 4th edn. London: Pharmaceutical Press.

Webster-Gandy J, Madden A (2011). *Oxford Handbook of Nutrition and Dietetics*, 2nd edn. Oxford: Oxford University Press.

Online resources

Bandolier is an excellent site with extensive summaries of recent clinical trials and experiments: www.medicine.ox.ac.uk/bandolier (accessed October 2015).

British National Formulary may be accessed and interacted with: www.bnf.org.uk (accessed October 2015).

Cochrane Collaboration for access to systematic reviews of healthcare interventions: www.cochrane.org (accessed October 2015).

Medicines and Healthcare products Regulatory Agency (MHRA) provides information on drug safety: www.mhra.gov.uk (accessed October 2015).

NHS Choices provides patient information on a range of conditions and treatments: www.nhs.uk (accessed October 2015)

The National Institute for Health and Care Excellence (NICE) provides guidance on prescribing policies: www.nice.org.uk (accessed October 2015).

Note to the reader

In producing this book we have attempted to provide a logical background to disease management. Although we have summarised some key guidelines, this book is not intended to provide definitive guidance, and the reader should of course consult appropriate national and local guidelines. The examples of drug interactions, adverse drug reactions and counselling points are not exhaustive and are included to illustrate common or important examples. Similarly, *Disease Management* is not intended to replace professional experience and the reader is reminded of the need to consult the latest information presented in the latest *British National Formulary,* summary of product characteristics and evidence-based resources for the latest drug information.

The case studies may deliberately contain less than ideal regimens and are intended to illustrate important therapeutic issues. Once again, the reader is reminded of the importance of consulting the *British National Formulary.*

Acknowledgements

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Despite the extensive help that we have received, any of the errors and omissions within *Disease Management* are the sole responsibility of the authors and we would very much appreciate any constructive comments directed to michael.randall@nottingham.ac.uk

About the authors

Michael D Randall read natural sciences at the University of Cambridge and specialised in pharmacology. After his first degree, he remained at Cambridge, carrying out research into the vascular actions of the endothelial factors, nitric oxide and the endothelins, and obtained a PhD in cardiovascular pharmacology. He was then a postdoctoral research fellow at the University of Wales College of Medicine (now Cardiff University's Medical School), continuing research into vascular pharmacology. In 1993 he was appointed to a lectureship, and is now a professor of pharmacology and Director of Teaching in the School of Life Sciences at the University of Nottingham Medical School, teaching pharmacology to both medical and pharmacy students.

Karen E Neil studied pharmacy at the University of Nottingham, before completing pre-registration training based at Broadgreen Hospital in Liverpool. She then returned to Nottingham to develop an interest in pharmacology gained during her final year as an undergraduate. She researched a variety of mechanisms involved in mediating second-messenger cross-talk, with particular interest in pathways associated with β-adrenoceptors, nitric oxide and phosphodiesterases, and achieved a PhD in molecular pharmacology. The application of pharmacology to clinical pharmacy beckoned and this developed from experience gained as a community pharmacist and researcher investigating adverse drug events and particularly drug interactions. She has been involved in teaching clinical pharmacy to pharmacy undergraduates, using problem-based learning, for a number of years. She has been a special lecturer in clinical pharmacology at the University of Nottingham Medical School.

Abbreviations

5ASA	5-aminosalicylate
5HT	5-hydroxytryptamine (serotonin)
ACE	angiotensin-converting enzyme
ACEI	angiotensin-converting enzyme inhibitor
ADH	antidiuretic hormone
ADME	absorption, distribution, metabolism, or excretion
ADP	adenosine diphosphate
ADR	adverse drug reaction
AED	antiepileptic drug
AF	atrial fibrillation
AIDS	acquired immune deficiency syndrome
AIN	acute interstitial nephritis
ALP	alkaline phosphatase
ALT	alanine transaminase
AMP	adenosine monophosphate
ANP	atrial natriuretic peptide
APTT	activated partial thromboplastin time
ARDS	adult respiratory distress syndrome
AST	aspartate transferase
AT	angiotensin
ATP	adenine triphosphate
AUC	area under the curve
AV	atrioventricular
BCG	bacille Calmette-Guérin
BHF	British Heart Foundation
BMI	body mass index
BNF	*British National Formulary*
BP	blood pressure
BTS	British Thoracic Society
CABG	coronary artery bypass grafting
CAD	coronary artery disease
CAI	cholesterol absorption inhibitors
cAMP	adenosine cyclic 3′:5′-monophosphate
CAPD	continuous ambulatory peritoneal dialysis
CAPP	Captopril Prevention Project
CBT	cognitive-behavioural therapy
CCK	cholecystokinin
CDH	chronic daily headache
CFC	chlorofluorocarbon
cGMP	guanosine cyclic 3′:5′-monophosphate
CGRP	calcitonin gene-related peptide
CHAOS	Cambridge Heart Antioxidant Study
CHD	coronary heart disease
CHF	chronic heart failure
CHM	Commission on Human Medicines
CK	creatine kinase
CKD	chronic renal disease
CL	clearance
CL_{cr}	creatinine clearance
C_{max}	maximum concentration
C_{min}	minimum concentration
CNS	central nervous system
CO_2	carbon dioxide
CoA	coenzyme A
COC	combined oral contraceptive
COMA	Committee on Medical Aspects of Food and Nutrition Policy
COMT	catechol-*O*-methyltransferase
CONSENSUS	Cooperative North Scandinavian Enalapril Survival Study
COPD	chronic obstructive pulmonary disease
COX	cyclo-oxygenase
CPK	creatine phosphokinase
CRF	corticotrophin-releasing factor
CRP	C-reactive protein
CSM	Committee on Safety of Medicines
C_{ss}	steady-state concentration
CTZ	chemoreceptor trigger zone
CVA	cerebrovascular accident
DCCT	Diabetes Control and Complications Trial

DCT	distal convoluted tubule
DDT	dichlorodiphenyltrichloroethane
DEET	diethyltoluamide (diethylmethylbenzamide)
DEXA	dual-energy X-ray absorptiometry
DHA	docosahexanoic acid
DHEA	dehydroepiandrosterone
DHP	dihydropyridine
DIG	Digitalis Intervention Group
DMARD	disease-modifying antirheumatoid drug
DNA	deoxyribonucleic acid
DPP-4	dipeptidyl peptidase-4
DSM-IV	*Diagnostic and Statistical Manual of Mental Disorders*
DVLA	Driver and Vehicle Licensing Agency
DVT	deep vein thrombosis
ECG	electrocardiogram
ECT	electroconvulsive therapy
EEG	electroencephalogram
eGFR	estimated glomerular filtration rate
EPA	eicosapentaenoic acid
EPO	erythropoietin; evening primrose oil
ESR	erythrocyte sedimentation rate
ET	endothelin
FBC	full blood count
FDA	(US) Food and Drug Administration
FEV_1	forced expiratory volume in the first second
FSH	follicle-stimulating hormone
FVC	forced vital capacity
GABA	γ-aminobutyric acid
GAD	general anxiety disorder
GFR	glomerular filtration rate
GGT	γ-glutamyl transferase (transpeptidase)
G6PD	glucose-6-phosphate dehydrogenase
GI	gastrointestinal
GLP-1	glycogen-like peptide-1
GLUT	glucose transporter
GORD	gastro-oesophageal reflux disease
GP	general practitioner
GTN	glyceryl trinitrate
Hb	haemoglobin
HbA_{1c}	glycated haemoglobin
Hct	haematocrit
HDL	high-density lipoprotein
HIV	human immunodeficiency virus
HMG	hydroxymethylglutaryl
HOPE	Heart Outcomes Prevention Evaluation
HOT	Hypertension Optimal Treatment
HPA	hypothalamic–pituitary–adrenal
HRT	hormone replacement therapy
IARC	International Agency for Research on Cancer
IBS	irritable bowel syndrome
IBW	ideal body weight
ICD-10	*International Statistical Classification of Diseases and Related Health Problems,* 10th edn
Ig	immunoglobulin
IHD	ischaemic heart disease
INR	international normalised ratio
IONA	Impact Of Nicorandil in Angina
IP_3	inositol triphosphate
JVP	jugular venous pressure
K_{ATP}	ATP-sensitive K^+ channels
K_m	Michaelis–Menten constant
LDH	lactate dehydrogenase
LDL	low-density lipoprotein
LFT	liver function test
LH	luteinising hormone
LIFE	Losartan Intervention For Endpoint reduction in hypertension
LMWH	low-molecular-weight heparin
LVH	left ventricular hypertrophy
MAOI	monoamine oxidase inhibitor
MCH	mean corpuscular haemoglobin
MCV	mean corpuscular (cell) volume
MDI	metered dose inhaler
MDMA	3,4-methylenedioxymethamfetamine or ecstasy
MDRD	modification of diet in renal disease
MHRA	Medicines and Healthcare products Regulatory Agency
MI	myocardial infarction
MMR	measles, mumps and rubella
MODY	maturity-onset diabetes of the young
MOH	medication overuse headache
MRSA	meticillin-resistant *Staphylococcus aureus*
MS	multiple sclerosis
NACC	National Association for Colitis and Crohn's Disease

NANC	non-adrenergic non-cholinergic
NARI	noradrenaline (norepinephrine) reuptake inhibitors
NaSSA	noradrenergic and specific serotonergic antidepressant
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NK	neurokinin
NMDA	*N*-methyl-D-aspartate
NO	nitric oxide
NPA	National Pharmaceutical Association
NPC	National Prescribing Centre
NPY	neuropeptide
NRT	nicotine replacement therapy
NSAIDs	non-steroidal anti-inflammatory drugs
NSF	National Service Framework
NSP	non-starch polysaccharide
OA	osteoarthritis
OCD	obsessive compulsive disorder
ORT	oral rehydration therapy
OTC	over-the-counter
PAF	platelet-activating factor
PCV	packed cell volume
PDEI	phosphodiesterase inhibitor
PE	pulmonary embolism
PEF	peak expiratory flow
PG	prostaglandin
PGRs	prandial glucose regulators
PI	phosphatidyl inositol
PLA_2	phospholipase A_2
PMR	patient medication record
POM	prescription-only medicine
POP	progestogen-only pill
PPAR	peroxisome proliferator-activated receptors
PPI	proton pump inhibitor
PRISM	Platelet Receptor Inhibition in Ischemic Syndrome Management
PROGRESS	Perindopril Protection Against Recurrent Stroke Study
PSA	prostate-specific antigen
PTCA	percutaneous transluminal coronary angioplasty
PTH	parathyroid hormone
PUFA	polyunsaturated fatty acid
RA	rheumatoid arthritis
RAAS	renin–angiotensin–aldosterone system
RAS	renin–angiotensin system
RBC	red blood cell
REIN	Ramipril Efficacy In Nephropathy
REM	rapid eye movement
RICE	rest, ice, compression and elevation
RIMA	reversible inhibitor of MAO-A
RPSGB	Royal Pharmaceutical Society of Great Britain
4S	Scandinavian Simvastatin Survival Study
SACN	Scientific Advisory Committee on Nutrition
SAD	seasonal affective disorder
SERM	selective oestrogen receptor modulator
SIADH	syndrome of inappropriate secretion of antidiuretic hormone
SIGN	Scottish Intercollegiate Guidelines Network
SLE	systemic lupus erythematosus
SM	smooth muscle
SMAC	Standing Medical Advisory Committee
SNRI	serotonin–noradrenaline (norepinephrine) reuptake inhibitors
SPC	summary of product characteristics
SRM	serotonin receptor modulator
SSRI	selective serotonin reuptake inhibitor
T_3	triiodothyronine
T_4	thyroxine
TB	tuberculosis
TCA	tricyclic antidepressant
TDM	therapeutic drug monitoring
TEN	toxic epidermal necrolysis
TENS	transcutaneous electrical stimulation
TFT	thyroid function test
THC	Δ^9-tetrahydrocannabinol
THR	traditional herbal registration
TIA	transient ischaemic attack
TNFα	tumour necrosis factor-α
TPN	total parenteral nutrition
tRNA	transfer ribonucleic acid
TrT	troponin T

TSH	thyroid-stimulating hormone
TxA_2	thromboxane
U&Es	urea and electrolytes
UKPDS	UK Prospective Diabetes Study
UT	urinary tract
UTI	urinary tract infection
UV	ultraviolet
V_d	volume of distribution
V_{max}	maximum rate of reaction
VLDL	very-low-density lipoprotein
VSM	vascular smooth muscle
VTE	venous thromboembolism
WBC	white blood cell
WFSBP	World Federation of Societies of Biological Psychiatry
WHO	World Health Organization

PART A

The patient

1

Signs and symptoms

Symptoms and patient histories in the pharmacy

Role

The pharmacist has a central role in assessing a patient's complaint or condition, with a view to providing information, recommending appropriate treatment or referring the patient to a general practitioner (GP). Indeed the pharmacist may be the first health professional consulted by many patients, especially as an appointment is not required.

The consultation

Unlike the hospital doctor or GP, the pharmacist is unlikely to have the luxury of carrying out a full medical history and may not have access to the patient's medical records or test results. Indeed, the consultation may well be happening in a busy shop. Hence, the pharmacist has to establish the relevant facts, to differentiate between minor complaints and potentially serious conditions, and make a judgement or even diagnosis 'on the spot'. First, the patient must be identified and once this is established the pharmacist might then ask the person to explain what he or she believes the problem to be; this should then prompt more specific questions related to the condition. Throughout the interview the pharmacist should take the opportunity to assess the patient to make a judgement about how ill he or she looks and also to examine the patient for any signs that may point to disease, e.g. the following might be revealed:

- Skin colour: signs of jaundice or changes in skin coloration.
- Coloration of the sclera (may reveal jaundice).
- Marks on the skin: e.g. a change in a mole, a rodent ulcer or spider naevi (see Chapter 36).
- Breathing: is the patient short of breath or having trouble completing a sentence?
- Digital clubbing: the fingers take on a 'drumstick' appearance and this can indicate chronic pulmonary, cardiac or liver diseases.
- Does the patient *appear* to have a fever?
- Does the patient appear anxious? Signs of anxiety might indicate how serious the patient feels that the problem is or reveal a hidden concern.

The pharmacist should also attempt to make a judgement about the educational background or medical knowledge of the person, so that the questioning and any subsequent counselling may be appropriately phrased. A patient volunteering specific facts or requesting a specific medicine may reveal their medical knowledge or lack of it.

Establishing the facts

The questioning should be directed towards aiding a diagnosis or making a judgement as to the need for referral or over-the-counter (OTC) treatment.

Relevant lines of questioning might be related to the following:

- What the problem appears to be.
- How bad the symptoms are.
- How long the patient has been aware of the problem.
- The main presenting symptoms.
- Any accompanying symptoms.
- What makes the condition worse?
- What provides relief?
- Any relevant social factors.
- Does the patient have a previously diagnosed medical condition?
- A drug history with particular attention to the use of OTC treatments.

The above may be summarised by the popular mnemonic, WWHAM (Blenkinsopp *et al.*, 2014):

Who is the patient?
What are the symptoms?
How long have the symptoms been present?
Action taken, medicines tried?
Medicines taken for other conditions?

The drug history may be relevant to the current symptoms or influence the recommendation for OTC medicines or referral. Patients may regard non-prescription medicines and herbal remedies as being less important and so they should be directly questioned about their usage. In addition, it is clearly important for the pharmacist to establish if the patient is suffering from a previously diagnosed chronic condition, such as diabetes mellitus, asthma, chronic obstructive pulmonary disease (COPD), epilepsy, liver disease, renal disease and cardiovascular disease, or receiving long-term treatment, e.g. corticosteroids. It may be that the presenting complaint is associated with this condition or its treatment but this may not be obvious to the patient. Chronic conditions will also influence the use of OTC medicines and the importance of referral.

Patients may also make direct requests for named OTC medicines. In such cases this may suggest that a patient has a previously diagnosed condition, for which an OTC medicine may be appropriate within the limitations of its licence, e.g. a patient may be requesting sumatriptan for previously diagnosed migraine (see Chapter 23). A request for simvastatin to reduce cholesterol (and cardiovascular risk) would prompt a full history to check that the patient fulfils the criteria to receive it as an OTC medicine (see Chapter 13), and also provides an opportunity to explore any health concerns and provide appropriate lifestyle advice

In the case of women of childbearing age it is important to establish if the patient *could be* pregnant and it may be sensible to assume that the patient is pregnant until proven otherwise. This level of caution is essential because many drugs may damage the fetus, especially in the early stages of pregnancy when the patient may not herself be aware that she is pregnant.

Once the presenting complaint has been established, the pharmacist should use his or her professional skills to select relevant searching questions, e.g. if a patient complains of a cough, an open and open-ended question may be:

'Tell me about the cough'

and, depending on the response, detailed questioning may enable the pharmacist to determine the underlying nature of the complaint (and thus course of action), e.g. the questioning might proceed as follows.

What are the symptoms?

'Is there any sputum?'
'What colour is the sputum?'
'Have you noticed any blood in the sputum?'
Alternatively, ask the patient to describe the sputum.

Indeed the last question is a more indirect approach than the question 'Have you coughed up any blood?' Using appropriate questions is important because patients may wish to deny to themselves sinister symptoms such as haemoptysis (coughing up blood) or by contrast they may not appreciate their importance.

How long?

'How long have you had the cough?'

Action taken, medicines tried?

> 'Are you taking any medicines prescribed by a doctor or bought from a pharmacy?'

This essential question enables the identification of iatrogenic problems such as drug-induced blood dyscrasias in patients prescribed immunosuppressants or a cough induced by an angiotensin-converting enzyme (ACE) inhibitor. It may also identify problems where a drug has already been prescribed but the treatment has failed. Medicines taken for other conditions should also be considered. A drug history is imperative when OTC medication is recommended, allowing the exclusion of contraindications and avoidance of drug interactions. Additional relevant questions might be:

> 'Have you ever smoked?'

This is a more searching question than 'Do you smoke?' because the person may have given up yesterday (perhaps in response to the symptom) and the answer would be no! Alcohol consumption is also likely to be under-reported by patients.

> 'Are you having any difficulty in breathing?'
> 'Have you noticed a wheezing noise or rattle?'

The outcome

The interview should enable the pharmacist to make a reasonable attempt at identifying the condition and then to decide on the appropriate course of action, whether advice, treatment or referral. If the outcome is that the pharmacist believes that it is in the patient's best interests to consult a GP, the importance of this should be emphasised without unduly worrying the patient. It is, however, important to give an indication of the urgency of referral, e.g. a patient presenting with cystitis and systemic symptoms such as fever should be seen urgently rather than wait for the next available appointment. In all cases the pharmacist should ensure that the patient understands fully the course of action that you recommend.

Signs and symptoms

In dealing with responding to symptoms the reader is referred to *Minor Illness or Major Disease* by Addison *et al.* (2016), *Symptoms in the Pharmacy* by Blenkinsopp *et al.* (2014) and *Community Pharmacy* by Rutter (2013), which deal with responding to a range of common symptoms (see end of chapter).

Symptoms

A symptom is a perceived change in well-being by the patient that may or may not be associated with significant illness. The patient complains of a symptom and it is different from 'normal'. Several symptoms may present together to suggest or exclude a disease; this forms part of differential diagnosis, e.g. a patient may report breathlessness and also notice swollen ankles, which may appear unrelated but to the pharmacist may point to chronic heart failure (see Chapter 16). The following are some examples of symptoms:

- cough
- tiredness
- aches
- chest pains
- breathlessness
- indigestion.

Signs

A sign is a clinical change in a person, which may be observed by a clinician and indicates a disease. The following are some common examples of signs:

- changes in skin (colour, markings)
- digital clubbing (fingers clubbed in lung and hepatic diseases)
- heart murmurs
- sounds on listening to the lungs (wheezes [rhonchi], crackles [crepitations])
- dullness to percussion of thorax (changes in sound on tapping)
- changes to the retina
- enlarged lymph nodes.

There is obviously some overlap between signs and symptoms as a patient might notice ankle oedema but not realise that it is a significant sign of heart failure.

Important examples of signs and symptoms

Cough

A cough may be a trivial symptom, either reflecting a minor ailment or possibly pointing to a serious underlying disease (Table 1.1).

Chest pains

Once again, chest pains represent an important symptom, which might be due to a minor illness or a serious condition and some common causes are detailed in Table 1.2.

Given the above (Table 1.2) presentations and diverse conditions, questioning should be directed towards establishing the following:

- The location and nature of the pain and additional symptoms.
- What provokes the pain?
- What relieves the pain (including the use of OTC medicines and rest)?
- Recent activity? For example, exertion that may have strained a muscle.
- Past medical history.
- If GTN (glyceryl trinitrate) failed to control the symptoms, is it actually in date?

Breathlessness

Similarly, breathlessness may be due to a whole range of conditions and the possible aetiologies include:

- congenital: cystic fibrosis
- infection: chest infection, tuberculosis
- inflammatory: asthma, anaphylaxis
- neoplastic: carcinoma
- haematological: secondary to anaemia
- psychogenic: panic attacks

Table 1.1 Some causes of a cough

Underlying condition	Comments
Coryza (cold) (Chapter 20)	Associated with cold symptoms
Acute bronchitis (Chapter 20)	Often following a cold: there may be production of sputum, with wheezing and a temperature
Tracheitis	A dry, rasping and painful cough which is often associated with a viral infection
Pneumonia (Chapter 20)	Infection of the alveoli which leads to sputum (which may be bloodstained and is often rusty in appearance), breathlessness, pleuritic chest pains and fever
COPD (Chapter 22)	• COPD • Associated with exacerbations • The 'smoker's cough' may herald the onset of COPD
Asthma (Chapter 22)	• May be associated with wheezing and breathlessness • Often a nocturnal cough and this may be the only symptom in a child
Drug-induced (Chapters 12 and 16)	For example, with ACE inhibitors
Anxiety	A long-term 'nervous cough'
Foreign body	Associated with recent inhalation of an object
Tuberculosis (Chapter 34)	Associated with tiredness, malaise, weight loss, fever and haemoptysis
Bronchiectasis	• Dilated bronchioles with persistent infections and mucus • Copious amounts of sputum which may be bloodstained
Congestive heart failure (Chapter 16)	Associated with breathlessness and oedema
Lung cancer	A history of smoking associated with haemoptysis. A change in a 'smoker's cough' is a serious alerting symptom

ACE, angiotensin-converting enzyme; COPD, chronic obstructive pulmonary disease.

Table 1.2 Some causes of chest pains

Underlying condition	Comments
Musculoskeletal in origin (Chapter 31)	Pain may be worse on moving an arm or follows strenuous or unusual exercise. This is a common explanation and is often the default diagnosis
Respiratory (Chapter 22)	The pain is likely to be associated with breathing and to be due to an underlying respiratory disease, e.g. asthma
Pleuritic pains	This may be due to some form of respiratory disease but, if associated with calf swelling, haemoptysis or risk factors for thromboembolism, it may point to pulmonary embolism
Gastric origin: peptic ulceration, reflux	Here there may be a relationship to food, being either brought on by a meal (gastro-oesophageal reflux disease) or temporarily relieved by food (peptic ulceration) (Chapter 8). It should be relieved rapidly by antacids. In patients >55 years of age, if this symptom is of recent onset it raises the suspicion of carcinoma, which should be excluded
Angina (Chapter 15)	Angina has the following characteristics, which often allow it to be diagnosed by a history: • A crushing feeling in the chest • Often accompanied by pains down the arm (often left) • Pains may radiate to the jaw • Stable angina is induced by exercise, emotional stress, cold weather or a meal • Unstable angina may occur at rest • It should be relieved by rest (unless unstable) or GTN • Characteristic ECG changes
Myocardial infarction (Chapter 15)	• This must be differentiated from angina and is characteristically severe chest pains, which are not relieved by rest or GTN • May be accompanied by nausea, breathlessness, pallor, sweating and pains down the arms and/or jaw • Often diagnosed by ECG changes and so-called 'cardiac enzymes' • Some patients may experience a silent myocardial infarction, which does not cause chest pains

ECG, electrocardiogram; GTN, glyceryl trinitrate.

- degenerative: COPD
- cardiac: chronic heart failure, acute left ventricular failure, myocardial infarction
- thromboembolic: pulmonary embolism
- functional: in pregnancy, ascent to altitude, obesity
- iatrogenic: bronchospasm secondary to drug treatment (e.g. (β blockers, non-steroidal anti-inflammatory drugs [NSAIDs]); chronic pulmonary damage (e.g. amiodarone). (See Chapter 6.)
- traumatic: physical damage to the chest.

In all cases, the serious nature of the potential conditions should lead to a referral, and the key question is the degree of urgency required.

Pain

Pain affects many parts of the body and represents an interesting complaint as it may point to a range of trivial or serious conditions, e.g. an uncomplicated tension headache would be treated by simple analgesia but a severe headache typical of migraine (see Chapter 23) with accompanying symptoms such as nausea and photophobia would require referral. A headache that is severe and explosive (the patient might describe it as feeling like being 'hit on the back of the head with a brick') might point to a subarachnoid haemorrhage, which is a medical emergency. In taking a history of pain it may help to ask the patient to describe the severity on a scale of 1–10, with 10 representing 'the worst ever'.

Pain affecting other systems in the body requires close questioning of the relevant system, e.g. musculoskeletal pain may be the response to a recent injury or due to a chronic condition such as arthritis – in which case a diagnosis might be suggested by the time course of onset and provoking factors.

Gastrointestinal pain similarly represents a challenge. The first issue is one of location, e.g. heartburn is an obvious indication of upper gastrointestinal

problems such as gastro-oesophageal reflux disease and would be exacerbated by eating. Lower gastrointestinal pain, which is colicky in nature, might point to a visceral cause, whereas pain with bloating, which is relieved by defecation, would be consistent with irritable bowel syndrome.

A 'funny turn'

This symptom encompasses a range of events from dizziness to total loss of consciousness that may involve fitting. As one might imagine, the range of events has a wide number of possible causes including the following.

Cardiovascular

Cardiovascular events such as a stroke (including a transient ischaemic attack), arrhythmias and postural hypotension, which is particularly prevalent in elderly people and those taking vasodilators or diuretics. Vaso-vagal syncope (fainting) may involve bradycardia with vasodilatation as a response to fear, pain, emotion or standing for a prolonged period and result in a faint.

Neurological

Neurological causes include epilepsy, strokes, migraine and infections including meningitis.

Endocrine

Endocrine causes include postural hypotension due to Addison's disease, thyrotoxicosis and diabetes with hypoglycaemia or hyperglycaemia.

Psychological

Psychological causes include panic attacks.

Iatrogenic

Iatrogenic causes include postural hypotension, in those taking vasodilators or diuretics as mentioned above or confusion with benzodiazepines. In response to a funny turn, the following questions may help to implicate or exclude certain causes:

- What provokes an attack? For example, flashing lights in certain forms of epilepsy.
- Were there any prodromal symptoms? For example, an aura in epilepsy.
- Was there loss of consciousness?
- Was there injury? Tongue biting would be consistent with epilepsy.
- Were there any unusual movements? This might implicate epilepsy.
- Was there incontinence? Incontinence of urine is common in epilepsy.
- What colour did the patient go? Extreme pallor during the episode and flushing after the attack might suggest a cardiac cause.
- How did the patient recover? With neurological causes there may be confusion.
- How long did it last?
- Does the patient have a current illness or is he or she receiving any drugs?

Given the potential seriousness of the above causes of a 'funny turn', it is likely that a referral would be made.

Referral

The pharmacist has a major role in responding to symptoms. Initially, the pharmacist should respond with advice and where necessary prescribe OTC medicines for 'minor' conditions that would respond. Compliance problems with prescribed medicines can often be rectified by the pharmacist. Equally, the pharmacist should be able to recognise potentially serious symptoms and refer patients to their GP, NHS drop-in centres or, in an emergency, a hospital accident and emergency department. Consultation via telephone, publications or online resources with NHS Choices is also a valuable source of referral information, triage and algorithms for patients.

In general, referral should be made for patients with potentially serious symptoms, for persistent symptoms and high-risk patients such as:

- babies
- children
- elderly people
- patients with diabetes
- pregnant or breastfeeding mothers
- immunocompromised patients.

In addition, many other disease states representing high risk (e.g. ischaemic heart disease, epilepsy, COPD, asthma) and then deterioration in the condition might warrant referral.

One should also be mindful of patients who frequently request OTC medicines for symptomatic relief, because they may be used to hide symptoms, e.g. the use of OTC H_2-receptor antagonists in peptic ulceration. Another reason to refer would be due to the failure of OTC medicines to control or relieve a condition or requests for OTC medicines that are not covered by their licence. In addition, the following examples of alerting symptoms should also prompt a referral.

Gastrointestinal

Some important gastrointestinal referral points are shown in Table 1.3.

Cardiorespiratory

Some important cardiorespiratory referral points are shown in Table 1.4.

Neurological and psychiatric

Some important neurological and psychiatric referral points are shown in Table 1.5.

Others

Some other important referral points are shown in Table 1.6.

This list of referrals is intended as a list of common examples that should prompt referral to the patient's GP or urgent referral to hospital. Obviously, if there is any doubt the patient should be referred and, as emphasised in Chapter 6, the pharmacist should be alert to the possibility of patients presenting with an adverse drug reaction (ADR). The list is clearly not exhaustive and local referral protocols may already be established with GPs.

Table 1.3 Some important gastrointestinal referral points

Leading feature	Features and comments
Mouth ulcers	• Recurrent and/or failure of OTC therapy • Possible ADR • Associated with agents that may cause neutropenia such as carbimazole, carbamazepine and clozapine (Chapter 6)
Swallowing	• Dysphagia (difficulty in swallowing) • Odynophagia (painful swallowing) that is not simply due to a sore throat
Vomiting (Chapters 9 and 10)	• Haematemesis (vomiting blood) – any and urgent referral if profuse. Bleeding may be profuse or present as 'ground coffee' in appearance (Chapter 8) • Symptoms of dehydration such as decreased output of urine, headache and confusion – care in special groups; taking laxatives or diuretics (advise to omit doses) • Nausea of more than 3–4 days
Dyspepsia/'indigestion' (Chapter 8)	• Indigestion persisting after 2 weeks of OTC histamine H_2-receptor antagonists or 4 weeks of OTC omeprazole • Pain consistent with peptic ulceration • Following use of NSAIDs • Prolonged indigestion, also new or changed symptoms in patients >45 years of age, or alerting symptoms including anorexia, weight loss, anaemia and upper abdominal masses
Bowel habits (Chapter 10)	• Sustained (>2 weeks) alteration in bowel habits (particularly in those over 45 years of age) • Passing blood (frank or melaena, black 'tarry' stools) – this may be due to gastrointestinal bleeding • Severe diarrhoea while taking antibiotics, especially clindamycin – antibiotics may lead to colitis • Steatorrhoea – significant if not explained by concomitant orlistat • Pale stools
Weight loss	Weight loss or wasting that is unexplained
Liver problems (Chapter 11)	Jaundice

ADR, adverse drug reaction; NSAIDs, non-steroidal anti-inflammatory drugs; OTC, over-the-counter.