

PAUL RUTTER



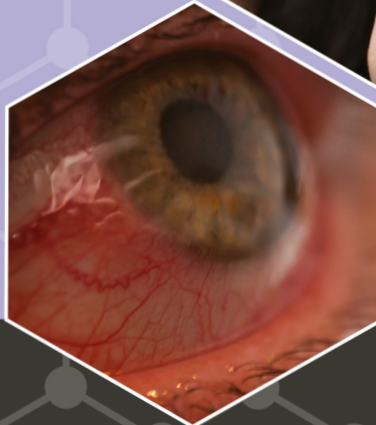
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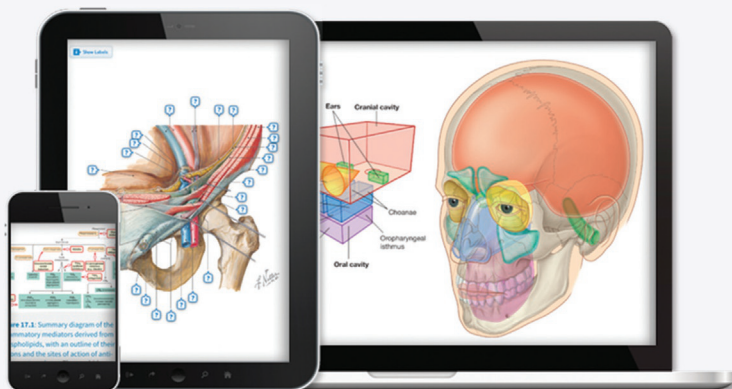
SYMPTOMS, DIAGNOSIS AND TREATMENT



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Community Pharmacy



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Community Pharmacy

Symptoms, Diagnosis and Treatment

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FIFTH EDITION



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Useful websites (addresses correct as of April 2020)

Evidence-Based Medicine

<http://www.bandolier.org.uk/>

Centre for Medicines Optimization

Centre for Reviews and Dissemination

Health Services Technology Assessment Texts (US Site)

King's Fund

National Institute for Health and Care Excellence

Regional Drugs and Therapeutic Centre

Medicine Information and Regulation

<https://www.medicines.org.uk/emc>

European Medicines Agency

Medicines and Healthcare Products Regulatory Agency

NICE Clinical Knowledge Summaries

Therapeutic Goods Administration (Australia)

UK Medicines Information

US Food and Drug Administration

Professional Bodies and Regulators

British Dental Association

British Medical Association

General Dental Council

General Medical Council

General Pharmaceutical Council

Health and care Professions Council

Pharmaceutical Society of Australia

Royal College of Nursing

Royal Pharmaceutical Society

The Nursing and Midwifery Council

UK Pharmacy Organizations and Trade Bodies

Association of the British Pharmaceutical Industry

British Pharmaceutical Students Association

<https://www.ghp.org.uk/>

National Pharmaceutical Association

Pharmaceutical Services Negotiating Committee

The Proprietary Association of Great Britain

UK Clinical Pharmacists Association

International Healthcare Organizations

International Pharmaceutical Federation (FIP)

International Pharmaceutical Students' Federation

World Health Organization

Pharmacy Journals

Chemist and Druggist

International Journal of Clinical Pharmacy

International Journal of Pharmacy Practice

Pharmaceutical Journal

Research in Social and Administrative Pharmacy

The Pharmacist

Wider Healthcare Journals of Interest to Community Pharmacy

British Journal of General Practice

British Medical Journal

Health and Social Care in the Community

Health Services Research

Journal of Evaluation in Clinical Practice

Journal of Prescribing Practice

Journal of Self Care

Nursing Standard

The Lancet

General Health Sites for Healthcare Workers

Medscape

Selfcare forum

General Health Sites for Patients

<http://www.patient.co.uk>

<http://www.healthfinder.gov/>

<http://www.bbc.co.uk/health/>

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Preface

Demand on healthcare professionals to deliver high-quality patient care has never been greater. A multitude of factors impinge on healthcare delivery today, including an aging population, more sophisticated medicines, high patient expectation and health service infrastructure, as well as adequate and appropriate staffing levels. In primary care, the medical practitioner role is still central in providing this care, but shifting the workload from secondary to primary care is placing greater demands on their time, resulting in new models of service delivery that increasingly involve other allied health professionals.

This is leading to a breakdown of the traditional boundaries of care among doctors, nurses and pharmacists. In particular, certain activities once seen as medical practitioner responsibility are now being performed by nurses and pharmacists as their scope of practice expands. The traditional role of supplying medicines safely and efficiently through the community pharmacy still exists, but greater patient-facing cognitive roles are now firmly established. Health prevention services are now routine; for example, smoking cessation, weight management and vaccination programmes. The pharmacy is now seen (by many governments) as a place where the general public can be managed for everyday healthcare needs without visiting a doctor. The most notable long-term global healthcare policy, which directly affects pharmacy, is the reclassification of prescription-only medicines to nonprescription status. In the UK, over 100 medicines have been deregulated since the

first switches took place in 1983. More recent switches have included products from new therapeutic classes, allowing community pharmacists to manage and treat a wider range of conditions.

Further deregulation of medicines to treat acute illness from different therapeutic areas seems likely in the medium to long term, especially because healthcare professional opinion to acute medicine deregulation is broadly positive, and the impact on the general practice workload associated with dealing with minor ailments is high (representing 100–150 million GP consultations per annum). Pharmacists, more than ever before, need to demonstrate that they can be trusted with this additional responsibility. Therefore, pharmacists require greater levels of knowledge and understanding about commonly occurring medical conditions. They will need to be able to recognise their signs and symptoms and use an evidence-based approach to treatment.

This was, and still is, the catalyst for this book. Although other books targeted for pharmacists about diagnosis have been published, this text aims to give a more in-depth view of minor conditions and explains how to differentiate them from more sinister pathology, which may present in a similar way. The book is intended for all nonmedical healthcare staff, but especially for pharmacists, from undergraduate students to experienced practitioners.

It is hoped that the information contained within the book is both informative and useful.

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Introduction

Community pharmacists are the most accessible healthcare professional. No appointment is needed to consult a pharmacist, and patients can receive free unbiased advice almost anywhere. A community pharmacist is often the first health professional from whom the patient seeks advice and, as such, provides a filtering mechanism whereby minor self-limiting conditions can be appropriately treated with the correct medication, and patients with more sinister pathology referred on to an appropriate practitioner for further investigation. On a typical day, a pharmacist practising in an 'average' community pharmacy can realistically expect to help between 5 and 15 patients a day who present with various symptoms for which they are seeking advice, reassurance, treatment or a combination of all three.

Probably of greatest impact to community pharmacy practice globally is the increased prominence of self-care. Self-care is not new; people have always taken an active role in their own health. What is different now is the attitude towards self-care by policy makers, healthcare organisations, not-for-profit agencies and front-line healthcare workers. Health improvements have been seen in people adopting health-enhancing behaviours rather than just through medical intervention. This has led to self-care being seen in a broader context than just the way in which people deal with everyday illness. In the UK, the self-care forum (<http://www.selfcareforum.org/>) was established; its purpose is to promote self-care and to embed it in everyday life.

So what is self-care?

Fundamentally, the concept self-care puts responsibility on individuals for their own health and well-being. The World Health Organization defines self-care as '*the ability of individuals, families and communities to promote health, prevent disease, and maintain health and to cope with illness and disability with or without the support of a health-care provider*'.

Self-care has been described as a continuum (Fig. 1), starting with individual choices on health (e.g., exercising), moving through to managing their own ill health (e.g., self-medicating) either on their own or with help. As people progress along the

continuum, more facilitation by others is required until a person needs fully managed care.

What is self-medication?

Self-medication is just one element of self-care and can be defined as the selection and use of medicines by individuals to treat self-recognised illness or symptoms. How these medicines are made available to the public vary from country to country, but all have been approved by regulatory agencies as being safe and effective for people to select and use without the need for medical supervision or intervention. In many countries (e.g. Australia, New Zealand, France, Sweden, Canada, UK), regulatory frameworks support the reclassification of medicines away from prescription-only control by having a gradation in the level of medicine availability, whereby certain medicines can only be purchased at a pharmacy. These 'pharmacy medicines' usually have to be sold by the pharmacist or under his or her supervision. Over the last 4 decades, this approach to reclassification has seen a wide range of therapeutic agents made available to consumers, including proton pump inhibitors (US, EU-wide), orlistat (EU-wide), triptans (UK, Germany) and beta-2 agonists (Singapore, Australia).

Facilitated self-medication

Most purchases of nonprescription medicines are by the consumer alone, who uses product information from packaging to make an informed decision on whether to make the purchase. When consumers seek help at the point of purchase, this can be termed *facilitated self-medication*. Where medicines are purchased through pharmacies, staff are in a strong position to facilitate self-care decision making by consumers because, in most pharmacies, the transaction takes place through a trained counter assistant or the pharmacist. Limited research has shown that consumer purchasing decisions are affected by this facilitation. Nichol et al. and Sclar et al. both demonstrated that consumers (25% and 43%, respectively) altered their purchasing decision when proactively approached by pharmacy students. Furthermore, a small

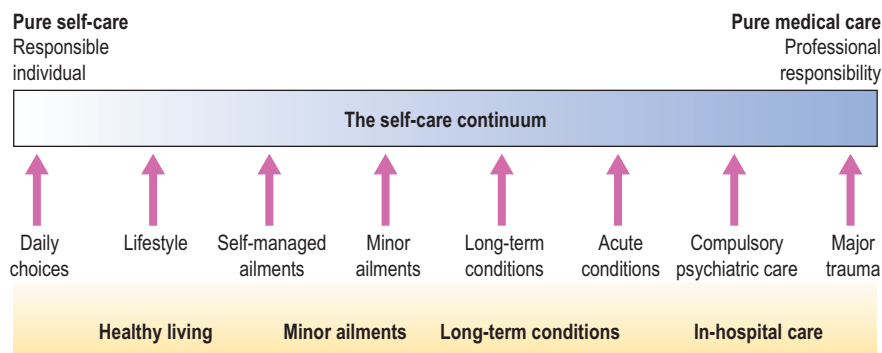


Fig. 1 The self-care continuum.

proportion of consumers did not purchase anything (13% and 8%) or were referred to their physician (1% and 4%). These studies highlight how the pharmacy team can positively shape consumer decisions and help guide them to arguably better alternatives.

Community pharmacy and self-care

Increasing healthcare costs, changes in societal lifestyle, improved educational levels, and increasing consumerism are all influencing factors on why people choose to exercise self-care. Of greatest importance are probably consumer purchasing patterns and controlling costs.

Consumerism

Changes in society have led people to have a different outlook on health and how they perceive their own health and ill health. Today, people have easy access to information; the Internet gives almost instantaneous access to limitless data on all aspects of health and care, which means that people across the globe have the means to query decisions and challenge medical opinion. This growing empowerment is also influenced by greater levels of education; having information is one thing, but being able to understand it and utilise it is another. This has proved challenging to healthcare systems and workers, having to move from traditional structures and paternalistic doctrines (e.g., 'doctor knows best') to a patient-focused and -centred type of care. This heightened public awareness about health, in the context of self-care, allows individuals to make informed choices and to recognise that much can be done by themselves. The extent of self-care is no better exemplified than by the level of consumer self-medication. The use of nonprescription medicines is the most prevalent form of medical care in the world. Sales are huge, with the global market estimated to be worth 73 billion euros.

Despite the enormous sums of money spent on nonprescription medicines, approximately only 25% of people regularly purchase them (25% tend to seek medical attention, and 50% do nothing). The extent to which this happens varies from country to country and, in some markets, this is considerably higher; for example, South Africa and the United States, where 35% to 40% of people use over-the-counter (OTC) medications on a regular basis.

Many papers and commissioned reports have shown that access and convenience shape the purchasing patterns of consumers. These factors seem to be unaffected by country or time. Reports spanning 30 years have repeatedly concluded that these play an important part in consumer decision making. The element of convenience does have a country context; for example, in Western countries, this is primarily due to ease of access that negates the need for doctor seeking that is often associated with higher cost and increased time. In developing countries, 'convenience' is more associated with 'need' due to lower levels of health infrastructure and access to medical resources.

Costs

As populations across the globe live longer lives, whether through better hygiene, nutrition or advances in medicine, providing medical care is becoming more and more expensive. In an attempt to control costs, many countries have gone through major healthcare reforms to maximise existing resources, both financial and staffing, to deliver effective and efficient healthcare. These reforms include integrating self-care into mainstream public health policy, including the management of long-term conditions.

Encouraging more people to exercise greater levels of self-care, for acute or chronic problems, has the potential to shift costs away from professional care. Figures from the UK give some indication as to the magnitude of potential

cost savings. Take primary care workload as an example. It has been reported that approximately 20% to 40% of general practice (GP) workload constitutes patients seeking help for minor illnesses at a cost of £2 billion.

Contribution of community pharmacy to self-care

Community pharmacists are uniquely placed to provide support and advice to the general public compared to other healthcare professionals. The combination of location and accessibility means that most consumers have ready access to a pharmacy where healthcare professional advice is available on demand. A high level of public trust and confidence in pharmacists' ability to advise on nonprescription medicines is afforded to community pharmacists. Although there is a general global move to liberalise nonprescription markets, pharmacies in many countries still are the main suppliers of nonprescription medicines. Pharmacists are,

therefore, in a unique position to facilitate consumer self-care and self-medication, which needs to be expanded and exploited.

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Self-Care Forum <http://www.selfcareforum.org/>

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How to use the book

The book is divided into 11 chapters. The first chapter lays the foundations of how to go about making a diagnosis. This is followed by nine systems-based chapters structured in the format shown in Fig. 2. The final chapter is product-based and has a slightly different format. A list of abbreviations and a glossary are included at the end of the book.

Key features of each chapter

At the beginning of each chapter, there is a short section addressing basic anatomy and history taking specific to that body system. A basic understanding of the anatomical location of major structures is useful when attempting to diagnose or exclude conditions from a patient's presenting complaint. It would be almost impossible to know whether to treat or refer a patient who presented with symptoms suggestive of renal colic if one didn't know the location of the kidneys. However, this is not intended to replace an anatomy text, and the reader is referred to further reading listed throughout the book for more detailed information on anatomical considerations.

Self-assessment questions

Twenty-five multiple-choice, extended matching questions, and at least two case studies are presented at the end of each chapter. These are designed to test factual recall and applied knowledge. Most questions are constructed to resemble those in the UK preregistration examination set by the General Pharmaceutical Council.

The case studies challenge you with real-life situations. All are drawn from practice and have been encountered by practising pharmacists but have been modified for inclusion in this book.

Elements included under each condition

The same structure has been adopted for every condition. This is intended to help the reader approach differential diagnosis from the position of clinical decision making (see Chapter 1). To help summarise the information, tables and algorithms are included for many of the conditions.

Arriving at a differential diagnosis

To contextualise how commonly conditions are seen by community pharmacists, a table listing the likelihood in which they are encountered is presented. This is designed to frame the questions that should be asked from the point of working from the most likely cause of symptoms. To help further, a table summarising the key questions that should be asked for each condition is included. The relevance (the rationale for asking the question) is given for each question. This will allow readers to determine which questions should be asked to enable a differential diagnosis to be reached.

Primer for differential diagnosis

A primer for differential diagnosis is available for a number of the conditions covered. This algorithmic approach to differential diagnosis is geared towards nearly or recently qualified practitioners. They are not intended to be solely relied on in making a differential diagnosis but to act as an aid to memory. It is anticipated that the primers will be used in conjunction with the text, thus allowing a broader understanding of the differential diagnosis of the condition to be considered.

Trigger points indicative of referral

A summary box of trigger factors explaining when it would be prudent to refer the patient to another healthcare practitioner is presented for each condition. In most cases, a rationale for referral and time scale is presented. These trigger factors are not absolute, and professional judgement needs to be exercised on a case by case basis. For example, a person with a cough of 3 days' duration would not normally constitute a referral but, if the person showed obvious visible signs of being in respiratory distress, this would require referral.

Evidence-based OTC medication and practical prescribing and product selection

These two sections present the reader first, with an evaluation of the current literature on whether OTC medicine works, and second, with a quick reference to the dose of the

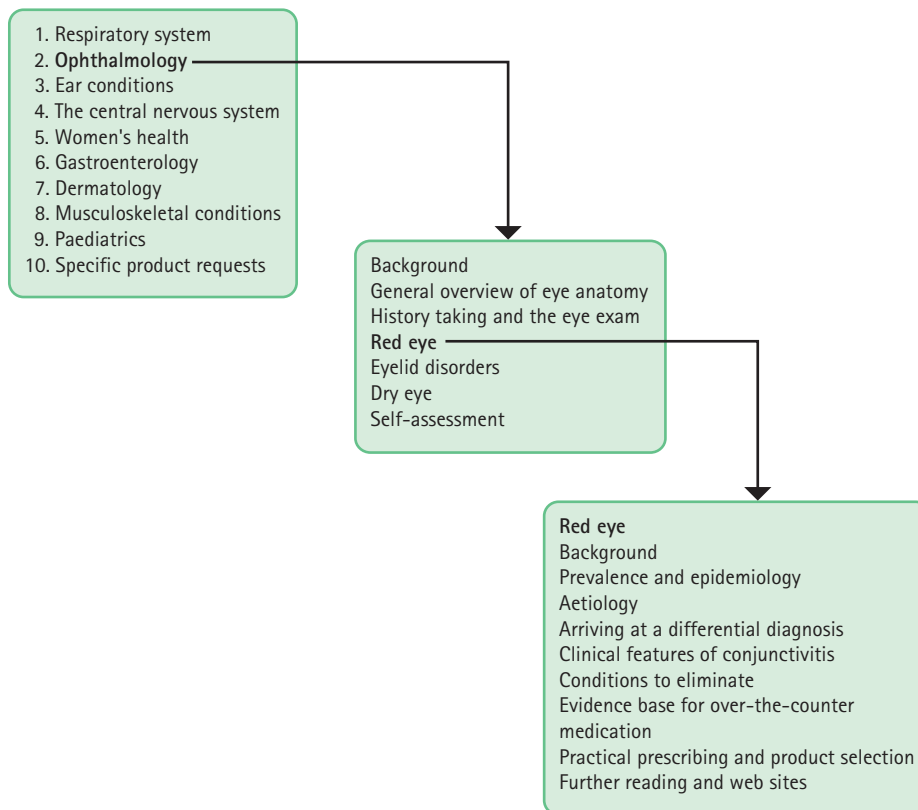


Fig. 2 Structure of the book.

medicine and when it needs to be prescribed with caution or when it should be avoided. This does not replace standard textbooks such as *Martindale* or *Stockley's Drug Interactions*, but it does allow the user to find basic data in one text without having to consult three or four other texts to answer simple questions.

Side effects listed for products are drawn from the Summary of Product Characteristics, which can be found via the electronic medicine compendium (<https://www.medicines.org.uk/emc>). Only side effects listed as very common ($\geq 1/10$) or common ($\geq 1/100$) are shown unless the product is associated with more unlikely but serious side effects of which the patient should be made aware.

The pregnancy and breastfeeding recommendations in this book are based largely on those from standard texts, such as Briggs and associates *Drugs in Pregnancy and Lactation* and, Schaefer and colleagues *Drugs During Pregnancy and Lactation*. Many manufacturers of OTC medicines advise against their products being used in these groups but, where possible, reference is made in the summary tables to the recommendations from these standard and trusted sources. This,

hopefully, will provide extra information for practitioners when faced with queries from pregnant and lactating women, and allow them to recommend products when manufacturer information stipulates avoidance.

Hints and tips boxes

A summary box of useful information is provided near the end of the discussion of each condition. This contains information that does not fall readily into any of the other sections but is nonetheless useful. For example, some of the hints and tips boxes give advice on how to administer eye drops, suppositories, and other forms of medicines.

Further reading and websites

To supplement the text, a list of selected references and further reading at the end of each condition is provided for those who wish to seek further information on the subject. Websites are

also provided, and all of these were checked, active and relevant at the time of this writing (Spring 2020).

Finally, all information presented in the book is accurate and factual as far as the author is aware. It is acknowledged that guidelines change, products become discontinued and new information becomes available over the lifetime of a book. Therefore, if any information in this book is not current or valid, the author would be grateful of any feedback, positive or negative, to ensure that the next edition is as up to date as possible.

Electronic resources

Access to additional material is hosted on Elsevier's electronic portal. The electronic resource holds additional material that includes the following:

- A chapter on evidence-based medicine
- Videos on physical examination
- Additional written case studies
- More multiple-choice questions

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Making a diagnosis

In this chapter

Community pharmacy performance when dealing with patients' signs and symptoms 1
Current pharmacy training in making a diagnosis 2
Clinical reasoning 3

Summary 4
Consultation and communication skills 6
Conclusion 7

Global health care policy now has a strong self-care focus, and various strategies have been put into place to encourage consumers to have a more active role in exercising self-care.

Pharmacies unquestionably handle and manage large numbers of consumers who seek help and advice for minor illness, and advocates of pharmacy have argued that this will decrease physicians' workloads regarding minor illness, allowing them to concentrate more on complex patient care.

The expansion of nonprescription medicines has contributed to the growth seen in the market and given consumers greater choice. It has also provided community pharmacy with an opportunity to demonstrate real and tangible benefits to consumers. For example, in the UK, government-endorsed (and funded) services such as Minor Ailment Schemes have shown the positive impact that community pharmacy can have on patient outcomes. However, research data on the effectiveness of community pharmacy staff to differentially diagnose patients is less convincing.

Community pharmacy performance when dealing with patients' signs and symptoms

Regardless what degree of control is placed on medicine availability in different countries, pharmacists can now manage and treat a wider number of conditions than ever before. This raises the question as to whether pharmacists are capable of selling these medicines appropriately. Early research of pharmacist-consumer interactions in pharmacy practice did

not address this but concentrated more on auditing questioning behaviour and analysing the advice people received (Cantrill et al., 1997). This body of work did illustrate the following: the basic nature of performance; types of questions asked; frequency of advice provided; and consumer perception to questioning. The findings were broadly critical of pharmacist performance. Over the same time period, covert investigation by the UK consumer organization, 'Which', also concluded that pharmacists generally performed poorly. (Consumers' Association, 1999).

Further practice research (mainly from developed countries) has sought to determine the outcome of these interactions rather than the mechanics of the interaction. Findings from all papers raise questions over pharmacist ability to consistently perform at expected levels. Lamsam & Kropff (1998), found that in one-third of interactions, the pharmacists made recommendations without assessing the patient's symptoms and, in a further third of cases, recommendations were poor, which could have potentially caused harm. Horsley et al. (2004) found that the expected outcome was only reached in half of observed cases. Driesen and Vandenplas (2009) and Bilkhu et al. (2013) also reported poor performance, and in each study – diarrhoea in a baby and allergic conjunctivitis in an adult – it was suggested that too few questions were asked. Tucker et al. (2013) compared pharmacist performance to doctors and nurses across a spectrum of dermatological conditions. Pharmacists performed more poorly than doctors, and only 40% of pharmacists were able to identify all lesions correctly. Data from developing countries are limited but a review by Brata et al. (2013) also highlighted inconsistent information gathering, leading to inappropriate recommendations.

Current pharmacy training in making a diagnosis

The use of protocols, guidelines and mnemonics seem to have been almost universally adopted by pharmacists. Many mnemonics have been developed, as highlighted in a 2014 review (Shealy, 2014). The use of these decision aids seems to have had little impact on improving performance, and recent research findings have shown that community pharmacists overrely on using this type of questioning strategy (Akhtar & Rutter, 2014; Iqbal & Rutter, 2013; Rutter & Patel, 2013).

Do not use mnemonics

At best, these tools allow for standardizing information gained from patients from and between pharmacists and the wider pharmacy team. The more fundamental and important point is not simply asking questions but determining how that information is used. Having a set of data still requires interpretation, and this inability to synthesize gathered information appropriately is where research has highlighted pharmacists' failings.

Mnemonics are rigid, inflexible and often inappropriate. Every patient is different, and it is unlikely that a mnemonic can be fully applied and, more importantly, using mnemonics can mean that vital information is missed, which could shape decision making. Some of the more commonly used mnemonics are discussed briefly in the next section.

WWHAM

This is the most common mnemonic in use and is widely taught and used in the UK. It is the simplest to remember but also the worst to use. It gives the pharmacist very limited information from which to establish a differential diagnosis. If used, it should be used with caution and is probably only helpful as a basic information-gathering tool. WWHAM

Meaning of the letter	Attributes of the mnemonic
W Who is the patient?	Positive points
W What are the symptoms?	Establishes presenting complaint
H How long have the symptoms been present?	Negative points
A Action taken?	Fails to consider general appearance of patient. No social or lifestyle factors taken into account; no family history sought; not specific or in-depth enough; no history of previous symptoms
M Medication being taken?	

might be appropriate to allow for counter assistants to gain a general picture of the person's presenting complaint but should not be advocated as a tool to establish a diagnosis.

Other examples of mnemonics that have been suggested as being helpful for pharmacists in a differential diagnosis are ENCORE, ASMETHOD and SIT DOWN SIR. Although these are more comprehensive than WWHAM, they still are limited. None take into consideration all factors that might affect a differential diagnosis. All fail to establish a full history from the patient with respect to lifestyle and social factors or the relevance of a family history. They are designed to establish the nature and severity of the presenting complaint, which in many cases will be adequate but for intermittent conditions (e.g., irritable bowel syndrome, asthma, hay fever) or conditions where a positive family history is important (e.g., psoriasis, eczema), they might miss important information that is helpful in establishing the correct diagnosis.

ENCORE

Meaning of the letter	Attributes of the mnemonic
E Explore	Positive points
N No medication	'Observe' section suggests taking into account the appearance of the patient – does he or she look poorly?
C Care	
O Observe	Negative points
R Refer	Sections on 'No medication' and 'Refer' add little to the differential diagnosis process; no social or lifestyle factors taken into account; no family history sought
E Explain	

AS METHOD

Meaning of the letter	Attributes of the acronym
A Age, appearance	Positive points
S Self or someone else	Establishes the nature of problem and if patient has suffered from previous similar episodes
M Medication	
E Extra medicines	Negative points
T Time persisting	Exact symptoms and severity of social or lifestyle factors not taken into account; no family history sought
H History	
O Other symptoms	
D Danger symptoms	

SIT DOWN SIR

Meaning of the letter	Attributes of the acronym
S Site or location	Positive points
I Intensity or severity	Establishes the severity and
T Type or nature	nature of problem and if the
D Duration	patient has suffered from
O Onset	previous similar episodes
W With (other symptoms)	Negative points
N Annoyed or aggravated	Fails to consider general
S Spread or radiation	appearance of patient; no
I Incidence or frequency pattern	social or lifestyle factors
R Relieved by	taken into account; no family history sought

Clinical reasoning

Decision making processes associated with clinical practice are an essential skill and are central to the practise of professional autonomy. Clinical reasoning is the cornerstone on which a diagnosis is made and relies on the practitioner being both knowledgeable and a good decision-maker. Clinical reasoning is an evidence-based, dynamic process in which the health professional combines scientific knowledge, clinical experience and critical thinking, with existing and newly gathered information about the patient against a backdrop of clinical uncertainty. It is a thinking process that allows the pharmacist to make wise decisions specific to individual patient context.

Whether we are conscious of it or not, most people will, at some level, use clinical reasoning to arrive at a differential diagnosis. It fundamentally differs from using mnemonics in that it is built around clinical knowledge and skills that are applied to the individual patient. It involves recognition of cues and analysis of data.

Steps to consider in clinical reasoning**1. Use epidemiology to shape your thoughts.**

What is the presenting complaint? Some conditions are much more common than others. Therefore, you can form an idea of what condition the patient is likely to be suffering from based on the laws of probability. For example, if a person presents with a cough, you should already know that the most common cause of cough is a viral infection. Other causes of cough are possible and need to be eliminated. Your line of questioning should therefore be shaped by thinking that this is the default

cause of the person's cough and ask questions based on this assumption (see step 4, below).

2. Take account of the person's age and sex

Epidemiological studies show that age and sex will influence the likelihood of certain conditions. For example, it is very unlikely that a child who presents with cough will have chronic bronchitis, but the probability of an elderly person having chronic bronchitis is much higher. Likewise, croup is a condition seen only in children. Sex can dramatically alter the probability of people suffering from certain conditions. For instance, migraines are three times more common in women than in men, yet cluster headache is four times more common in men than in women. Use this to your advantage. It will allow you to internally change your thought processes as to which conditions are most likely for that person.

3. General appearance of the patient

Does the person look well or poorly? This will shape your thinking about the severity of the problem. If a child is running around a pharmacy, they are likely to be healthier than a child who sits quietly on a chair, not talking.

Taking these three points into consideration, you should be able to form some initial thoughts about the person's health status and ideas of what may be wrong with them. At this point, questions should be asked.

4. Hypothetical-deductive reasoning

Based on this (limited) information, the pharmacist should arrive at a small number of hypotheses. The pharmacist should then set about testing these hypotheses by asking the patient a series of questions.

Ask the right question, at the right time, for the right reason

The answer to each question asked allows the pharmacist to narrow down the possible diagnosis by eliminating particular conditions or confirming his or her suspicions of a particular condition. In effect, the pharmacist asks questions with knowledge of the expected answer. For example, a confirmatory type of question asked of a patient suspected of having allergic conjunctivitis might be 'Do your eyes itch?' In this case, the pharmacist is expecting the patient to say 'yes' and thus helps support your differential diagnosis. If a patient states 'no', this is an unexpected answer that casts doubt on the differential diagnosis; therefore, further questions will be asked and other diagnostic hypotheses explored. This cycle of testing and retesting the hypotheses continues until you arrive at a differential diagnosis.

Good questioning following these principles means that you will end up with the right diagnosis about 80% of the time.

5. Pattern recognition

In addition, clinical experience (pattern recognition) also plays a part in the process. Certain conditions have very characteristic presentations and, with experience, it is relatively straightforward to diagnose the next case drawing on previous cases seen. Therefore, much of daily practice will consist of seeing new cases that strongly resemble previous encounters and comparing new cases to old.

Pattern recognition is therefore much more commonly used by experienced or expert diagnosticians compared with novices. This is generally because there is a gap between the expert-novice knowledge and clinical experience. Research has shown that experienced doctors tend to only use hypothetical-deductive strategies when presented with difficult cases.

6. Physical examination

The ability to perform simple examinations (e.g., eye, ear, mouth and skin examinations) increases the probability of arriving at the correct diagnosis. Where appropriate (provided that pharmacists are suitably trained), examinations should be conducted. Seeing a rash or viewing an eardrum will provide much better data on which to base a decision than purely a patient description. Throughout this text, where examinations are possible, instruction is given in how to perform these examinations. Student consult has some videos on how to perform these physical examinations.

7. Safety netting

Even if you are confident of your differential diagnosis, it is important to use a safety net. You are not going to get it right all the time; making an incorrect diagnosis is inevitable. It has been reported that more than 50% of patients do not receive a definitive diagnosis at the end of a consultation with a family doctor (Heneghan et al., 2009).

Many people will present to the pharmacist at an early stage in the evolution of their illness. This means that they may not present with classical textbook symptoms or have not yet developed any red flag – type symptoms when seen by the pharmacist. For example, a child may have a headache but no other symptoms yet later go on to develop a stiff neck and rash and be diagnosed with meningitis, or a person may have an acute cough that subsequently develops into pneumonia. Using a safety net attempts to manage these situations.

This should take one of two forms:

- Conditional referrals

This should be built into every consultation. It is more than a mere perfunctory 'If you don't get better come back to me or see the doctor'. It has to be tailored and specific to the individual and the symptoms. For example, if a person presents with a cough of 10 days' duration, after how many more days would you ask them to seek further medical help – 3 days? 5 days? 7 days? Longer?

In this case, knowledge of cough duration is important. If the differential diagnosis is a viral cough, then we know that this symptom typically lasts 10 to 14 days, but it is not unusual for the symptom to last 21 days. Longer than 21 days suggests that the cough is becoming chronic and requires further investigation. A conditional referral in this case would be anything between 5 and 10 days; in other words, the person has had the cough for between 2 and 3 weeks, which is starting to become longer than one would expect for a viral cough. Conversely, if the cough had been present for just 2 days, a conditional referral after a further 2 more weeks would be appropriate.

- Advise patients on warning symptoms

It is entirely reasonable to highlight to patients signs and symptoms that they may develop subsequent to your consultation. For example, a child suffering with diarrhoea is managed by the pharmacist, but the pharmacist highlights the signs of dehydration to the child's parents. This would be good practice because the consequence of dehydration is clinically more significant than the diarrhoea itself.

Summary

In practice, family doctors tend to use a mixture of hypothetico-deductive reasoning and pattern recognition augmented with physical examination and, where needed, laboratory tests. It can seem to some patients that the doctor asks very few questions, spends very little time with them, and closes the consultation even before they have 'warmed the seat'. In these cases, the doctor is probably exhibiting very good clinical reasoning. Research has shown that with greater experience, doctors tend to rely more on nonanalytical decision making (e.g., pattern recognition), whereas novice practitioners use analytical models (hypothetico-deductive reasoning) more frequently.

Most pharmacists will exhibit some degree of clinical reasoning but most likely at a subconscious level. The key to better performance is shifting this activity from the subconscious to conscious. Gaining clinical experience is fundamental to this process. Critical for pharmacists is the need to learn from uncertainty. When referrals are made, every attempt should be made to follow up with the doctor about the outcome of the referral or encourage the patient to return to the pharmacy to see how they got on. Knowing what another person (usually a more experienced diagnostician) believed what the diagnosis was allows you to build up experience and, when faced with similar presenting symptoms, have a better idea of the cause. Without this feedback, pharmacists reach a 'glass ceiling', where the outcome is always the same – referral – which might not be necessary.

Differential diagnosis – an example

A 35-year-old female patient, Mrs JT, asks to speak to the pharmacist about getting some painkillers for her headache. She appears smartly dressed and in no obvious great discomfort but appears a little distracted.

Step 1: Use epidemiology to shape your thoughts

In primary care, headache is a very common presenting symptom that can have many causes. Table 1.1 highlights the conditions associated with headache that can be seen by community pharmacists.

From this background information, you should already be thinking that the probability of Mrs JT's headaches are going to be caused by the four conditions that are commonly seen by community pharmacists – tension-type headache, migraine, sinusitis and eye strain. This is not to say that it could not be caused by the other conditions, but the likelihood that they are the cause is much lower.

Step 2: Take account of the person's age and sex

Does age or sex have any bearing on shaping your thoughts? The person is a woman, and we know that migraines are more common in women compared with men. So, although tension-type headache is the most common cause of headache, the chances of it being caused by migraine needs to be given more prominence in your thinking. Will age affect your thinking? In this case, probably not, because the common causes of headache do not really show any real variation with age.

At this point, you should still be considering all four conditions as likely, but migraine as a cause should now be thought of more seriously along with the most common cause of headache: tension.

Table 1.1

Conditions associated with headache that can be seen by community pharmacists

Incidence	Cause
Most likely	Tension-type headache
Likely	Migraine, sinusitis, eye strain
Unlikely	Cluster headache, medication overuse headache, temporal arteritis, trigeminal neuralgia, depression
Very unlikely	Glaucoma, meningitis, subarachnoid haemorrhage, raised intracranial pressure

Step 3: The general appearance of the patient

Nothing obvious from her physical demeanour is constructive regarding your thinking. Her 'distracted' state might be as a consequence of the pain from the headache and worth exploring.

Step 4: Hypothetico-deductive reasoning

Each question asked should have a purpose; again, it is about asking the *right question, at the right time and for the right reason*. In this case, we are initially considering the conditions of tension-type headache, migraine, sinusitis and eye strain (listed in that sequence in terms of likelihood). It is important that your clinical knowledge be sufficiently sound to know how these different conditions present so that similarities and differences are known, allowing questions to be constructed to eliminate one type of headache from another. This will allow you to think of *targeted questions* to ask. Table 1.2 highlights associated signs and symptoms of these four conditions.

We can see that the location and nature of pain for the four conditions vary, as do the severity of pain experienced (although pain is subjective and difficult to measure reliably).

A reasonable first question would be about the *location* of pain. If the patient says, 'It is bilateral and towards the back', this points towards the tension-type headache (other causes are frontal or unilateral).

Given this information, if we asked about the *nature* of pain next, and working on the hypothesis of tension-type headache, we would be expecting a response from the patient of an 'aching, nonthrobbing headache', which might worsen as the day goes on. If patients describe symptoms similar to our expectation, this further points to tension-type headache as being the correct diagnosis.

To further confirm your thinking, you could ask about the *severity* of pain. In tension-type headache, we are expecting a response that does not suggest debilitating pain. Again, if we found that the pain was bothersome but not severe, this would point to tension-type headache.

At this point, we might want to ask other questions that *rule out* other *likely causes*. We know that migraine is associated with a positive family history. We would expect the patient to say there was no family history if our working differential diagnosis is tension-type headache. Likewise, asking about previous episodes of the same type of headache would help rule out migraine due to its episodic and recurrent nature. Similarly, eye strain is closely associated with close visual work. If the person has not been doing this activity more than normal, it tends to rule out eye strain. Finally, sinusitis is a consequence of upper respiratory tract infection so, if the person has not had a recent history of colds, this will rule out sinusitis.

Table 1.2
Associated signs and symptoms

Type of headache	Duration	Timing and nature	Location	Severity (pain score, 0–10)	Precipitating factors	Who is affected?
Tension-type	Can last days	Symptoms worsen as day progresses; nonthrobbing pain	Bilateral; Most often at back of head	2–5	Stress due to changes in work or home environment	All age groups; both sexes equally affected
Migraine	Average attack lasts 24 hours	Associated with menstrual cycle and weekends; throbbing pain and nausea; dislike of bright lights and loud noises	Usually unilateral	4–7	Food (in 10% of sufferers); family history	Three times more common in women
Sinusitis	Days	Dull ache that begins as unilateral	Frontal	2–6	Valsalva movements	Adults
Eye strain	Days	Aching	Frontal	2–5	Close vision work	All ages

Therefore, we are expecting certain responses to these questions if the symptoms are a consequence of suffering from a tension-type headache. If the patient answers in a negative way, this would start to cast doubt on your differential diagnosis. If this happens, you need to revisit your hypothesis and test another one – that is, think that the symptoms are caused by something else, and recycle your thought processes to test a hypothesis of a different cause of headache.

Consultation and communication skills

The ability of the community pharmacist to diagnose the patient's presenting signs and symptoms is a significant challenge given that unlike most other healthcare professionals, community pharmacists do not normally have access to the patient's medical record and thus have no idea about the person's problem until a conversation is initiated.

For the most part, pharmacists will be totally dependent on their ability to question patients to arrive at a differential diagnosis. It is therefore vital that pharmacists possess excellent consultation and communication skills as a prerequisite to determining a differential diagnosis. This will be drawn from a combination of good questioning technique, listening actively to the patient and picking up on nonverbal cues.

Many models of medical consultation and communication have been developed. Probably the most familiar and

most widely used model is the *Calgary-Cambridge model* of consultation. This model is widely taught in pharmacy and medical education and provides an excellent platform in which to structure a consultation. The model is structured into the following:

1. Initiating the session
 - Establishing initial rapport
 - Identifying the reason(s) for the consultation
2. Gathering information
 - Exploration of problems
 - Understanding the patient's perspective
 - Providing structure to the consultation
3. Building the relationship
 - Developing rapport
 - Involving the patient
4. Explanation and planning
 - Providing the correct amount and type of information
 - Aiding accurate recall and understanding
 - Achieving a shared understanding: Incorporating the patient's perspective
 - Planning: Shared decision making
 - Closing the session

For more detailed information on this model, there are numerous Internet references available, and the authors of the model have written a book on communication skills (Silverman et al., 2013).

Conclusion

The way in which one goes about establishing what is wrong with the patient will vary from practitioner to practitioner. However, it is important that whatever method is adopted, it must be sufficiently robust to be of benefit to the patient. Using a clinical reasoning approach to differential diagnosis has been shown to be effective in differential diagnosis and is the method advocated throughout this book.

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Respiratory system

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Background

Diseases of the respiratory tract are among the most common reasons for consulting a general practitioner (GP). The average GP sees approximately 700 to 1000 patients each year with respiratory disease. Although respiratory disease can cause significant morbidity and mortality, the vast majority of conditions are minor and self-limiting.

General overview of the anatomy of the respiratory tract

The basic requirement for all living cells to function and survive is a continuous supply of oxygen. However, a byproduct of cell activity is carbon dioxide, which, if not removed, poisons and kills the cells of the body. The principal function of the respiratory system is therefore the exchange of carbon dioxide and oxygen between blood and atmospheric air. This exchange takes place in the lungs, where pulmonary capillaries are in direct contact with the linings of the lung's terminal air spaces, the alveoli. All other structures associated with the respiratory tract serve to facilitate this gaseous exchange.

The respiratory system is divided arbitrarily into the upper and lower respiratory tracts. In addition to these structures, the respiratory system also includes the oral cavity, rib cage and diaphragm.

Upper respiratory tract

The upper respiratory tract comprises those structures located outside the thorax – the nasal cavity, pharynx and larynx.

Nasal cavity

The internal portion of the nose is known as the *nasal cavity* and lies over the roof of the mouth. It is a hollow structure but is separated by a midline partition known as the *septum*. The septum has a rich blood supply, which means that direct blows to the nose result in nosebleed. The cavity is divided into a larger respiratory region and a smaller olfactory region. The nasal cavity is connected to the pharynx through two openings called the *internal nares*. The respiratory region is lined with cilia and plays an important part in respiration because it filters out large dust particles. The inhaled air circulates, allowing it to be warmed by close contact with blood from the capillaries. Mucus secreted from goblet cells also helps moisten the air.

Pharynx

The pharynx is a tubelike structure approximately 12 cm long that serves as a common pathway for the respiratory and digestive tracts. It has three anatomical divisions – the nasopharynx, oropharynx and laryngopharynx. It is lined with a ciliated mucous membrane that helps with the removal of dust particles as it does the larynx. It also affects speech production by changing shape to allow vowel sounds to be formed.

Larynx (voice box)

The triangular shaped larynx is a short passageway that connects the pharynx with the trachea that lies in the mid-line of the neck. It protects the airway against the entrance of liquids and foods during swallowing via the glottis and epiglottis, which act like trap doors to ensure that liquids and food are routed into the oesophagus and not the trachea.

Lower respiratory tract

The lower respiratory tract is located almost entirely within the thorax. It is comprised of the trachea, bronchial tree and lungs.

Trachea (windpipe) and bronchi

The trachea is an 11-cm-long tube that lies in front of the oesophagus and extends from the larynx to the fifth thoracic vertebra, where it divides into the right and left primary bronchi. The bronchi divide and subdivide into bronchioles and resemble an inverted tree trunk, giving rise to the term *bronchial tree*. Eventually, these divisions form terminal bronchioles, giving rise to alveolar ducts and sacs, the walls of which consist of alveoli where gaseous exchanges take place. The epithelial lining of the bronchial tree acts as a defence mechanism known as the *mucociliary escalator*. Cilia on the surface of cells beat upwards in organized waves of contraction, thus expelling foreign bodies.

Lungs

The lungs are paired, cone-shaped organs divided into lobes; the left lung has two lobes and the right lung three lobes, which occupy the thoracic cavity. The thoracic cavity plays an important part in respiration because it becomes larger when the chest is raised and smaller when it is lowered, affecting inspiration and expiration. Enclosing the lungs are the pleural membranes; the inner membrane covers the lungs, and the outer membrane is attached to the thoracic cavity. Between the membranes is the pleural cavity, which contains fluid and prevents friction between the membranes during breathing. If the pleura is inflamed, respiration becomes painful.

History taking and physical examination

Cough, cold, sore throat and rhinitis often coexist, and an accurate history is therefore essential to differentially diagnose a patient who presents with symptoms of respiratory disease. A number of similar questions must be asked for

each symptom, although symptom-specific questions are also needed (and are discussed under each heading that follow). Currently, examination of the respiratory tract is outside the remit of the community pharmacist unless they have additional qualifications (e.g., independent prescriber status). An examination involving palpation, percussion and auscultation may support a differential diagnosis after history taking.

Cough

Background

Coughing is the body's defence mechanism in an attempt to clear the airways of foreign bodies and particulate matter. This is supplemented by the mucociliary escalator – the upward beating of the finger-like cilia in the bronchi that move mucus and entrapped foreign bodies to be expectorated or swallowed. Cough is the most common respiratory symptom and one of the few ways whereby abnormalities of the respiratory tract manifest themselves. Cough can be very debilitating to the patient's well-being and can also be disruptive to family, friends and work colleagues.

Coughs can be described as productive (chesty) or nonproductive (dry, tight, tickly). However, many patients will say that they are not producing sputum, although they may go on to say that they 'can feel it on their chest'. In these cases, the cough is probably productive in nature and should be treated as such.

The British Thoracic Society Guidelines (2019) state that cough is usually self-limiting and will resolve in 3 or 4 weeks without the need for antibiotics. Coughs are classified as *acute* or *chronic* in nature, and guidance from current Clinical Knowledge Summaries define cough as follows:

- Acute when present for less than 3 weeks
- Subacute when present for 3 to 8 weeks
- Chronic when present for more than 8 weeks

Although these times are only considered indicative, patients who present with cough, other than acute cough (not being systemically unwell), are usually best referred to a medical practitioner for further investigation.

Prevalence and epidemiology

Statistics from UK general medical practice show that respiratory illness accounts for more patient visits than any other disease category. Acute cough is usually caused by a viral upper respiratory tract infection (URTI) and constitutes 20% of consultations. This translates to 12 million GP visits per year and represents the largest single cause of primary care consultation. These data are echoed elsewhere; for example,

episodes of URTI are the most common acute condition seen in Australian general practice (Cooke G, et al., 2013). In community pharmacy, the figures are even higher, with at least 24 million visits per year (or 2000 visits per UK pharmacy each year).

Schoolchildren experience the greatest number of coughs, with an estimated 7 to 10 episodes per year (compared with adults, with two to five episodes per year). Acute viral URTIs exhibit seasonality, with a higher incidence seen in the winter months.

Aetiology

The vast majority (90%) of URTIs are caused by viruses. These include respiratory syncytial virus, rhinovirus and viral influenza. The remaining 10% of infections involve bacteria and include *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Staphylococcus aureus* and *Klebsiella pneumoniae*, although these infections often have a viral element. A five-part cough reflex is responsible for cough production. Receptors located mainly in the pharynx, larynx, trachea and bifurcations of the large bronchi are stimulated via mechanical, irritant or thermal mechanisms. Neural impulses are then carried along afferent pathways of the vagal and superior laryngeal nerves, which terminate at the cough centre in the medulla. Efferent fibres of the vagus and spinal nerves carry neural activity to the muscles of the diaphragm, chest wall and abdomen. These muscles contract and are followed by the sudden opening of the glottis, which creates the cough.

Arriving at a differential diagnosis

As stated above, the most likely cause of acute cough in primary care for all ages is a viral infection. Recurrent viral bronchitis is most prevalent in preschool and young school-aged children, and is the most common cause of persistent cough in children of all ages. [Table 2.1](#) highlights those conditions that can may be encountered by community pharmacists and their relative incidence.

As viral infection is by far the most likely cause of cough in all age groups, it is logical to hypothesize that this will be the cause of the cough, and questions should be directed to help confirm or refute this assumption (using hypothetico-deductive reasoning; see chapter 1). Asking symptom-specific questions will help the pharmacist establish a differential diagnosis ([Table 2.2](#)).

Clinical features of acute viral cough

Viral coughs typically present with sudden onset and associated fever. Sputum production is minimal, and symptoms are often worse in the evening. Associated cold symptoms are

Table 2.1
Causes of cough and their relative incidence in community pharmacy

Incidence	Cause
Most likely	Viral infection
Likely	Upper airways cough syndrome (formerly known as <i>postnasal drip</i> ; includes allergies), acute bronchitis
Unlikely	Croup, chronic bronchitis, COPD, asthma, pneumonia, ACE inhibitor induced
Very unlikely	Heart failure, bronchiectasis, tuberculosis, cancer, pneumothorax, lung abscess, nocardiosis, GORD, psychogenic cough

ACE, Angiotensin-converting enzyme; *COPD*, chronic obstructive pulmonary disease; *GORD*, gastro-oesophageal reflux disease.

also often present; these usually last between 7 and 10 days. A duration of longer than 14 days might suggest postviral cough or possibly indicate a bacterial secondary infection, but this is clinically difficult to establish without sputum samples being analysed. A common misconception is that cough with mucopurulent sputum is bacterial in cause and requires referral. This is almost never the case, and people should not be routinely referred to the GP for cough associated with mucopurulent sputum.

Conditions to eliminate

Likely causes

Upper airways cough syndrome

This was previously referred to as *postnasal drip* or *rhinosinusitis*. Postnasal drip has been broadened to include a number of rhinosinus conditions related to cough. The umbrella term of *upper airways cough syndrome* (UACS) is now routinely adopted (Pratter, 2016).

UACS is characterized by a sinus or nasal discharge that flows behind the nose and into the throat, experienced by patients as abnormal sensations arising from the throat (i.e., patients describe something stuck in the throat). Patients should always be asked whether they are swallowing mucus or notice that they are clearing their throat more than usual. Chronic cough is also characteristically associated with UACS.

Allergies are one cause of UACS. Coughs caused by allergies are often nonproductive and worse at night. However, there are usually other associated symptoms, such as



Table 2.2
Specific questions to ask the patient: Cough

Question	Relevance
Sputum colour	Mucoid (clear and white) normally of little consequence, suggests that no infection is present; yellow, green or brown sputum normally indicates infection; <i>mucopurulent sputum is generally caused by a viral infection and does not require automatic referral.</i> Haemoptysis can be rust coloured (pneumonia), pink tinged (left ventricular failure), or dark red (carcinoma); occasionally, patients can produce sputum with bright red blood as a single event due to the force of coughing, causing a blood vessel to rupture. This is not serious and does not require automatic referral.
Nature of sputum	Thin and frothy suggests left ventricular failure; thick, mucoid to yellow, can suggest asthma. Offensive foul-smelling sputum suggests bronchiectasis or lung abscess.
Onset of cough	Cough worse in the morning – may suggest upper airways cough syndrome, bronchiectasis or chronic bronchitis.
Duration of cough	Acute cough can sometimes take 4 weeks or more to resolve (British Thoracic Society Guidelines Guidelines, 2019). However, coughs lasting longer than 3 weeks should be viewed with caution – the longer the cough is present, the more likely serious pathology is responsible. For example, the likely diagnosis at 3 days will be upper respiratory tract infection (URTI); at 3 weeks acute, or chronic bronchitis; and at 3 months, conditions such as chronic bronchitis, gastro-oesophageal reflux disease (GORD), and carcinoma.
Periodicity	Adult patients with recurrent cough might have chronic bronchitis, especially if they smoke. Care should be exercised in children who present with recurrent cough and have a family history of eczema, asthma or hay fever. This might suggest asthma and referral would be required for further investigation.
Age of the patient	Children will most likely be suffering from a URTI but asthma and croup should be considered; with increasing age, conditions such as bronchitis, pneumonia and carcinoma become more prevalent.
Smoking history	Patients who smoke are more prone to chronic and recurrent cough. Over time, this might develop into chronic bronchitis and chronic obstructive pulmonary disease (COPD).

sneezing, nasal discharge or blockage, conjunctivitis and an itchy oral cavity. Cough of an allergic origin might show seasonal variation; for example, hay fever. Other causes include vasomotor rhinitis (caused by odours and changes in temperature/humidity) and postinfectious UACS after a URTI. If UACS is present, it is better to direct treatment at the cause of the UACS (e.g., antihistamines or decongestants) rather than just treat the cough.

Acute bronchitis

Most cases are seen in autumn or winter, and symptoms are similar to those of viral URTI, but patients also tend to exhibit dyspnoea and wheeze. The cough usually lasts for 7 to 10 days but can persist for 3 weeks. The cause is normally viral, but is sometimes bacterial. Symptoms will resolve without antibiotic treatment, regardless of the cause. If the person is systemically unwell, referral is appropriate.

Unlikely causes

Laryngotracheobronchitis (croup)

Symptoms are triggered by a recent infection with parainfluenza virus and account for 75% of cases; other viral pathogens include rhinovirus and respiratory syncytial virus. It affects infants aged between 3 months and 6 years and affects 2% to 6% of children. The incidence is highest in those between 1 and 2 years of age and occurs slightly more in boys than in girls; it is more common in the autumn and winter months. Symptoms occur in the late evening and night. The cough can be severe and violent and is described as having a barking (seal-like) quality. In between coughing episodes, the child may be breathless and struggle to breathe properly. Typically, symptoms improve during the day and often recur again the following night, with most children seeing symptoms resolve in 48 hours. Warm moist air as a

treatment for croup has been used since the 19th century. However, current guidelines do not advocate humidification because there is no evidence to support its use.

Croup management is based on an assessment of severity. Parents should be advised that if the child's symptoms persist beyond 48 hours, or they exhibit any symptoms of stridor or distress, medical intervention is required. Standard treatment for children with stridor would be oral or intramuscular dexamethasone or nebulized budesonide (Gates et al., 2018).

Chronic obstructive pulmonary disease

Chronic obstructive pulmonary disease (COPD) is characterized by the destruction of lung tissue and is the preferred term for chronic bronchitis (CB), emphysema and chronic obstructive airways disease. It is characterized by cough, sputum production and increasing breathlessness; it is treatable although not curable. The prevalence of COPD in the UK is uncertain, but figures from the British Lung Foundation (2019) estimated that more than 1.2 million individuals had a diagnosis of COPD, which accounts for approximately 30 000 deaths each year. COPD prevalence increases with age and is more common in men. Typical symptoms include chronic cough, breathlessness on exertion, wheezing and recurrent chest infections. Confirmation of the diagnosis is by spirometry testing. Patients with established COPD often experience acute exacerbations marked by a reduction in activities and more pronounced breathlessness. In such cases, the patient requires referral to the GP for potential antibiotics and steroid therapy.

A history of smoking is the single most important factor in the cause of CB. Therefore, early intervention by community pharmacy teams to stop patients smoking could help prevent deterioration in lung function. In nonsmokers, the likely cause of CB is UACS, asthma or gastro-oesophageal reflux. One study has shown that 99% of nonsmokers with CB and a normal chest x-ray suffered from one of these three conditions (Simpson & Amin, 2006).

Asthma

The exact prevalence of asthma is unknown due to differing terminologies and definitions, plus difficulties in correct diagnosis, especially in children, and comorbidity with COPD in older adults. Best estimates of adult asthma prevalence are approximately 4% to 10%. In children, the figures are higher (10%–15%) because a proportion of children will grow out of it and be symptom-free by adulthood. This equates to 5.4 million people receiving asthma treatment.

Asthma is a chronic inflammatory condition of the airways characterized by coughing, wheezing, chest tightness, and shortness of breath. Typically, these symptoms tend to be variable, intermittent, worse at night, and provoked by triggers (e.g., allergens, infections, irritant exposure). In

addition, possible risk factors associated with the development of asthma include a family or personal history of atopy.

In the context of presentations to a community pharmacist, asthma can also present as a nonproductive cough (or minimally productive) especially in young children, in whom the cough is often worst at night and recurrent.

Pneumonia (community-acquired)

Every year, between 0.5% and 1% of adults in the UK will have community-acquired pneumonia. Bacterial infection is usually responsible for pneumonia and is most commonly caused by *S. pneumoniae* (80% of cases), although other pathogens are also responsible (e.g., *Chlamydia*, *Mycoplasma*). Initially, the cough is nonproductive and painful (first 24–48 hours), but it rapidly becomes productive, with sputum being stained red. The intensity of the redness varies, depending on the causative organism. The cough tends to be worst at night. The patient will be unwell, with a high fever (>38°C), malaise, headache, and breathlessness and experience pleuritic pain (inflammation of pleural membranes, manifested as pain to the sides) that worsens on inspiration. Older patients are often afebrile and may present with confusion. Most cases occur during the autumn and winter months. Urgent referral to a doctor is required so antibiotics can be started as soon as possible.

Medicine-induced cough or wheeze

A number of medicines may cause bronchoconstriction, which presents as coughing or wheezing. Angiotensin-converting enzyme (ACE) inhibitors are most commonly associated with cough. The incidence might be as high as 16%; it is not dose-related, and time to onset is variable, ranging from a few hours to more than 1 year after the start of treatment. Cough invariably ceases after withdrawal of the ACE inhibitor but takes 3 to 4 weeks to resolve. Other medications associated with cough or wheeze are nonsteroidal antiinflammatory drugs (NSAIDs) and beta blockers. If an adverse drug reaction (ADR) is suspected, the pharmacist should discuss an alternative medicine with the prescriber; for example, the incidence of cough with angiotensin II receptor blockers is half that of ACE inhibitors.

Very unlikely causes

Heart failure

Heart failure is a condition of older adults. The prevalence of heart failure rises with increasing age; it is rare in those younger than 65 years but thereafter increases rapidly with increasing age, affecting one in seven people older than 85 years. Heart failure is characterized by an insidious progression; diagnosing early mild heart failure is extremely difficult because symptoms are not pronounced and are

nonspecific. Often, the first symptoms patients experience are fatigue, shortness of breath, orthopnoea and dyspnoea at night. As the condition progresses from mild to moderate to severe heart failure, patients will show ankle swelling and might complain of a productive frothy cough, which may have pink-tinged sputum and may worsen at night.

Bronchiectasis

Bronchiectasis is caused by irreversible dilation of the bronchi, often brought on by a previous lower respiratory tract infection. It might be underdiagnosed because some sufferers are often thought to have COPD. It appears to be more common in women, and prevalence increases with age. Characteristically, the patient has a chronic cough of very long duration. Over 75% of patients will cough daily with sputum production. Breathlessness is a very common accompanying symptom. Approximately one-third of patients will also suffer from wheezing and chest pain.

Tuberculosis

Tuberculosis (TB) is a bacterial infection caused by *Mycobacterium tuberculosis* that is transmitted primarily by inhalation. In 2017, English figures showed there were 5102 cases notified, a drop of almost 40% from a peak in 2011. People born outside the UK (predominantly from India, Pakistan, Romania, Bangladesh and Somalia) represent 70% of cases, and TB still remains concentrated in the most deprived populations. As in previous years, London accounted for the highest proportion of cases (38%), followed by the West Midlands area (13%).

TB is characterized by its slow onset and initial mild symptoms but should be considered in those at high risk and have symptoms of fever, weight loss, night sweats, anorexia or malaise. Cough associated with TB is chronic in nature, and sputum production can vary from mild to severe, with associated haemoptysis, although this feature tends to be late in symptom presentation. A patient with a productive cough for more than 3 weeks and who exhibits one or more of the associated symptoms should be referred for further investigation, which includes chest x-rays and sputum smear tests.

Carcinoma of the lung

Lung cancer is the third most common cancer in the UK, with almost 50 000 new cases each year, and is strongly related to increasing age – those older than 40 to 45 years. Multiple symptoms can be present, such as cough, fatigue, shortness of breath, chest pain, weight loss and appetite loss. If a person older than 40 years has two or more of these symptoms, he or she needs to be referred to the GP for a chest x-ray. Cough is common, reportedly affecting 47% to 86% of patients at

some point during the progression of the carcinoma (Malassiotis et al., 2010). The cough produces small amounts of sputum that might be blood-streaked. The possibility of carcinoma increases in long-term cigarette smokers who have had a cough for a number of months or who have developed a marked change in the character of their cough.

Lung abscess

A typical presentation is initially a nonproductive cough with pleuritic pain and dyspnoea, with signs of infection such as malaise and fever. Later, the cough produces large amounts of purulent and often foul-smelling sputum. It is more common in older adults.

Spontaneous pneumothorax (collapsed lung)

Rupture of the bullae – the small air or fluid-filled sacs in the lung – can cause spontaneous pneumothorax, but normally there is no underlying cause. It affects approximately 1 to 2 people in every 10 000, and is most common in young men. Smoking is the most important risk factor, although approximately 10% of patients have a family history of the disease. Key presenting symptoms are sharp unilateral pleuritic pain and shortness of breath. The patient is likely to show signs of distress. This can be a life-threatening disorder, and immediate onward referral to hospital is required.

Gastro-oesophageal reflux disease

Gastro-oesophageal reflux disease (GORD) does not usually present with cough, but patients with this condition might cough when recumbent (lying down). The patient might show symptoms of reflux or heartburn. Patients with GORD have increased cough reflex sensitivity and respond well to proton pump inhibitors. GORD should always be considered in all cases of unexplained cough.

Nocardiosis and psychogenic cough

It is very unlikely that a pharmacist will ever encounter these conditions; they are included here for the sake of completeness. Nocardiosis is an extremely rare bacterial infection caused by *Nocardia asteroides*; it is transmitted primarily by inhalation. It has a higher incidence in older adults, especially in men. The sputum is purulent, thick and possibly blood-tinged. Fever is prominent, and night sweats, pleurisy, weight loss and fatigue might also be present. If no organic cause of cough can be found, psychogenic cough should be considered. In such cases, cough is absent at night. In children, it is associated with attention seeking, and in adults it is linked to anxiety disorders.

Fig. 2.1 will aid in the differentiation between serious and nonserious conditions of cough in adults.

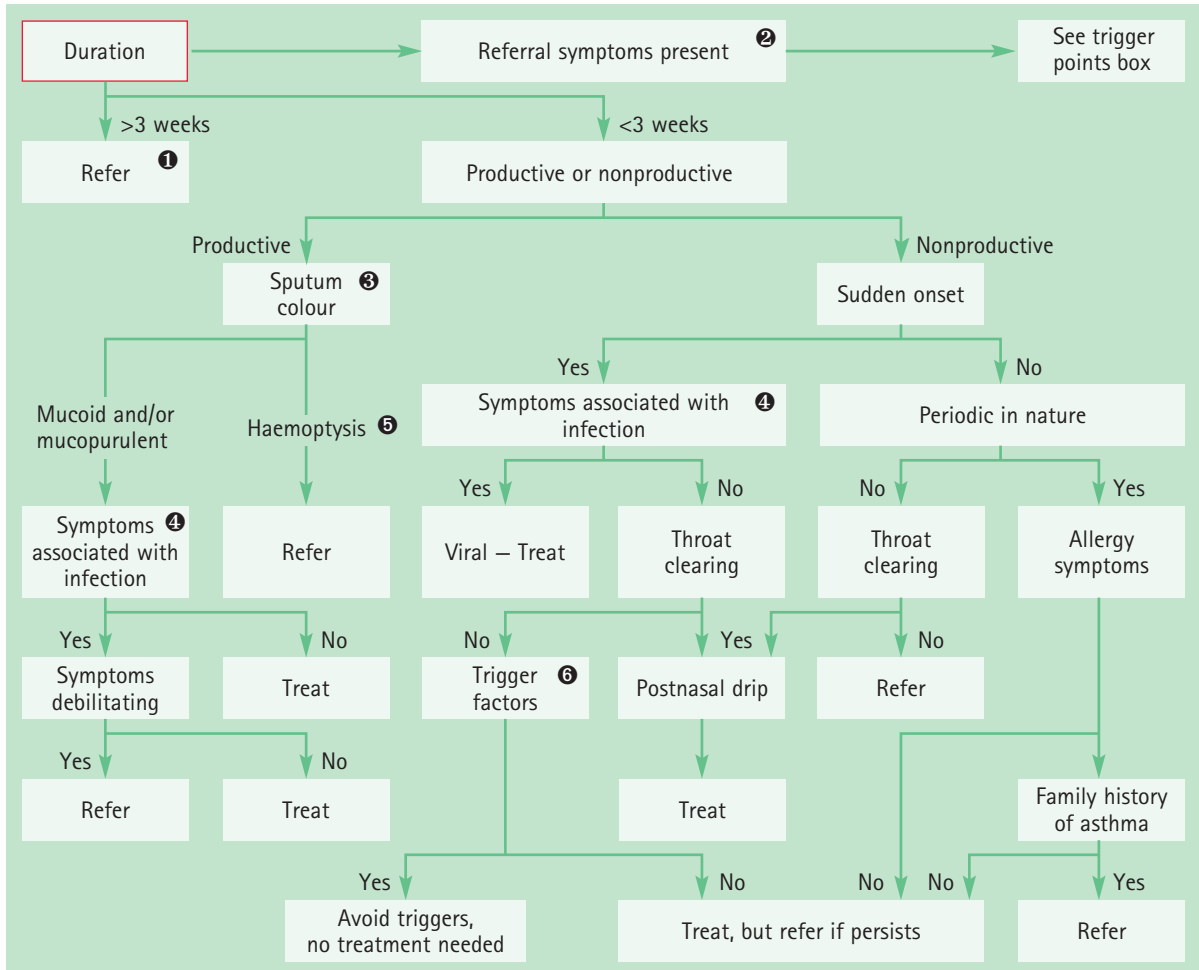


Fig. 2.1 Primer for differential diagnosis of cough in adults.

1 Duration of cough. Coughs lasting longer than 3 weeks are considered not to be acute in nature; conditions with sinister pathology are more likely the longer the cough has been present. However, not all coughs that have lasted 3 weeks have to be referred automatically. For example, upper airways cough syndrome (UACS) can persist for weeks and be managed by community pharmacists.

2 Referral symptoms. Certain symptoms warrant direct referral to the general practitioner (GP) or even casualty. The severity of these symptoms should dictate which referral option is most appropriate.

3 Sputum colour. Sputum colour can be helpful in deciding when to refer. However, there is a common misconception that patients who present with green-yellow or brown sputum have a bacterial infection; this is not the case – almost all will be viral in origin. If the cough has persisted

for more than 2 weeks, it is possible that an initial viral infection has become secondarily infected with a bacterial infection. This could indicate referral, especially if the symptoms are debilitating or if the patient is an older adult.

4 Symptoms associated with infection. The patient might have associated symptoms of fever, rhinorrhoea and sore throat.

5 Haemoptysis. Blood in the sputum requires further investigation, especially if the person has had the symptoms for a period of time.

6 Trigger factors. Certain atmospheric factors can trigger cough. These factors include air temperature changes, pollution (e.g., cigarette smoke) and dry atmospheres (e.g., air conditioning).


TRIGGER POINTS indicative of referral: Cough

Symptoms/signs	Possible danger/ reason for referral	Urgency of referral
Chest pain Haemoptysis Pain on inspiration Wheezing and/ or shortness of breath	All symptoms suggest possible sinister pathology or severe cases of simple viral infection	Urgent same- day referral. Depending on severity, may mean referring to hospital rather than GP
Duration > 3 weeks Cough that recurs on a regular basis	Suggests nonacute cause of cough and requires further investigation	As soon as practicable
Debilitating symptoms in older adults	This patient group at greater risk of complications	Urgent same- day referral
Persistent nocturnal cough in children	Suggests possible asthma	As soon as practicable

Evidence base for over-the-counter medication

Cough is often trivialized by practitioners, but coughing can impair quality of life and cause anxiety to parents of children with cough (Dicpinigaitis et al., 2009). Patients who exercise self-care will be confronted with a plethora of over-the-counter (OTC) medication, and many will find the choice overwhelming. All active ingredients to treat cough were brought to the market many years ago when clinical trials suffered from flaws in study design compared with today's standards; thus, their clinical efficacy is difficult to establish. Compounding these problems is the self-limiting nature of acute cough, which further hinders the differentiation between clinical efficacy and normal symptom resolution. However, there is growing evidence of the lack of demonstrable efficacy and potential safety concerns, in particular in children.

Expectorants

A number of active ingredients have been formulated to help expectoration, including guaifenesin, ammonium salts, ipecacuanha, creosote and squill. Most products marketed in the UK for productive cough contain guaifenesin, although products containing squill (e.g., Buttercup Original Cough

Syrup, Covonia Chesty Cough Mixture Mentholated) and ipecacuanha (e.g., Covonia Herbal Mucus Cough Syrup) are available.

However, the clinical evidence available for any active ingredient is limited. Older ingredients, such as ammonium salts, ipecacuanha and squill, were traditionally used to induce vomiting, and it was believed that at subemetic doses, they would cause gastric irritation, triggering reflex expectoration; but this has never been proven and belongs in the annals of folklore. Guaifenesin is thought to stimulate secretion of respiratory tract fluid, increasing sputum volume and decreasing viscosity, thus assisting in the removal of sputum. Guaifenesin is the only active ingredient that has any evidence of effectiveness. Three studies identified by Smith et al. (2014) in their systematic review found conflicting results for guaifenesin as an expectorant. In the largest study ($N = 239$), participants stated that guaifenesin significantly reduced cough frequency and intensity compared with placebo. In a smaller trial ($N = 65$), guaifenesin was found to have no effect on cough frequency or severity compared with placebo.

A more recent study comparing extended-release guaifenesin with placebo ($N = 378$) found no difference in spontaneous symptom severity scores on day 7 but found a reduction from baseline in scores on day 4 (7.1 vs 5.7; $P = .04$). The clinical significance of this difference is uncertain.

Summary

Based on studies, guaifenesin is the only expectorant with any evidence of effectiveness. However, trial results are not convincing, and guaifenesin is probably little or no better than placebo. Given its proven safety record, absence of drug interactions, and the public's desire to treat productive coughs with a home remedy, it would seem reasonable to supply OTC cough medicines containing guaifenesin.

Cough suppressants (antitussives)

Cough suppressants act directly on the cough centre to depress the cough reflex. Their effectiveness has been investigated in patients with acute and chronic cough, as well as citric acid-induced cough. Although trials on healthy volunteers, in whom coughing was induced by citric acid, allowed reproducible conditions to assess the activity of antitussives, they are of little value because they do not represent physiological cough. Of greatest interest to OTC medication are trials investigating acute cough because patients suffering from chronic cough should be referred to a doctor.

Codeine

Codeine is generally accepted as a standard or benchmark antitussive against which all others are judged. A review

by Eddy et al. (1970) showed codeine to be an effective antitussive in animal models, and cough-induced studies in humans have also shown codeine to be effective. However, these findings appear to be less reproducible in acute and pathological chronic cough. More recent studies have failed to demonstrate a significant clinical effect of codeine compared with placebo in patients suffering with acute cough. Greater voluntary control of the cough reflex by patients has been suggested for the apparent lack of effect of codeine on acute cough.

Pholcodine

Pholcodine, like codeine, has been subject to limited clinical trials, with most being animal models or citric acid-induced cough studies in humans. These studies have shown pholcodine to have antitussive activity. A review by Findlay (1988) concluded that on balance, pholcodine appeared to possess antitussive activity but advocated the need for better, well-controlled studies. Of interest, a Cochrane review by Smith et al. (2014) failed to identify any studies using pholcodine that met their inclusion criteria to include in the review, suggesting that there are no robust data supporting the use of pholcodine.

Dextromethorphan

Trial data for dextromethorphan, like that for codeine and pholcodine, are limited. The Cochrane review of cough mixtures (Smith et al., 2014) identified three studies comparing dextromethorphan with placebo in adults. Two studies found an improvement in cough counts and cough effort, which in one study equated to a difference of up to 8 to 10 coughing bouts every 30 minutes. The third study found no difference between dextromethorphan and placebo in terms of cough frequency and subjective cough scores. It appears to have limited abuse potential and fewer side effects than codeine.

Antihistamines

Antihistamines have been included in cough remedies for decades. Their mechanism of action is thought to be through the anticholinergic-like drying action on the mucous membranes and not via histamine. There are numerous clinical trials involving antihistamines for the relief of cough and cold symptoms, most notably with diphenhydramine.

Citric acid-induced cough studies have demonstrated significant antitussive activity compared with placebo, and results from chronic cough trials support an antitussive activity for diphenhydramine. However, trials that showed a significant reduction in cough frequency suffered from having small patient numbers, thus limiting their usefulness. Additionally, poor methodological design of trials

investigating the antitussive activity of diphenhydramine in acute cough makes assessment of its effectiveness difficult. One review concluded that 'Presumptions about efficacy of diphenhydramine against cough in humans are not unequivocally substantiated in literature' (Bjornsdottir et al., 2007). Less sedating antihistamines have also not been shown to have any benefit in treating coughs compared with placebo (Smith et al., 2014).

Demulcents

Demulcents, such as simple linctus and honey, are pharmacologically inert and are used on the theoretical basis that they reduce irritation by coating the pharynx and thus prevent coughing. However, there is no evidence for their efficacy, and they are used mainly for their placebo effect. A Cochrane review explored the evidence for the use of honey in acute cough in children (Oduwole et al., 2018). The review included six trials involving 899 children. The review found moderate- to low-quality evidence that honey was probably more effective than no treatment or placebo, and giving honey for up to 3 days is probably more effective in relieving the duration of cough symptoms compared with placebo.

Combination cough mixtures

Many OTC cough preparations are combinations of agents. Some of these include ingredients, such as decongestants, that target other symptoms of URTIs. It should be noted that some combination products contain subtherapeutic doses of the active ingredients, and a few contain illogical combinations such as cough suppressants with an expectorant or an antihistamine with an expectorant. If possible, these should be avoided.

Summary

Antitussives have traditionally been evaluated for efficacy in animal studies or cough-induced models on healthy volunteers. This presents serious problems in assessing their effectiveness because support for their antitussive activity does not come from patients with acute cough associated with URTI. Furthermore, there appear to be no comparative studies of sound study design to allow for judgements to be made on their comparable efficacy.

Antitussives, therefore, have a limited role in the treatment of acute nonproductive cough. Patients should not be routinely prescribed antitussives but instead encouraged to drink more fluids and told that their symptoms will resolve in time on their own. If recommended, dextromethorphan is the only agent with any evidence of effectiveness; its side effect profile and abuse tendency rather than clinical efficacy may drive this choice. On this basis, dextromethorphan

would be first-line therapy and pholcodine second-line treatment. The use of codeine or antihistamines seems difficult to justify.

Cough medications for children

Very few well-designed studies have been conducted in children. A review published in the *Drug and Therapeutics Bulletin* (Anonymus, 1999) identified just five trials of sound methodological design. However, of these five trials, one study used illogical drug combinations (expectorant combined with suppressant), and a further three studies used combination products not available on the UK market. In addition, there has been growing evidence of the potential harm that these agents can pose to young children, either due to adverse effects or from accidental inappropriate dosing (Isbister et al., 2012; Vassilev et al., 2010). In 2014, a Cochrane review examining the treatment of acute cough in adults and children concluded there was no good evidence to support the effectiveness of cough medicines in acute cough (Smith et al., 2014).

It therefore seems difficult to justify the use of such products in children. Simple measures of keeping well hydrated and the use of demulcents are more appropriate.

Herbal products

A number of herbal ingredients are included in cough medicines; for example, *Pelargonium sidoides* (geranium), echinacea, *Andrographis paniculata* (green chiretta), ivy, primrose and thyme (Wagner et al., 2015). In Wagner's review, very low-quality evidence was found that ivy, primrose or thyme significantly reduced cough compared with placebo in people with acute cough. Commercially, in the UK, thyme is included in the product Bronchostop but, based on this evidence, should not be routinely recommended.

Practical prescribing and product selection

Prescribing information relating to the cough medicines reviewed in the section 'Evidence base for over-the-counter medication' is discussed and summarized in [Table 2.3](#); useful tips relating to patients presenting with cough are given in 'Hints and Tips' in [Box 2.1](#). Due to a series of Medicines and Healthcare products Regulatory Agency (MHRA) announcements on cough products, many manufacturers have taken the opportunity to revise their prescribing information and no longer recommend cough products in children younger than 12 years. The use of antitussives, and codeine, is now widely discouraged and, in Australia, codeine is no longer available OTC.

Cough expectorants

Guaifenesin

Almost all manufacturers (e.g., in the Benylin, Lemsip, and Robitussin products) include guaifenesin. Adults and children 12 years and older should take 200 mg four times a day; in products licensed for children, the dose is 100 mg four times a day. Guaifenesin-based products have no cautions in their use and no side effects; they are also free from clinically significant drug interactions so can be given safely with prescribed medication. Sugar-free versions (e.g., Robitussin products) are available.

Cough suppressants

Codeine, pholcodine and dextromethorphan are all opiate derivatives and therefore, broadly, have the same interactions, cautions in use and side effect profiles. They do interact with prescription-only medications (POMs) and also with OTC medications, especially those that cross the blood-brain barrier. Their combined effect is to potentiate sedation, and it is important to warn the patient of this, although short-term use of cough suppressants with the interacting medication is unlikely to warrant dosage modification.

Dextromethorphan may increase the risk of serotonin syndrome if given with other drugs that contribute to serotonin syndrome, such as monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors (SSRIs) and tramadol, and manufacturers specifically warn against the combination with MAOIs.

Care should be exercised when giving cough suppressants to asthmatics because, in theory, cough suppressants can cause respiratory depression. In practice, however, this is very rarely observed and does not preclude the use of cough suppressants for asthmatic patients.

Codeine

The dose for adults and children older than 18 years is 5 mL three or four times a day.

Pholcodine

The adult dose is 5 to 10 mL (5–10 mg) three or four times a day. Most marketed products now state avoidance in children, but the British National Formulary (BNF) still states that it can be given to children aged 6 years and older. If given, the standard dose is 2 to 5 mg three or four times a day. Sugar-free versions (e.g., Pavacol-D) are available.

Dextromethorphan

For adults and children aged over 12, there are a number of products available (e.g., Benylin dry coughs; Covonia Original Bronchial Balsam, and Robitussin Dry Cough medicine).



Table 2.3
Practical prescribing: Summary of cough medicines

Name of medicine	Use in children: Age (years)	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy & breastfeeding
<i>Cough expectorants</i>					
Guaifenesin	>6	None	None	None	OK
<i>Cough suppressants</i>					
Codeine (best avoided)	>18	Sedation, constipation	Increased sedation with alcohol, opioid analgesics, anxiolytics, hypnotics, antidepressants	Asthmatics	Pregnancy – best avoided in third trimester; short periods OK in breastfeeding; reports of dextromethorphan causing drowsiness and poor feeding in the baby
Pholcodine	>6 ^a	Possible sedation			
Dextromethorphan	>12 ^a				
<i>Antihistamines</i>					
Diphenhydramine	>6	Dry mouth, sedation, constipation	Increased sedation with alcohol, opioid analgesics, anxiolytics, hypnotics, antidepressants	Glaucoma, prostate enlargement	Pregnancy – standard references state OK, although some manufacturers advise avoidance; breastfeeding OK, because amount secreted into breast milk is small but may, however, reduce milk supply; reports of poor feeding in the baby
<i>Demulcents</i>					
Simple linctus	>1 month	None	None	None	OK

^aNot recommended for adolescents (aged 12–18 years) who have problems with breathing.

HINTS AND TIPS BOX 2.1: COUGH

Treatment for children <6 years	Parents should be advised to make the child drink more fluid and potentially try a nonpharmacological cough mixture, such as a demulcent.
Insulin-dependent diabetics	People with insulin-dependent diabetes should be asked to monitor their blood glucose level more frequently because insulin requirements increase during acute infections.
Avoid theophylline	Theophylline is available as a pharmacy-only medicine, but is best avoided because patients requiring medication to help with shortness of breath or wheeze need further assessment.

The dosing for these listed products is standard, 10 mL four times a day.

Antihistamines

The routine use of antihistamines is unjustified in treating nonproductive cough. However, the sedative side effects from antihistamines can, on occasion, be useful to allow the patient an uninterrupted night's sleep. Diphenhydramine is included in some Benylin and Covonia products.

All antihistamines included in cough remedies can interact with other sedating medication, resulting in potentiation of the sedative properties of the interacting medicines. They also possess antimuscarinic side effects, which commonly result in dry mouth and possibly constipation. Because of these antimuscarinic properties, patients with glaucoma and prostate enlargement should ideally avoid their use because it could lead to increased intraocular pressure and precipitation of urinary retention.

Demulcents

Demulcents – for example, simple linctus and glycerine – provide a safe alternative for at-risk patient groups, such as older adults, pregnant women, young children and those taking multiple medications. They are being increasingly used because manufacturers have reformulated their cough products in light of restrictions placed on antitussives. They can act as useful placebos when the patient insists on a cough mixture. If recommended, they should be given three or four times a day.

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- The British Thoracic Society: <https://www.brit-thoracic.org.uk/>

The common cold

Background

Colds, along with coughs, represent the largest caseload for primary healthcare workers. Because the condition has no specific cure and is self-limiting, with two-thirds of sufferers recovering within 1 week, it would be easy to dismiss the

condition as unimportant. However, because of the very high number of cases seen, it is essential that pharmacists have a thorough understanding of the condition so that severe symptoms or symptoms suggestive of influenza are identified.

Prevalence and epidemiology

The common cold is extremely prevalent and, like cough, is caused by a viral URTI. Children contract colds more frequently than adults, with on average 5 to 6 colds per year compared with 2 to 4 colds in adults, although in children this can be as high as 12 colds per year. Children aged between 4 and 8 years are most likely to contract a cold, and it can appear to a child's parents that one cold follows another, with no respite. By the age of 10, the number of colds contracted is half that observed in preschool children. In the UK, colds peak in December and January, possibly due to increased crowding indoors during cold weather.

Aetiology

More than 200 subtypes of viruses can produce symptoms of the common cold, including rhinoviruses (accounting for 30%–50% of all cases), coronaviruses, parainfluenza virus, respiratory syncytial virus, and adenovirus. Transmission is primarily by the virus coming into contact with the hands, which then touch the nose, mouth and eyes (direct contact transmission). Droplets shed from the nose coat surfaces such as door handles and telephones. Cold viruses can remain viable on these surfaces for several hours and, when an uninfected person touches the contaminated surface, transmission occurs.

Transmission by coughing and sneezing does occur, although it is a secondary mechanism. This is why good hygiene (washing hands frequently and using disposable tissues) remains the cornerstone of reducing the spread of colds.

Once the virus is exposed to the mucosa, it invades the nasal and bronchial epithelia, attaching to specific receptors and causing damage to the ciliated cells. This results in the release of inflammatory mediators, which, in turn, leads to inflammation of the tissues lining the nose. Permeability of capillary cell walls increases, resulting in oedema, which is experienced by the patient as nasal congestion and sneezing. Fluid might drip down the back of the throat, spreading the virus to the throat and upper chest, causing cough and sore throat. Colds are most contagious during the first 1 to 2 days of symptoms.

Arriving at a differential diagnosis

It is extremely likely that someone presenting with cold symptoms will have a viral infection. [Table 2.4](#) highlights conditions that may be encountered by community pharmacists and their relative incidence.

Table 2.4
Causes of cold and their relative incidence in a community pharmacy

Incidence	Cause
Most likely	Viral infection
Likely	Rhinitis, rhinosinusitis, otitis media
Unlikely	Influenza

Most people will accurately self-diagnose a common cold, and it is the pharmacist's role to confirm this self-diagnosis and assess the severity of the symptoms because some patients – for example, the elderly, infirm and those with existing medical conditions, might need greater support and care. In the first instance, the pharmacist should make an overall assessment of the person's general state of health. Anyone with debilitating symptoms that effectively prevents him or her from doing normal daily routines should be managed more carefully. Although it is likely that a patient will have a common cold, severe colds can mimic symptoms of flu, which is the only condition of any real significance that has to be eliminated before treatment can be given, although secondary complications associated with the common cold can occur. Asking symptom-specific questions will help the pharmacist establish a differential diagnosis ([Table 2.5](#)).



Table 2.5
Specific questions to ask the patient:
The common cold

Question	Relevance
Onset of symptoms	Peak incidence of flu is in the winter months; the common cold occurs any time throughout the year. Flu symptoms tend to have a more abrupt onset than the common cold – a matter of hours rather than 1 or 2 days. Summer colds are common, but they must be differentiated from seasonal allergic rhinitis (hay fever).
Nature of symptoms	Marked myalgia, chills and malaise are more prominent in flu than in the common cold. Loss of appetite is also common with flu.
Aggravating factors	Headache and pain that is worsened by sneezing, coughing and bending over suggests sinus complications. If ear pain is present, especially in children, middle ear involvement is likely.

Clinical features of the common cold

Symptoms of the common cold are well known. However, the nature and severity of symptoms will be influenced by factors such as the causative agent, patient age and underlying medical conditions. Following an incubation period of between 1 and 3 days (although this can be as short as 10–12 hours), the patient develops a sore throat and sneezing, followed by profuse nasal discharge and congestion. Cough and UACS commonly follow. In addition, headache, mild to moderate fever ($<38.9^{\circ}\text{C}$; [102°F]), and general malaise may be present. Most colds resolve in 1 week, but up to 25% of people will have symptoms lasting 14 days or more.

Conditions to eliminate

Likely causes

Rhinitis

A blocked or stuffy nose, whether acute or chronic in nature, is common. Rhinitis is covered in more detail later in this chapter, and the reader is referred to this section for the differential diagnosis of rhinitis from the common cold.

Acute rhinosinusitis

Rhinosinusitis (formerly referred to as sinusitis) is an inflammation of one or more of the paranasal sinuses. Up to 2% of patients will develop acute rhinosinusitis as a complication of the common cold. Anatomically, the sinuses are described in four pairs: frontal sinuses, ethmoid sinuses, maxillary sinuses and sphenoid sinuses (Fig. 2.2). All are air-filled spaces that drain into the nasal cavity. Following a cold, sinus air spaces can become filled with nasal secretions, which stagnate because of a reduction in ciliary function of the cells lining the sinuses. Bacteria, commonly *Streptococcus* and *Haemophilus*, can then secondarily infect these stagnant secretions. It is clinically defined by at least two of these symptoms:

- Blockage or congestion
- Discharge or UACS
- Facial pain or pressure
- Reduction or loss of smell

The pain in the early stages tends to be relatively mild and localised, usually unilateral and dull, but becomes bilateral and more severe the longer the condition persists. Bending forward often exacerbates the pain (moving the eyes from side to side and coughing or sneezing can also increase the pain), and sinuses will be tender when gently palpated. If the ethmoid sinuses are involved, retro-orbital pain

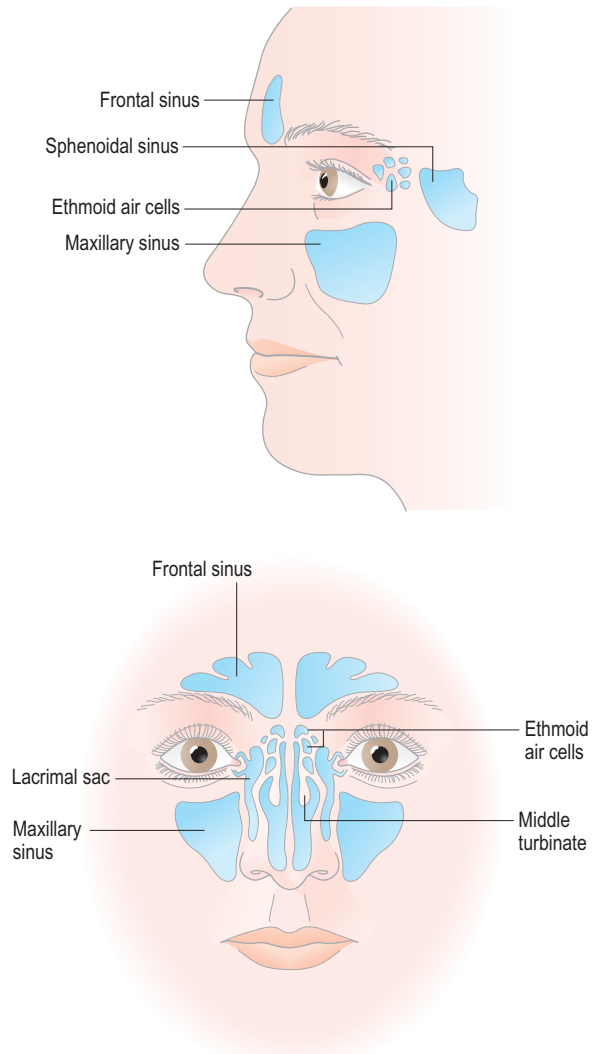


Fig. 2.2 Location of the sinuses.

(behind the eye) is often experienced. Symptoms usually resolve in 2 to 3 weeks but analgesics for pain relief and oral or nasal sympathomimetics to remove the nasal secretions can be tried. Antibiotics are not routinely recommended (NICE, 2017) unless the person is systemically unwell, at risk of complications due to underlying medical conditions, or has had symptoms for at least 10 days. If antibiotics are to be prescribed, then phenoxymethylpenicillin or co-amoxiclav (amoxicillin-clavulanic acid) are first-line agents (doxycycline or clarithromycin if the patient has a penicillin allergy).

Acute otitis media

Acute otitis media is commonly seen in children following a common cold and results from the virus spreading to the middle ear via the Eustachian tube, where an accumulation of pus in the middle ear or inflammation of the tympanic membrane (eardrum) results. The overriding symptom is ear pain, but the child may rub or tug at the ear and become more irritable. Referral to the GP would be appropriate for auroscopical examination unless the pharmacist is competent to perform this procedure. Examination reveals a bulging tympanic membrane, loss of normal landmarks, and a change in colour (red or yellow). See Student Consult (<https://studentconsult.inkling.com>) for eardrum images. Rupture of the eardrum causes purulent discharge and relieves the pain. For management of acute otitis media, see page 90.

Unlikely causes

Influenza

Influenza is caused by RNA viruses, for which there are three types: A, B, and C. Types A and B are most virulent, giving rise to flu symptoms, whereas type C produces mild coldlike symptoms. There are many different strains because they constantly alter their antigenic structure, necessitating yearly recommendations about which strains of influenza should be included in vaccines. Its spread is the same as the common cold: via droplet inhalation or direct contact with an infected person's nasal secretions.

Patients often use the word *flu* when describing a common cold. However, subtle differences in symptoms between the two conditions should allow for differentiation. It is helpful to remember that the flu season tends to occur between December and March, whereas the common cold, although more common in the winter months, can occur at any time. The onset of influenza is sudden; the typical symptoms are shivering, chills, malaise, marked aching of limbs, insomnia, fatigue, a nonproductive cough (cough in the common cold is usually productive) and loss of appetite. Influenza is therefore normally debilitating, and a person with flu is much more likely to send a third party into a pharmacy for medication than present in person. Symptoms improve after approximately 5 days, with resolution after 1 week or more. Flu vaccination programmes are the most important preventive measure to reduce flu cases and the associated complications of flu in at-risk populations. In 2018, English community pharmacies administered over 1 million vaccines under the community pharmacy contractual framework.



TRIGGER POINTS indicative of referral: The common cold

Symptoms/ signs	Possible danger/ reason for referral	Urgency of referral
Acute sinus involvement that fails to respond to OTC decongestant therapy	Possible need for nasal steroids or antibiotics	As soon as practicable
Middle ear pain that fails to respond to analgesia	Possible need for antibiotics	As soon as practicable
Patients with symptoms indicative of flu; vulnerable patient groups, such as the very old	Need an assessment of symptom severity by physician	Same-day referral

Evidence base for over-the-counter medication

Many of the active ingredients found in cold remedies are also constituents of cough products. Often, they are combined and marketed as cough and cold or flu remedies. For information relating to cough ingredients, the reader is referred to the sections on OTC medication for coughs.

Antihistamines

A Cochrane review (De Sutter et al., 2009; subsequently withdrawn) found that antihistamines when used as monotherapy had a small effect on nasal congestion, rhinorrhoea or sneezing in older children and adults on the first 2 days of treatment but did not have significant benefit with mid-term (3–4 days) or long-term (6–10 days) use. Only two trials were evaluated in young children, with conflicting results. However, the larger study, which was more robustly conducted, showed no benefit of antihistamines on the common cold.

Sympathomimetics

Trial data specifically looking at the effects of decongestants in the common cold are limited. A Cochrane review (Deckx et al., 2016) identified 15 trials that met their inclusion criteria, which involved topical oxymetazoline and oral pseudoephedrine and phenylpropanolamine (no longer used in the UK). The authors found a small but significant improvement in symptoms of nasal congestion in adults. However, the studies were generally of low quality, and there were insufficient data to compare oral and topical treatment. Also, data were lacking in children younger than 12 years.

A systematic review of single-dose phenylephrine studies found a statistically significant improvement in nasal airway resistance at 60 minutes compared with placebo (Kollar et al., 2007). However, the studies did not measure clinical outcomes (e.g., subjective improvement in symptoms), and the difference was small (16% at 60 minutes). In addition, four of the eight studies showed no benefit for phenylephrine compared with placebo. Importantly the manufacturers of phenylephrine conducted this review; the studies included were from a US Food and Drug Administration (FDA) submission and have not been subject to peer review. A systematic review (Hatton et al., 2007) concluded that there was insufficient evidence for the efficacy of phenylephrine as a nasal decongestant. This was supported by a more recent randomized controlled trial using doses up to 40 mg every 4 hours that found no significant difference compared with placebo (Meltzer et al., 2015).

Multiingredient preparations

There is no shortage of cold and flu remedies marketed. Many combine three or more ingredients. In most cases, the patient will not require all the active ingredients to treat symptoms, or the 'drug cocktail' administered will not contain active ingredients that have proven efficacy. A more sensible approach to medication management would be to match symptoms with active ingredients with known evidence of efficacy. In many cases, this can be achieved by providing the patient with monotherapy or a product containing two active ingredients. Preparations with multiple ingredients, therefore, have a very limited role to play in the management of coughs and colds. However, patients might perceive an all-in-one medicine as better value for money and, potentially, adherence with such preparations might be improved. The only review conducted on combination therapies was by De Sutter et al. (2012). They investigated oral antihistamine-decongestant-analgesic combinations for the common cold. The review involved 27 trials and over 5000 patients,

concluding that for adults and older children, all four combinations (antihistamine-analgesic-decongestant, analgesic-decongestant, analgesic-antihistamine, and decongestant-antihistamine) were effective, although they had an increased risk of adverse effects, in particular analgesic-decongestant formulations.

Anticholinergics

One intranasal preparation in combination with xylometazoline is available on the UK market. A Cochrane review identified seven trials that explored the effect of intranasal ipratropium on the severity of congestion and rhinorrhoea in patients with the common cold (AlBalawi et al., 2013). The review found that four studies showed a statistically significant improvement in the severity of rhinorrhoea and two that demonstrated a significantly greater global assessment of overall improvement with ipratropium compared with placebo. However, no studies found an improvement in nasal congestion. The authors concluded that ipratropium is likely to be effective in ameliorating rhinorrhoea associated with the common cold.

Alternative therapies

Many products are advocated to help treat cold symptoms. Three products in particular have received much attention and are widely used.

Zinc lozenges

The argument for zinc as a plausible treatment in reducing symptoms of the common cold can be traced back to 1984. Since that time, a number of studies have looked at zinc's effect on treating the common cold. A systematic review by Hemilä (2011) identified 13 randomized controlled trials that compared zinc with placebo. The results indicated differences in efficacy depending on the dose and the salt of zinc used. The authors found no significant difference in the duration of colds compared with placebo at doses less than 75 mg per day. For doses of more than 75 mg per day using an acetate salt, the investigators found a statistically significant 42% reduction in the duration of colds and a 20% reduction in duration with nonacetate salts. This equated to a 1- to 3-day reduction in the duration of the cold. It should be noted that this systematic review is of low to moderate quality because there are limited details on the methods, including whether or not study selection and data extraction for the review were done in duplicate. A protocol for a newer Cochrane review was published in late 2017 to review the role of zinc in treating the common cold. It seems prudent that until this review is published, zinc should not be recommended to treat the common cold.

Vitamin C

Vitamin C has been widely recommended as a cure for the common cold by many sources, medical and nonmedical. However, controversy still remains whether it is effective in combating the common cold. A large number of clinical trials have investigated the effect of vitamin C on the prevention and treatment of the common cold.

A Cochrane review examining the role of vitamin C at doses higher than 200 mg per day in preventing and treating the common cold identified 29 studies involving 11 306 subjects (Hemilä et al., 2013). The review found that vitamin C prophylaxis had no effect on the incidence of the common cold in the general community and only a small effect (8% reduction) on the duration of the cold. However, they found a 50% reduction in the incidence of the common cold in people undergoing high physical stress (e.g., marathon runners, skiers, and soldiers on subarctic exercises) with the prophylactic use of vitamin C. The review found that the use of vitamin C, once a cold had started, had no consistent effect on the duration or severity of the cold. The authors concluded that routine prophylaxis with vitamin C in the general community is unjustified, but could be beneficial to those exposed to brief periods of intense physical exercise.

Echinacea

The herbal remedy echinacea is marketed as a treatment for URTIs, including the common cold. Several reviews have reported echinacea's effect as being inconsistent. This is in part due to the limited number of trials that are comparable because different echinacea species are used, as well as different plant parts and extraction methods. A Cochrane review has attempted to take these factors into consideration (Karsch-Völk et al., 2014). The authors reviewed 24 trials involving 4631 participants in an attempt to determine echinacea's effectiveness in preventing and treating the common cold. Overall, they concluded that evidence was weak for echinacea in preventing and treating colds, although there was stronger evidence for its use as a preventive treatment.

Vapour inhalation

Steam inhalation has long been advocated to aid relief of symptoms of the common cold, usually with the addition of menthol crystals. Trial data (review of six trials [$N = 387$], all involving adults) shows conflicting evidence in symptom relief of the common cold (Singh et al., 2017). However, it is cheap and does not carry any significant risks, apart from minor discomfort and irritation of the nose. It appears that steam is the key to symptom resolution and not any additional ingredient that is added to the water.

Saline sprays

Saline sprays have been shown to work in observational studies. A Cochrane review exploring the use of saline irrigation on acute upper respiratory tract infections identified five randomized controlled trials involving 205 adults and 544 children (King et al., 2015). The studies generally found no difference between saline treatment and control, although one study involving children did demonstrate statistically significant reductions in nasal secretion scores. Whether this translates into clinical improvement is uncertain. The authors noted that there were no serious side effects, but saline irrigation could cause minor irritation and discomfort, with up to 40% of babies not tolerating saline nasal drops. In conclusion, it remains unclear if saline irrigation is beneficial.

Garlic

A Cochrane review (Lissiman et al., 2014) identified one trial that randomly assigned 146 participants to a garlic supplement (with 180 mg of allicin content) or a placebo once daily for 12 weeks. The trial relied on self-reported episodes of the common cold and reported 24 occurrences of the common cold in the garlic intervention group compared with 65 in the placebo group ($P < .001$). This single trial suggests that garlic may prevent occurrences of the common cold, but more studies are needed to substantiate these findings.

Summary

Evidence of efficacy for Western and alternative medicines in preventing and treating the common cold are weak. Decongestants used on an as-needed basis probably have the strongest evidence base in treating symptoms.

Practical prescribing and product selection

Prescribing information relating to OTC cold medicines is discussed and summarized in [Table 2.6](#), and useful tips relating to patients presenting with a cold are given in [Box 2.2](#).

Antihistamines

First-generation antihistamines are now included in relatively few cough and cold remedies. Further information on antihistamines can be found on page 20.

Sympathomimetics

Sympathomimetics serve to constrict dilated blood vessels and swollen nasal mucosa, easing congestion and helping breathing. Sympathomimetics interact with MAOIs (e.g., phenelzine, isocarboxazid, tranilcypramine, moclobemide), which can result in a fatal hypertensive crisis. The danger



Table 2.6
Practical prescribing: Summary of cold medicines

Name of medication	Use in children (age, years)	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy & breastfeeding
Antihistamines					
Diphenhydramine	>6	Dry mouth, sedation, constipation	Increased sedation with alcohol, opioid analgesics, anxiolytics, hypnotics, antidepressants	Glaucoma, prostate enlargement	Pregnancy – standard references state OK, although some manufacturers advise avoidance. Breastfeeding OK because amount secreted into breast milk is small. It may, however, reduce milk supply.
Systemic sympathomimetics					
Phenylephrine	>12	Insomnia	Avoid concomitant use with MAOIs and moclobemide due to risk of hypertensive crisis. Avoid in patients taking beta blockers and TCAs.	Control of hypertension and diabetes may be affected, but a short treatment course is unlikely to be clinically important.	Best avoided in pregnancy because mild foetal malformations have been reported. Breastfeeding OK because amount secreted into breast milk is small. It may, however, reduce milk supply.
Pseudoephedrine	>6				
Topical sympathomimetics					
Oxymetazoline	>12	Possible local irritation in ~5% of patients	Avoid concomitant use with MAOIs and moclobemide due to risk of hypertensive crisis.	None	Pregnancy – not adequately studied, avoid. Breastfeeding OK
Xylometazoline	>6 (Otrivine Child Nasal Drops)				
Ephedrine	>12				
Anticholinergic (ipratropium, xylometazoline)	>18	Nosebleeds, nasal irritation, dryness	Avoid concomitant use with MAOIs and moclobemide due to risk of hypertensive crisis.	Narrow-angle glaucoma, urinary retention	Manufacturers recommended avoiding

MAOI, Monoamine oxidase inhibitor; OTC, over-the-counter; TCA, tricyclic antidepressant.

HINTS AND TIPS BOX 2.2: THE COMMON COLD

Limiting viral spread	Use disposable tissues rather than handkerchiefs. Wash hands frequently, especially after nose blowing. Do not share hand towels. Try to avoid touching your nose.
Stuffy noses in babies	Saline nose drops can be used from birth to help with congestion. This would be a more suitable and safer alternative than a topical sympathomimetic.
General sales list of cold remedies	Products such as Lemsip and Beecham contain paracetamol. It is important to ensure that patients are not taking excessive doses of analgesia unknowingly. Also, many products contain subtherapeutic doses of sympathomimetics.
Administration of nasal drops	The best way to administer nose drops is to have the head in the downward position facing the floor. Tilting the head backward and towards the ceiling is incorrect because this facilitates the swallowing of the drops. However, most patients will find the latter way of putting drops into the nose much easier than the former.

of the interaction persists for up to 2 weeks after treatment with MAOIs is discontinued. In addition, systemic sympathomimetics can also increase blood pressure, which might, although unlikely with short courses of treatment, alter control of blood pressure in hypertensive patients and disturb blood glucose control in diabetics. However, coadministration of medicines, such as beta blockers, is probably clinically unimportant and does not preclude patients on beta blockers from taking a sympathomimetic. A topical sympathomimetic could be given to such patients to negate this potential interaction. The most likely side effects of sympathomimetics are insomnia, restlessness, and tachycardia. Patients should be advised not to take a dose just before bedtime because their mild stimulant action can disturb sleep.

As with cough remedies, the MHRA has stated that sympathomimetics (oral or nasally administered) should not be given to children younger than 6 years; for those aged between 6 and 12 years, duration of treatment should be limited to a maximum of 5 days. Additionally, maximum pack sizes are limited to 720 mg (the equivalent of 12 tablets, or capsules of 60 mg or 24 tablets or capsules of 30 mg), and sales are restricted to one pack per person owing to concerns over illicit manufacture of methylamphetamine (crystal meth) from OTC sympathomimetics.

*Systemic sympathomimetics***Phenylephrine**

Phenylephrine is available in a number of proprietary cold remedies – for example, Lemsip, Sudafed, and Beecham products – in doses ranging from 5 to 12 mg, three or four times a day, for adults and children over the age of 12 (although some restrict it to those >16 years). It is often combined with paracetamol and other ingredients and marketed as a cold and flu remedy.

Pseudoephedrine

Pseudoephedrine is widely available as a single ingredient (e.g., Sudafed Decongestant Tablets) or in multiingredient products in cold and cough remedies (e.g., Benylin 4 Flu Tablets). The standard adult dose is 60 mg three or four times a day, and half the adult dose (30 mg) is suitable for children between 6 and 12 years of age. Some products only recommend use in adults and children over 12.

Nasal sympathomimetics

Nasal administration of sympathomimetics represents the safest route of administration. They can be given to most patient groups, including pregnant women after the first trimester and patients with preexisting heart disease, diabetes, hypertension, and hyperthyroidism. However, a degree of systemic absorption is possible, especially when using drops, because a small quantity might be swallowed; therefore, they should be avoided in patients taking MAOIs. All topical decongestants should not be used for longer than 5 to 7 days (British National Formulary [BNF] 76) states a maximum of 5 days in children older than 6 years; otherwise, rhinitis medicamentosa (rebound congestion) can occur.

Ephedrine

Adults and children older than 12 years should put one or two drops into each nostril up to four times daily when required.

Oxymetazoline and xylometazoline

These agents are longer acting than ephedrine and require less frequent dosing, typically two or three times a day. They are made by a number of manufacturers (e.g., Otrivine, Sudafed, Vicks) who all recommend use from 12 years upwards, except Otrivine Child Nasal Drops, which can be

given to children over the age of 6 (one or two drops into each nostril once or twice daily).

Anticholinergic-decongestant combination

In 2017, ipratropium was reclassified to allow OTC sales. It is available as a combination product with xylometazoline and marketed under the brand name Otrivine Extra Dual Relief Nasal Spray (ipratropium bromide, 0.6 mg/mL, and xylometazoline hydrochloride, 0.5 mg/mL). It is licensed for the symptomatic treatment of nasal congestion and rhinorrhoea in connection with common colds in people over 18 years. Dosing is one puff in each nostril three times a day. It should be restricted to a maximum of 7 days' use (presumably because of the potential for rebound effects associated with xylometazoline). Side effects include nasal dryness and nose bleeds. The manufacturer does not recommend use in pregnancy and lactation.

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Sore throats

Background

Any part of the respiratory mucosa of the throat can exhibit symptoms of pain. This includes the pharynx (pharyngitis) and tonsils (tonsillitis), yet clinical distinction between pharyngitis and tonsillitis is unclear. Pain can range from irritation to severe pain. Sore throats are often associated with the common cold. However, in this section, people who present with sore throat as the principal symptom are considered.

Prevalence and epidemiology

Sore throats are extremely common. UK figures show that a GP with 2000 patients will see about 120 people each year with a throat infection. However, four to six times as many people will visit the pharmacy and self-treat. Figures from other countries such as New Zealand and Australia broadly support UK findings. On average, an adult will experience two to three sore throats each year.

Aetiology

Viral infection accounts for between 70% and 90% of all sore throat cases. Remaining cases are nearly all bacterial, with the most common cause being group A beta-haemolytic

Streptococcus (also known as *Streptococcus pyogenes*). A fuller account of the viral and bacterial pathogens that affect the upper respiratory tract appears under aetiology of colds.

Arriving at a differential diagnosis

The overwhelming majority of cases will be acute and self-limiting, whether viral or bacterial in origin. Clinically, differentiation between viral and bacterial infection is extremely difficult, although specific symptom clusters are suggestive for sore throat of bacterial origin (see conditions to eliminate), but these are not foolproof. Other causes of sore throat also need to be considered; Table 2.7 highlights those conditions that can be encountered by community pharmacists and their relative incidence. Asking symptom-specific questions will help the pharmacist establish a differential diagnosis (Table 2.8).

Physical examination

After questioning, the pharmacist should inspect the mouth and cervical glands (located just below the angle of the jaw) to aid the differential diagnosis (Fig. 2.3). The examination requires a good light source (e.g., pen torch). These steps should be followed:

1. Get the person seated so that the examiner can be at eye level.
2. Ask the patient to say 'ah'; this should allow you to see the posterior throat. Pay particular attention to the size of the tonsils. Are they red and swollen? Is there any exudate present? Is there any sign of ulceration?
3. Check for the posterior wall of the throat. It should appear pink and moist, without exudate or lesions when healthy. Redness or exudate suggests pharyngitis.

Clinical features of viral sore throat

Acute pharyngitis is characterized by the rapid onset of sore throat and pharyngeal inflammation (with or without



Table 2.8
Specific questions to ask the patient: Sore throat

Question	Relevance
Age of the patient	Although viruses are the most common cause of sore throat, there are epidemiological variances with age: <i>Streptococcus</i> is uncommon those <3 years, <i>Streptococcal</i> infections more prevalent in people <30 years, particularly those of school age (5–10 years) and young adults (15–25 years); glandular fever is most prevalent in adolescents.
Tender cervical glands	On examination, patients suffering from glandular fever and streptococcal sore throat often have markedly swollen glands. This is less so in viral sore throat.
Tonsillar exudate present	Marked tonsillar exudate is more suggestive of a bacterial rather than a viral cause.
Ulceration	Herpetiform and herpes simplex ulcers can also cause soreness in the mouth, especially in the posterior part of the mouth.

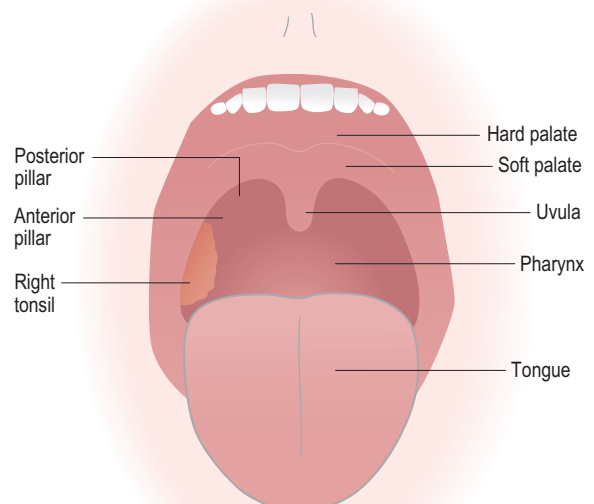


Fig. 2.3 Major structures of the mouth.

Table 2.7
Causes of sore throat and their relative incidence in community pharmacy

Incidence	Cause
Most likely	Viral infection
Likely	Streptococcal infection
Unlikely	Glandular fever, trauma
Very unlikely	Carcinoma, medications

exudate). Many studies have now shown that it is exceedingly difficult to differentiate viral and bacterial infection on patient history and clinical findings. Patients will present with a sore throat as an isolated symptom or as part of a cluster of symptoms that include rhinorrhoea, cough, malaise, fever, headache and hoarseness (laryngitis). Symptoms are relatively short-lived, with 40% of people being symptom free after 3 days and 85% of people symptom free after 1 week.

Conditions to eliminate

Likely cause

Streptococcal sore throat

Patients who present with pharyngeal or tonsillar exudates, swollen anterior cervical glands, nasal congestion, history of or current high-grade fever (over 39.4°C; 101°F), and absence of cough are more likely to have a bacterial infection (Table 2.9). These are known as the *Centor criteria*; a person exhibiting three or all four symptoms should be referred to their physician for potential antibiotics. However, even if the patient exhibits all of these four classic symptoms, up to 40% will still not have a bacterial infection. It tends to be more common during winter months. To further compound the difficulty of diagnosis, the routine use of throat swabs is not recommended because asymptomatic carriage of *Streptococcus* affects up to 40% of people, making it impossible to differentiate between infection and carriage. The use of antibiotics in such situations is debatable; studies have shown that they only decrease symptom duration by less than 1 day. If antibiotics are prescribed, the drug of choice is phenoxymethylpenicillin, with erythromycin or clarithromycin reserved for those with penicillin allergy. Doctors are encouraged to adopt delayed prescription strategies to reduce the number of inappropriate antibiotics taken by patients.

Complications arising from strep throat include otitis media and acute sinusitis.

Unlikely causes

Glandular fever (infectious mononucleosis)

Glandular fever is caused by the Epstein-Barr virus and is often called the *kissing disease* because transmission primarily occurs from saliva. It has a peak incidence in adolescents and young adults (15–19 years of age). The signs and symptoms of glandular fever can be difficult to distinguish from sore throat because it is characterized by pharyngitis (occasionally with exudates), fever and cervical lymphadenopathy. The person generally suffers from general malaise, which is disproportionate to the symptoms experienced. A rash can also occur in 10% of patients, appearing in the first days of the illness, and lasts 1 week. Spleen enlargement occurs in approximately 50% of patients.

Trauma-related sore throat

Occasionally, patients develop a sore throat from direct irritation of the pharynx. This can be due to substances such as cigarette smoke, a lodged foreign body or from acid reflux.

Very unlikely causes

Medicine-induced sore throat

A rare complication associated with certain medication is agranulocytosis, which can manifest as a sore throat. The patient will also probably present with signs of infection, including fever and chills. Agents known to cause this adverse event are listed in Table 2.10.

Laryngeal and tonsillar carcinoma

Both these cancers have a strong link with smoking and excessive alcohol intake and are four times more common in men than in women. Sore throat, hoarseness, dysphonia and dysphagia are the common presenting symptoms. In addition, patients with tonsillar cancer often develop referred ear pain. Any person, regardless of age, who presents with dysphagia should be referred.

Fig. 2.4 will help in the differentiation of serious and non-serious conditions in which sore throat is a major presenting complaint.

Table 2.9
Features of viral and bacterial sore throat

Infection	Age	Tonsillar, pharyngeal exudate	Duration	Cervical glands	Cough present	Other symptoms
Viral	Any age	Possible, but generally limited	3–7 days	Normal	Common	Low-grade fever, headache
Bacterial	Schoolchildren	Often present and can be substantial	3–7 days	Swollen	Rare	High-grade fever, possible rash

Table 2.10
Examples of medications known to cause agranulocytosis

Captopril
Carbimazole
Cytotoxics
Neuroleptics (e.g., clozapine)
Penicillamine
Sulfasalazine
Sulphur-containing antibiotics

! TRIGGER POINTS indicative of referral: Sore throat

Symptoms/signs	Possible danger/reason for referral	Urgency of referral
Duration >2 weeks	Suggests nonacute cause and requires further investigation	As soon as practicable
Marked tonsillar exudate, accompanied with high temperature and swollen glands	Possible bacterial cause and may require antibiotics	
People taking medications that can interfere with the immune response (e.g., immunosuppressants, disease-modifying antirheumatics) or those known to cause agranulocytosis	Requires doctor involvement to monitor	
Dysphagia	Suggests sinister pathology	Urgent referral

Evidence base for over-the-counter medication

Because most sore throats are viral in origin and self-limiting, medication aims to relieve symptoms and discomfort while the infection runs its course. Lozenge and spray formulations incorporating antibacterial and anaesthetics provide the mainstay of treatment. In addition, systemic analgesics and antipyretics will help reduce the pain and fever associated with sore throat.

Local anaesthetics

Lidocaine and benzocaine are included in a number of marketed products. Very few published clinical trials involving products marketed for sore throat have been conducted, yet local anaesthetics have proven efficacy. A study reported on clinicaltrials.gov (US National Library of Medicine, 2013) compared two strengths of lidocaine (1 and 8 mg) in lozenges for sore throat associated with the common cold. The study found no difference in pain relief between the two strengths at 2 and 4 hours. In the absence of a placebo arm, it is difficult to assess whether the pain relief obtained was any different from no treatment.

Antibacterial and antifungal agents

Antibacterial agents include chlorhexidine, tyrothricin, dequalinium chloride, and benzalkonium chloride. In vitro testing has shown that many of the proprietary products do have antibacterial activity, and some inhibit *Candida albicans* growth. In vivo tests have also shown antibacterial effects.

The use of antibacterial and antifungal agents should not be routinely recommended because the vast majority of sore throats are caused by viral infections against which they have no action. However, because adverse effects are rare, and stimulation of saliva from sucking the lozenge may confer symptomatic relief, the use of such products may possibly be justified.

Antiinflammatories

Benzydamine is available as a spray or mouthwash; one small trial involving benzydamine as a gargle resulted in significantly greater relief of pain compared with placebo (Thomas et al., 2000). Similar results were shown in another study comparing a mouth spray containing benzydamine to placebo in patients with viral sore throat (Cingi et al., 2010).

Analgesics

There is good evidence to indicate that simple systemic analgesia (e.g., paracetamol, aspirin, ibuprofen) is effective in reducing the pain associated with sore throat. Thomas et al. (2000) reviewed treatments other than antibiotics for sore throats. They identified 22 trials, 13 of which involved NSAIDs (primarily ibuprofen) or paracetamol, and found that both

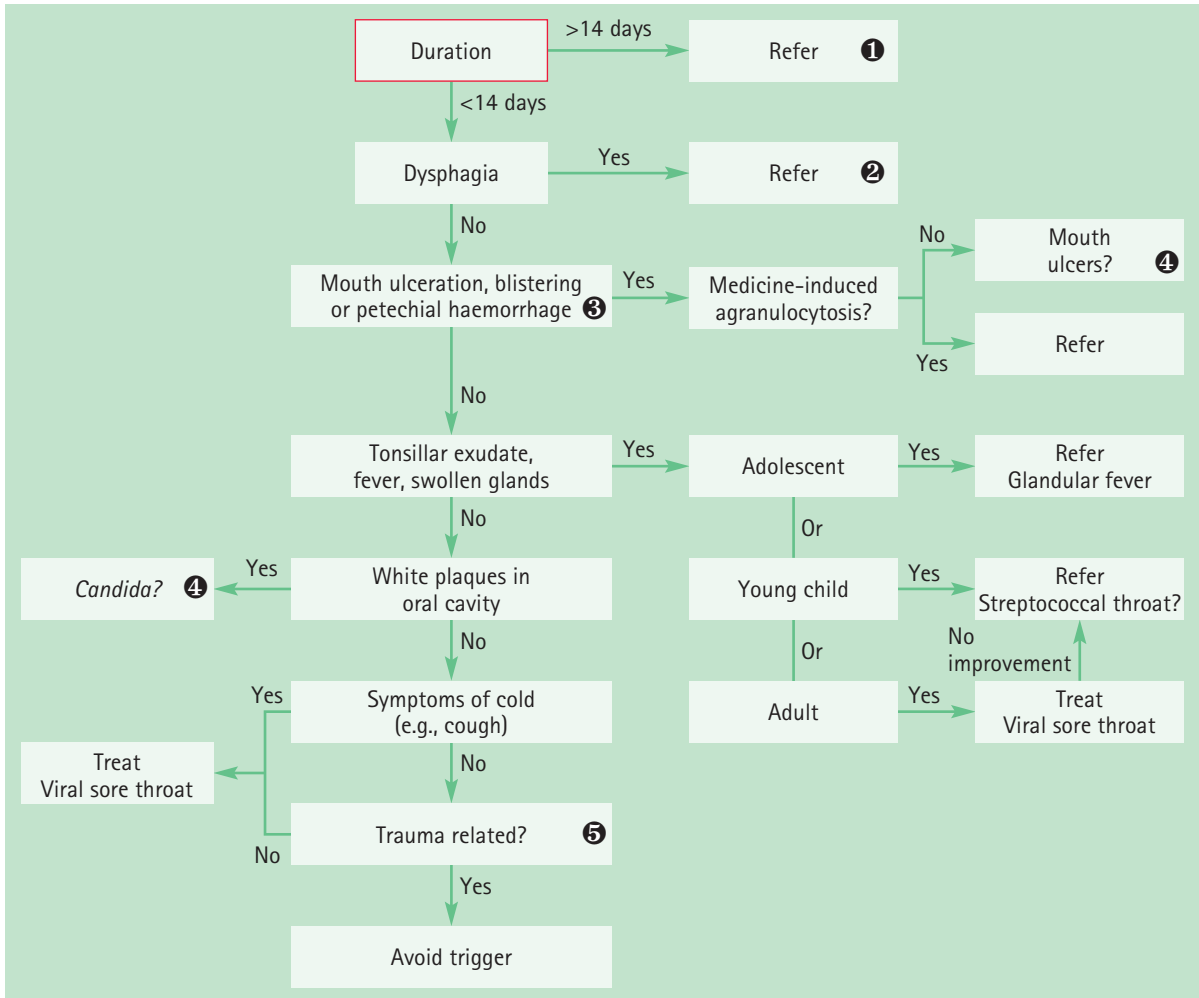


Fig. 2.4 Primer for differential diagnosis of sore throat.

① Duration longer than 2 weeks. The overwhelming majority of cases resolve spontaneously in this time; it is therefore prudent to refer these cases for further investigation. 1, Duration longer than 2 weeks. The overwhelming majority of cases resolve spontaneously in this time; it is therefore prudent to refer these cases for further investigation.

② Dysphagia. True difficulty in swallowing (i.e., not just caused by pain but by a mechanical blockage) should be referred. Most patients with sore throat will find it less easy to swallow, but this has to be differentiated from actual difficulty in swallowing. Severe inflammation of the throat can cause restriction of the airways and thus hinder breathing. Additionally, rare causes of sore throat also have associated dysphagia symptoms, such as peritonsillar abscess, thyroiditis and oesophageal carcinoma.

③ Signs of agranulocytosis. A severe reduction in the number of white blood cells can result in neutropenia, which is manifested as fever, sore throat, ulceration and small haemorrhages under the skin.

④ Mouth ulceration and *Candida* (oral thrush) primers. See Chapter 7 and Figs 7.6 and 7.7 for further differentiation of these conditions.

⑤ Trauma related. Simple acts of drinking fluids that are too hot can give rise to ulceration of the pharynx. It is worth asking whether any such factors could have triggered the sore throat.

NSAIDs and paracetamol were effective. However, the authors noted that patients took the medications regularly in the studies, not on an as-needed basis, and this should be stressed to patients presenting with sore throats. Flurbiprofen lozenges have also been shown to be more effective than placebo in reducing pain associated with sore throat (Benrimoj et al., 2001). However, the clinical significance of the benefit is uncertain, and comparisons with active treatments are lacking. In a review in *Prescribe International* in 2007, the conclusion was that 'flurbiprofen lozenges have a negative risk-benefit balance. ... it is better to suck real sweets and, if necessary, take paracetamol' (Anonymous, 2007).

Aspirin and saltwater gargles

Gargling with aspirin or saltwater is a common lay remedy for sore throat. No trials appear to have been conducted on their effectiveness and until evidence becomes available, they should not be recommended.

Practical prescribing and product selection

Prescribing information relating to the sore throat medicines is discussed and summarized in [Table 2.11](#), and useful tips relating to patients presenting with a sore throat are given in 'Hints and Tips' in [Box 2.3](#).

Local anaesthetics (lidocaine, benzocaine)

All local anaesthetics have a short duration of action, and frequent dosing is required to maintain the anaesthetic effect, whether formulated as a lozenge or spray. They appear to be free from any drug interactions, have minimal side effects, and can be given to most patients, including pregnant and breastfeeding women. A small number of patients may experience a hypersensitivity reaction with either ingredient, although it appears to be more common with benzocaine. Owing to differences in the chemical structure of these products, cross-sensitivity is unusual;



Table 2.11
Practical prescribing: Summary of sore throat medicines

Name, type of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy & breastfeeding
<i>Local anaesthetics</i>					
Lidocaine	>12 years	Can cause sensitization reactions	None	None	OK
Benzocaine	Lozenge: >3 years Spray: >6 years				
<i>Antiinflammatory</i>					
Benzydamine	Rinse: >12 years Spray and lozenge: >6 years	Oral rinse may cause stinging	None	None	OK, but in pregnancy, limit use after 30 weeks.
Flurbiprofen	>12 years	None reported	None	Avoid in patients with peptic ulcers.	Avoid if possible.

HINTS AND TIPS BOX 2.3: SORE THROAT

Stimulation of saliva production	Sucking a lozenge or pastille promotes saliva production, which will lubricate the throat and thus exert a soothing action.
Gargles or lozenges?	Gargles have a very short contact time with inflamed mucosa and therefore any effect will be short lived. A lozenge or a pastille is preferable because contact time will be longer.
Benzydamine (Difflam) rinse	The manufacturers advise that the product should be stored in the box away from direct sunlight, even though the stability of the product is not known to be affected by sunlight.

therefore, if a patient experiences side effects with one, the other can be tried. Most products do contain a sugar base, but the amount of sugar is too small to affect blood glucose control substantially and therefore can be recommended to diabetic patients.

Lidocaine spray (Boots Anaesthetic Sore Throat Relief 2% and Covonia Throat Spray – 0.05%)

Both are licensed for adults and children over the age of 12. The dosing for the 2% product is three sprays every 3 hours when needed, up to a maximum of six times per day. For Covonia, the dose is three to five sprays between six and ten times per day.

Benzocaine

Unlike lidocaine, benzocaine can be given to children in lozenge and spray formulations. Lozenges are available and can be given to children age 3 years and older (Tyrozets, one lozenge, 5 mg every 3 hours when needed; maximum of six in 24 hours); adults can take up to eight in 24 hours every 2 to 3 hours when needed (e.g., Tyrozets, Boots anaesthetic and antibiotic throat lozenges). Additionally, children over the age of 6 can also use a spray formulation (Ultra Chloraseptic, 0.71%, or AAA Spray, 1.5%), for which the dose is one spray every 2 to 3 hours, up to a maximum of eight doses per day. The adult dose is up to three sprays (Ultra Chloraseptic) and two sprays (AAA Sore Throat Spray) repeated every 2 to 3 hours.

Antiinflammatories

Benzydamine (Difflam Sore Throat Rinse, Difflam Spray and Lozenge)

The rinse should be used by adults and children over the age of 12 every 1½ to 3 hours when required. It occasionally causes stinging, in which case the rinse can be diluted with water.

The dosing frequency for the spray is the same as the rinse (every 1½–3 hours when required) but, unlike the rinse, it can be used in children. For those younger than 6 years, the number of sprays is based on mg/kg dosing; for those aged 6 to 12 years, it is four puffs. In adults four to eight puffs can be used. The lozenge (3 mg) is for adults and children over the age of 6, and the dose is to suck one lozenge three times a day. Benzydamine has no drug interactions of note and can be used by all patient groups.

Flurbiprofen

Strefen lozenges (8.75 mg flurbiprofen) can only be given to adults and children older than 12 years. The dose is one lozenge to be sucked every 3 to 6 hours, with a maximum of five lozenges in 24 hours. They are contraindicated in patients with peptic ulceration, and must be avoided in the last trimester of pregnancy but are suitable for breastfeeding women. If a patient has a known hypersensitivity reaction to an NSAID or aspirin, they should be avoided.

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Website

Sinus Care Center: <http://www.sinuscarecenter.com>

Rhinitis

Background

Rhinitis is simply inflammation of the nasal lining. It is characterized by rhinorrhoea, nasal congestion, sneezing, and itching. Most cases that present in a community pharmacy will be a viral infection or allergic in origin. This section concentrates on the differentiation of allergic rhinitis (AR) from other causes. For AR, there are currently different classifications but the ARIA (Allergic Rhinitis and its Impact on Asthma) guidelines classify

AR into intermittent and persistent categories, with both subdivided into mild or moderate–severe disease (Brozek et al., 2017). The ARIA classification is based on the timing of the symptoms and is divided into intermittent (occurring on less than 4 days per week and less than 4 weeks at a time) or persistent (occurring on more than 4 days per week and more than 4 weeks at a time). Rhinitis can have a significant impact on quality of life, impairing performance at work and school and disrupting sleep.

Prevalence and epidemiology

AR is a global health problem that has dramatically increased over the last 20 years, with studies suggesting that the prevalence has at least doubled in that time. The UK has one of the highest levels of AR in the world, with estimates ranging from 10% to 25% of adults and as many as 40% of children affected. These figures might, however, represent an underestimate, because many people do not consult their doctor and choose to self-medicate. Seasonal intermittent allergic rhinitis (hay fever) commonly affects school-aged children, with 10% to 30% of the adolescent population suffering from the condition. The mean age of onset is 10 years; the incidence peaks between the ages of 13 and 19 years. It is believed that improved living standards and reduced risk of childhood infections might increase susceptibility to hay fever. Allergic rhinitis is a recognized risk factor for the development of asthma.

Aetiology

AR is a mucosal reaction in response to allergen exposure. Initially, the patient must come into contact with an allergen; for intermittent AR, this is usually pollen or fungal spores. The allergen lodges within the mucus blanket lining the nasal membranes, and activates immunoglobulin E (IgE) antibodies – formed from previous allergen exposure – on the surface of mast cells. Potent chemical mediators are released, primarily histamine, but also leukotrienes, kinins and prostaglandins, which exert their action via neural and vascular mechanisms. This immediate response to an allergen is known as the *early-phase allergic reaction* and gives rise to nasal itch, rhinorrhoea, sneezing and nasal congestion. A late-phase reaction then occurs 4 to 12 hours after allergen exposure, with nasal congestion as the main symptom.

Also of importance is the phenomenon of nasal priming. Patients, after a period of continuous allergen exposure, may find that they experience the same level of severity in symptoms with lower levels of allergen exposure. Similarly, symptoms will be worse than previously experienced when levels of the allergen are the same. This may explain why patients complain of worsening hay fever symptoms the longer the season goes on. [Table 2.12](#) highlights the main allergens responsible for AR.

Table 2.12
Allergens responsible for rhinitis

Type	When present	Causative allergen
Intermittent allergic rhinitis	February to April	Tree pollens (hazel and alder associated with early symptoms and silver birch in March and April)
	May to August (peaks in June and July)	Grass pollen
	September to October	Fungal spores
Persistent allergic rhinitis (e.g., perennial rhinitis)	Year-round	House dust mite; animal dander, especially cats

Arriving at a differential diagnosis

In the community pharmacy setting, most patients who present with rhinitis will be suffering from a cold or intermittent AR. Diagnosis is largely dependent on the patient having a family history of atopy, the presenting clinical symptoms, and when these worsen. Asking symptom-specific questions will help the pharmacist establish a differential diagnosis ([Table 2.13](#)); [Table 2.14](#) highlights conditions that may be encountered by community pharmacists and their relative incidence.

Clinical features of intermittent allergic rhinitis

The patient will experience a combination or all four of the classic rhinitis symptoms of nasal itch, sneeze (especially paroxysmal), watery rhinorrhoea, and nasal congestion. Bilateral symptoms typically develop within minutes following allergen exposure. In addition, the patient might also suffer from ocular irritation, giving rise to allergic conjunctivitis. The symptoms will occur intermittently (i.e., at times of pollen exposure) and tend to be worse in the morning and evening because pollen levels peak at this time, as they do when the weather is hot and humid.

In terms of classifying symptoms as mild or moderate to severe (as per ARIA), the following criteria are used:



Table 2.13
Specific questions to ask the patient:
Rhinitis

Question	Relevance
Seasonal variation	Symptoms in the summer months suggest intermittent allergic rhinitis, whereas year-round symptoms suggest perennial rhinitis.
History of asthma, eczema, or intermittent allergic rhinitis in the family	If a first-degree relative suffers from atopy, intermittent allergic rhinitis is much more likely.
Triggers	When pollen counts are high, symptoms of intermittent allergic rhinitis worsen. Infective rhinitis and vasomotor rhinitis will be unaffected by pollen count. Patients with persistent rhinitis might suffer from worsening symptoms when pollen counts are high, but symptoms should still persist when indoors compared with intermittent rhinitis sufferers who usually see relief of symptoms when away from pollen.

Table 2.14
Causes of allergic rhinitis and their relative incidence in community pharmacy

Incidence	Cause
Most likely	Intermittent allergic rhinitis
Likely	Persistent allergic rhinitis, infective rhinitis
Unlikely	Nonallergic rhinitis, pregnancy, medicines, nasal foreign bodies or blockage

Moderate to severe: one or more of the following are present:

- Sleep disturbance
- Impairment of daily activities, leisure, and/or sport
- Impairment of school or work
- Troublesome symptoms.

If none of these symptoms are present, this is classified as mild.

Conditions to eliminate

Likely causes

Persistent allergic rhinitis

Persistent AR is much less common than intermittent AR. As its name suggests, the problem tends to be persistent and does not exhibit seasonality. In addition to not having a seasonal cause, there are a number of other clues to look for that aid in differentiation. Nasal congestion is much more common, which often leads to hyposmia (poor sense of smell), and ocular symptoms are uncommon. Additionally, persistent AR sufferers also tend to sneeze less frequently and experience more episodes of chronic sinusitis. The most common allergen causing persistent AR is the house dust mite but animal dander (particularly from cats, dogs and horses) are common causes of symptoms, so it is prudent to ask about any pets the patient may have.

Infective rhinitis

This is normally viral in origin and associated with the common cold. Symptoms are acute in onset. Nasal discharge tends to be more mucopurulent than in AR, and nasal itching is uncommon. Sneezing tends not to occur in paroxysms, and the condition resolves more quickly, whereas AR lasts for as long as the person is exposed to the allergen. Other symptoms, such as cough and sore throat, are much more prominent in infective rhinitis than in AR.

Unlikely causes

Nonallergic rhinitis (vasomotor rhinitis or intrinsic rhinitis)

Nonallergic rhinitis is thought to be due to either an overactive parasympathetic nervous system response or hypoactive sympathetic nervous system response to irritants such as dry air, pollutants or strong odours. The symptoms can be similar to AR, but an allergy test will be negative. Itching and sneezing are less common, and patients might experience worsening nasal symptoms in response to climatic factors, such as a sudden change in temperature. Onset of symptoms tend to be after the age of 20 years.

Rhinitis of pregnancy

Nearly 10% of women will experience rhinitis during pregnancy that is unrelated to URTI or allergy (Namazy & Schatz, 2014). It is thought that this occurs because of hormonal changes; however, evidence is lacking (Wallace et al., 2008). It usually starts after the second month of the pregnancy and resolves spontaneously after childbirth. Nasal congestion is the prominent feature.

Rhinitis medicamentosa and medicine-induced rhinitis

Rhinitis medicamentosa is due to prolonged use of topical decongestants (>5–7 days), which causes rebound vasodilation of the nasal arterioles, leading to further nasal congestion. Although the exact pathophysiology is unclear, it is thought to be due to desensitization of the alpha-adrenoceptors as a result of constant stimulation. A number of oral medications are implicated in causing rhinitis through other mechanisms, including ACE inhibitors, reserpine, alpha blockers (e.g., terazosin), sildenafil, chlorpromazine, oral contraceptives, aspirin and other NSAIDs.

Nasal blockage

In the absence of rhinorrhoea, nasal itch and sneezing, it is possible that the problem is mechanical or anatomical. If the blockage is continuous and unilateral, this may relate to a deviated nasal septum in adults, which may develop or be a result of trauma. Referral is needed, and surgery is recommended. If the obstruction is bilateral, this may relate to nasal polyps in adults. Nasal obstruction is progressive and is often accompanied by hyposmia. Referral is needed for corticosteroids or surgery.

Nasal foreign body

A trapped foreign body in a nostril commonly occurs in young children, often without the parent's knowledge. Within a matter of days of the foreign body being lodged, the patient experiences an offensive nasal discharge. Any unilateral discharge, particularly in a child, should be referred for nasal examination, because it is highly likely that a foreign body is responsible.

Fig. 2.5 will aid in differentiating the different types of rhinitis.

! TRIGGER POINTS indicative of referral: Rhinitis

Symptoms/signs	Possible danger/ reason for referral	Urgency of referral
Failed medication Medicine-induced rhinitis	Requires discussion with a doctor for alternative treatment	As soon as practicable
Nasal blockage that fails to clear	Suggests polyp	
Unilateral discharge, especially in children	Possible trapped foreign body	Same-day GP referral

Evidence base for over-the-counter medication

Before medication is started, it is clearly important to try and identify the causative allergen. If this can be achieved, measures to limit exposure to the allergen will be beneficial in reducing the symptoms experienced by the patient. This is more easily accomplished in persistent AR than in seasonal intermittent rhinitis.

Allergen avoidance

Avoidance of pollen is almost impossible but, if the patient follows a few simple rules, exposure to pollen can be reduced. Patients may choose to stay indoors when pollen counts are high. Windows should be closed (when in the house and when travelling in cars) and wrap-around sunglasses may be worn. Air conditioning in cars fitted with a pollen filter is also beneficial. Patients should avoid walking in areas with the potential for high pollen exposure (e.g., grassy fields, parks, gardens), as well as areas such as city centres, because many intermittent allergy sufferers will have increased sensitivity to other irritants, such as car exhaust fumes and cigarette smoke.

The two main causative agents of persistent AR – house dust mites and animal dander – can be more easily avoided. Pets, for example, can be excluded from certain parts of the house, such as living areas and bedrooms, and acaricidal sprays and strict bedroom cleaning regimens have been shown to be of some benefit in reducing rhinitis symptoms (Sheikh et al., 2010). Cleaning regimens should include regular washing of bedding and mattress covers with hot water (to try and kill the mites), replacing carpets with hard wood floors, minimizing soft furnishings, and avoiding drying clothes on radiators.

Medications

Pharmacists now possess a wide range of therapeutic options to treat AR, allowing the vast majority of sufferers to be appropriately managed in the pharmacy. Management of AR falls broadly into two categories, systemic and topical.

Systemic therapy: Antihistamines

Both sedating and nonsedating antihistamines are clinically effective in reducing the symptoms associated with AR. However, given the sedative effects of first-generation antihistamines, they should not be routinely recommended.

Of the second-generation antihistamines, community pharmacists in the UK currently have a choice between acrivastine, cetirizine or loratadine. All are equally effective and are considered to be nonsedating, although they are not truly nonsedating and cause different levels of sedation. Loratadine has been shown to have the lowest affinity for histamine

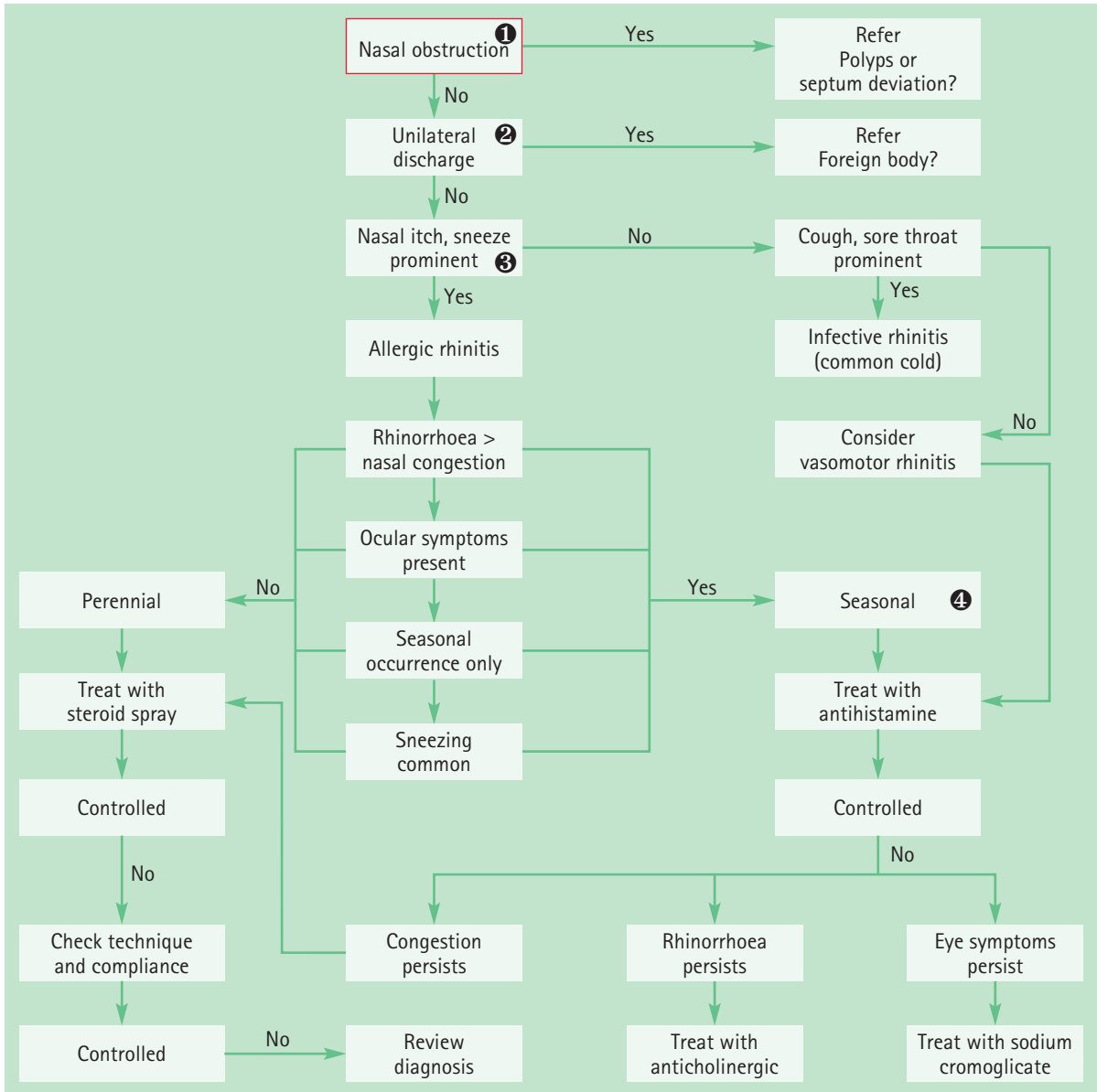


Fig. 2.5 Primer for differential diagnosis of rhinitis.

❶ Nasal obstruction. Nasal obstruction differs from nasal congestion in that obstruction refers to a physical blockage of the nasal passage and is normally due to an anatomical fault, whereas congestion refers to the nasal passages being temporarily blocked by nasal secretions that can easily be cleared by nose blowing. Obstruction therefore warrants referral.

❷ Unilateral discharge. Any one-sided nasal discharge must be viewed with suspicion. Accidental lodging of a foreign body by young children is the usual cause.

❸ Nasal itch and sneeze prominent. Nasal itching and sneezing are typically associated with hay fever, although these symptoms are also associated with perennial rhinitis, but to a lesser extent. Sneezing is often said to occur in multiple bouts, which is unlike infective rhinitis. Coughing can occur but is infrequent.

❹ Treatment of vasomotor rhinitis. Because symptoms are similar to hay fever, it is reasonable to assume that first-line therapy for vasomotor rhinitis would be a systemic antihistamine.

receptors in the brain; a study by Mann et al. (2000) reviewing reported sedation with second-generation antihistamines showed loratadine to be the least sedating of the nonsedating antihistamines. In comparison, cetirizine was 3.5 times more likely to cause sedation and acrivastine, 2.5 times more likely to cause sedation than loratadine. On this basis, loratadine would be the antihistamine of choice.

Topical therapy

To combat nasal congestion and ocular symptoms, a range of topically administered medications is available, including antihistamines, corticosteroids, mast cell stabilizers and decongestants.

Intranasal medication: Corticosteroids

Intranasal corticosteroids are the most effective overall treatment for AR – a number of clinical trials have confirmed their efficacy and they have demonstrated superiority to antihistamines in the treatment of allergic rhinitis for all nasal symptoms, and equivalence for ocular symptoms (Wallace et al., 2017). There is little difference in efficacy between the intranasal corticosteroids, and clinical evidence does not support the use of one intranasal corticosteroid over another. They have a slow onset of action (12 hours), and maximum clinical efficacy can take up to 2 weeks. Patients who regularly suffer from nasal congestion associated with AR should be advised to commence therapy before exposure to the allergen to maximize symptom control.

Decongestants

Topical decongestants are effective in the treatment of nasal congestion but are of limited value in treating AR because prolonged use is associated with rebound congestion; however, they may be useful for treating intermittent symptoms. Their place in therapy is probably best reserved when nasal congestion needs to be treated quickly and can provide symptom relief while corticosteroid therapy is initiated and has time to begin to exert its action.

Intraocular medication

Mast cell stabilizers

Sodium cromoglicate has proven efficacy and is significantly better than placebo (Lindsay-Miller, 1979). However, it does require dosing four times a day, and adherence might be a problem. Further, cromoglicate takes 4 to 6 weeks to reach maximal response; therefore, mast cell stabilizers alone only have a role when patients can predict the onset of the symptoms well in advance.

Antihistamines

The only ocular antihistamine available OTC is antazoline. It is available in combination with xylometazoline. There appear to be few trial data in the public domain regarding

decongestant-antihistamine combinations, although one small trial concluded that a combination of the two drugs was superior to either alone (Abelson et al., 1990). At best it should be used short term to avoid possible rebound conjunctivitis caused by xylometazoline, which has been well documented.

Sympathomimetics

OTC ocular sympathomimetics are commonly used to control ocular redness and discomfort. There appear to be no significant differences between ocular decongestants on the basis of their vasoconstrictive effectiveness. Like nasal sympathomimetics, they should be restricted to short-term use (<7 days) to avoid rebound effects.

Complementary therapies

Butterbur (*Petasites hybridus*) is promoted as having antiallergic properties. Two clinical trials have reported favourable outcomes of butterbur in controlling symptoms (Lee et al., 2004; Schapowal, 2002). Both trials found butterbur to be as effective as its comparator drug (cetirizine and fexofenadine, respectively). However, the comparison of butterbur to cetirizine used quality of life measures as the main outcome, and the study with fexofenadine was short (1 week) and involved only 16 participants. Another trial found butterbur to be no better than placebo in terms of peak nasal inspiratory flow or nasal symptom scores (Gray et al., 2004). A systematic review of complementary and alternative medicines for rhinitis concluded that the current available evidence does not support the use of complementary (alternative) medicines to treat rhinitis (Passalacqua et al., 2006), and a more recent review also concluded that further evidence is required (Garbo et al., 2013). Until further larger studies are conducted to assess butterbur's effect, it should not be routinely recommended.

Summary

Oral antihistamines are effective and popular with patients due to easy dosing and quick onset of action. They should be used if the patient suffers from mild intermittent general symptoms. Loratadine should be recommended as first-line therapy due to its propensity to cause the least sedation. Corticosteroid nasal sprays are, however, the most effective overall treatment and should be the first-line treatment in adults suffering from moderate to severe cases of AR or those who are still symptomatic, despite regular use of antihistamines.

Practical prescribing and product selection

Prescribing information relating to the rhinitis medicines reviewed earlier is presented in [Table 2.15](#), and their relative effect on symptom control is summarized in [Table 2.16](#).



Table 2.15
Practical prescribing: Summary of rhinitis medicines

Name of medicine	Use in children (age, years)	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy & breastfeeding
Systemic antihistamines					
Acrivastine	>12	None	None	None	Manufacturers advise avoidance, but safety data have shown them to be safe.
Cetirizine	>2				
Loratadine	>2				
Chlorphenamine	>1	Dry mouth, sedation, constipation	Increased sedation with alcohol, opioid analgesics, anxiolytics, hypnotics, antidepressants.	Glaucoma, prostate enlargement.	Standard references state OK, although some manufacturers advise avoidance.
Ocular antihistamines					
Antazoline ^a	>12	None	Avoid concomitant use with MAOIs and moclobemide due to risk of hypertensive crisis.	Avoid in glaucoma.	Safety not established, but probably OK.
Nasal corticosteroids					
Beclometasone	>18	Nasal irritation, bitter taste,	None	Avoid in glaucoma.	Manufacturers advise avoidance, but safety data have shown them to be safe.
Fluticasone		Nasal irritation, bitter taste, nosebleeds, headache			
Triamcinolone		Headache, nosebleeds, dyspepsia, bronchitis, flulike symptoms, sore throat, cough			
Budesonide		Nasal irritation, nosebleeds			
Mometasone		Headache, sneezing, nose bleeds			Consult with doctor before use.
Ocular mast cell stabilizer					
Sodium cromoglicate	>6	None	None	None	OK.
Ocular sympathomimetics					
Naphazoline	>12	Local irritation	Avoid concomitant use with MAOIs and moclobemide due to risk of hypertensive crisis.	None	Not adequately studied but not yet shown to be a risk; probably OK.

^aOnly available in combination with sympathomimetics.
MAOI, Monoamine oxidase inhibitor.

Table 2.16
Efficacy and properties of drug treatments used in allergic rhinitis

Characteristic	Oral antihistamine	Nasal steroid	Nasal decongestant	Ipratropium bromide
Rhinorrhoea	++	+++	-	++
Sneezing	++	+++	-	-
Itching	++	+++	-	-
Blockage	+	+++	++++	-
Eye symptoms	++	++	-	-
Onset of action	1 hour	12 hours	5–15 minute	15–20 minute
Duration	12–24 hours	12–48 hours	3–6 hours	4–12 hours

-, No effect; +, marginal effect; +++, substantial effect (under natural exposure conditions).

From Farooque, S. (2012). Allergic rhinitis: Guide to diagnosis, allergen avoidance and treatment. *The Prescriber*, 23, 330–339.

HINTS AND TIPS BOX 2.4: RHINITIS

Breakthrough symptoms with once-daily antihistamines

Patients who suffer breakthrough symptoms using a once-daily preparation (e.g., loratadine, cetirizine) may benefit from changing to acrivastine because three times a day dosing may result in better symptom control.

Corticosteroid nasal sprays

These are suspensions, and the bottle should be shaken before use. Regular usage is essential for full therapeutic benefit. It should also be explained to the patient that maximum relief might not be obtained for several days. However, most begin to act in 3–7 hours.

Useful tips relating to patients presenting with rhinitis are given in 'Hints and Tips' in [Box 2.4](#).

Systemic antihistamines

Systemic antihistamines selectively inhibit histamine H₁ receptors and suppress many of the vascular effects of histamine. They have rapid onset of action (~30–60 minutes) and relieve ocular symptoms, rhinorrhoea and nasal irritation, but have less effect on nasal congestion. For maximum effect, they are best taken on a regular basis but will still be effective if taken when required. Patient response is variable among the differing antihistamines, and more than one type may have to be tried to provide symptom control. They possess very few side effects and can be given safely with other prescribed medications. They can also be prescribed to all patient groups, although manufacturers advise against prescribing to older adults.

First-generation sedating antihistamines are the preferred antihistamines in pregnancy because the risk of foetal toxicity appears low, with chlorphenamine being the medicine of choice. Of the nonsedating antihistamines, loratadine is the most widely studied; available data do not indicate an increased risk of teratogenicity, yet manufacturers advise avoidance (presumably on the basis of being outside their product licences). For breastfeeding mothers, nonsedating antihistamines should be avoided because infant drowsiness has been associated with their use. Expert opinion has noted that cetirizine and loratadine can be used if absolutely required.

Nonsedating antihistamines

Acrivastine (Benadryl Allergy Relief)

Acrivastine is recommended for adults and children above 12 years. The dose is one capsule (8 mg) as necessary, up to three times a day. Acrivastine can also be purchased as

a combination product (Benadryl Allergy Relief Plus Decongestant), which contains a sympathomimetic (pseudoephedrine). However, if nasal congestion is a problem, corticosteroids should be considered in preference to a decongestant.

Cetirizine (e.g., *Benadryl Allergy One-a-Day, Benadryl Allergy Oral Solution and Liquid Capsules, Piriteze range, Zirtek range*)

Cetirizine is available as tablets, capsules or solution. The dose for adults and children 6 years and older is 10 mg daily. The adult dose is as a single dose (10 mL, or one tablet), whereas for children older than 6 years this is given as 5 mg (5 mL, or half a tablet) twice daily. For children between 2 and 5 years of age, the dose is 2.5 mL (2.5 mg) twice daily. Not all manufacturers have a licence for children under 6 years of age, so it is important to refer to specific manufacturer literature before making recommendations.

Loratadine (e.g., *Clarityn range*)

Loratadine is available as a tablet or syrup. The dose for those older than 12 years is 10 mg daily. The syrup (1 mg/mL) can be given to children 2 to 12 years old (providing they are >30 kg) at a dose of 5 mg (5 mL) daily.

Sedating antihistamines

Chlorphenamine (e.g., *Piriton Allergy Tablets and Syrup*)

This can be given to children from 1 to 2 years of age (2.5 mL [1 mg] twice daily). The dose for children 2 to 6 years of age is 2.5 mL (1 mg) every 4 to 6 hours, and for children 6 to 12 years of age it is 2 mg (5 mL [2 mg] or half a tablet) every 4 to 6 hours. The adult dose is 4 mg every 4 to 6 hours.

Sympathomimetics

For information about sympathomimetics and product information on nasally administered products, see earlier in the chapter under cold products.

Nasal corticosteroids (beclometasone, budesonide, fluticasone, mometasone, triamcinolone) can be used in most patient groups older than 18 years, although avoidance is recommended in glaucoma. (Glaucoma and/or cataracts have been reported in patients receiving nasal corticosteroids) In addition, manufacturers other than the makers of budesonide (Benacort) recommend that they should not be used during pregnancy and breastfeeding due to insufficient evidence to establish safety. Beclometasone and fluticasone can cause unpleasant taste and smell, as well as nasal and throat irritation. Beclometasone is also reported, rarely, to cause hypersensitivity reactions. Fluticasone and

triamcinolone also cause headaches and nosebleeds. Dyspepsia, bronchitis, flu-like symptoms, sore throat, and cough have also been reported with triamcinolone. Budesonide is associated with nasal irritation and nosebleeds.

Beclometasone (*Beconase Hayfever*)

The recommended dose is two sprays into each nostril twice daily (400 µg/day). Once symptoms have improved, it might be possible to decrease the dose to one spray twice daily. However, should symptoms recur, patients should revert to the standard dosage.

Fluticasone (*Pirinase Hayfever Nasal Spray*), **triamcinolone** (*Nasacort Allergy Nasal Spray*), **budesonide** (*Benacort Nasal Spray*), and **mometasone** (*Clarinaze Allergy Control*)

The dose is two sprays into each nostril once daily. Like beclometasone, once symptoms are controlled, the patient should use the lowest effective dose.

Ocular cromoglicate (e.g., *Opticrom range, Optrex Allergy and Hayfever Relief, Murine hayfever relief*)

One or two drops should be administered in each eye four times a day. It is a prophylactic agent and needs to be started at least 1 week before required and given continuously while exposed to the allergen. Instillation of the drops can rarely cause a transient blurring of vision. It has no drug interactions and can be given to all patient groups. Clinical experience has shown cromoglicate to be safe in pregnancy, and expert opinion considers sodium cromoglicate to be safe in breastfeeding.

Ocular sympathomimetics

These contain a combination of a sympathomimetic and antihistamine (antazoline-xylometazoline, Otrivine Antistin) or sympathomimetic alone (e.g., Naphazoline, 0.01%). They are useful in reducing redness in the eye but will not treat the underlying pathology that is causing the eye to be red. Like all sympathomimetics, they can interact with monoamine oxidase inhibitors (MAOIs) and should not be used by patients receiving such treatment or within 14 days of ceasing therapy.

Otrivine Antistin

Used in adults and children over 12 years, the dose is one or two drops two or three times a day. Patients with narrow-angle glaucoma should avoid this product due to the potential of the antihistamine component to increase intraocular pressure. Local transient irritation and a bitter taste after application have been reported.

Naphazoline

The use of products containing naphazoline (e.g., Murine Irritation & Redness Relief Eye Drops, Murine Bright & Moist Eyes, Optrex Bloodshot Eyes Eye Drops, Optrex Brightening Eye Drops) is restricted to adults and children older than 12 years. One to two drops should be administered into the eye three or four times a day.

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Further reading

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Websites

- Action Against Allergy: <https://actionagainstallergy.org/>
- Allergic Rhinitis and its Impact on Asthma (ARIA): <https://www.euforea.eu/aria>
- Allergy UK: <http://www.allergyuk.org/>
- British Society for Allergy and Clinical Immunology: <https://www.bsaci.org/>

Self-assessment questions

The following questions are intended to supplement the text. Two levels of questions are provided, multiple-choice questions and case studies. The multiple-choice questions are designed to test knowledge and application of knowledge, and the case studies allow this knowledge to be put into context in patient scenarios.

Multiple choice questions

- 2.1** Which of the following conditions causing cough is most prevalent in the immigrant population?
- Chronic bronchitis
 - Asthma
 - Heart failure
 - Pneumonia
 - Tuberculosis
- 2.2** Which of the following conditions with cough as a major presenting symptom is least likely to produce a productive cough?
- Chronic bronchitis
 - Asthma
 - Bronchiectasis
 - Pneumonia
 - Tuberculosis
- 2.3** Mrs Jones visits your pharmacy complaining of having a dry cough for the last 7 days. After questioning, you decide it is a simple viral infection and recommend simple linctus. If symptoms persist, after how many further days would referral to the physician be appropriate?
- 3 days
 - 5 days
 - 7 days
 - 10 days
 - 14 days
- 2.4** Mr Patel, who is 48 years old, presents with a nonproductive cough. Based on epidemiology, what is the most likely cause of the cough?
- Acute bronchitis
 - Upper airways cough syndrome (postnasal drip)
 - Asthma
 - Viral infection
 - Pneumothorax
- 2.5** Dyspnoea is a symptom most closely associated with which condition?
- Chronic bronchitis
 - Asthma
 - Heart failure
 - Pneumonia
 - Tuberculosis
- 2.6** You are recommending treatment for a young woman to treat a common cold (primary symptom of nasal congestion). She tells you that she is breastfeeding. What would be the most suitable option?
- Vitamin C
 - Steam inhalation
 - Oral sympathomimetics
 - Topical sympathomimetics
 - Antihistamines
- 2.7** Simon, who is 32 years old, presents with a nonproductive cough of 6 days' duration. He has no other symptoms and takes no medication. What would be the most appropriate course of action to take?
- Give pholcodine, 5 mL qds.
 - Advise only on drinking more fluids.
 - Give dextromethorphan, 10 mL qds.
 - Give guaifenesin, 10 mL qds.
 - Give glycerine lemon and honey, 10 mL qds.
- 2.8** Steven Blake, who is 37 years old, visits the pharmacy wanting treatment for his cough. After questioning him, you find out he has had a nonproductive cough for the last 7 to 10 days. He also states he has had some nasal congestion and been suffering from occasional shortness of breath. Based on the signs and symptoms listed, what is the most likely diagnosis?
- Upper airways cough syndrome (UACS)
 - Acute bronchitis
 - Chronic bronchitis
 - Pneumonia
 - Pneumothorax

- 2.9** Jane Thompson, a 19-year-old woman, has a nonproductive cough. You believe it to be a viral infection. Jane is asthmatic and suffers from type 1 diabetes. What would be the most appropriate treatment or course of action?
- No treatment
 - A demulcent
 - A cough suppressant
 - An antihistamine
 - An expectorant
- 2.10** Joanne Martin presents with a productive cough. She tells you that is yellow-green in colour. Given this information, what condition is most likely?
- Acute viral infection
 - Heart failure
 - Pneumonia
 - Chronic bronchitis
 - Acute bacterial infection
- 2.11** David Daly, a 52-year-old man, presents with symptoms of nasal congestion, slight sore throat, headache, and loss of smell. The pharmacist decides to make a referral to the physician because the differential diagnosis suggests the following:
- Influenza
 - Sinusitis
 - Postnasal drip
 - Rhinitis
 - Glandular fever
- 2.12** A middle-aged man presents with sore throat. He has had the symptoms for 3 days. From the list of other symptoms, which would warrant referral to the physician?
- Rhinorrhoea, cough, malaise, fever, headache and hoarseness
 - Rhinorrhoea, malaise, fever, headache and hoarseness
 - Rhinorrhoea, cough, malaise, headache and hoarseness
 - Rhinorrhoea, cough, malaise and fever
 - Rhinorrhoea, cough, malaise, fever and hoarseness
- 2.13** A 28-year-old patient presents with a cold and tells you the following: 'I developed a sore throat a few days ago and now, as you can hear, my voice is very hoarse. My nose is all bunged up and I have a headache. I have taken paracetamol, which has not helped that much'. Which of the following is the most appropriate advice to give?
- See a GP; the paracetamol should have helped ease the symptoms.
 - See a GP; it sounds like you may now have sinusitis.
 - See a GP; the symptoms sound more like a bacterial infection than a viral infection.
 - It sounds like a typical cold; try some vitamin C and keep taking the paracetamol.
 - It sounds like a typical cold; keep taking the paracetamol and try pseudoephedrine to ease the nasal congestion.
- 2.14** From the list below, what symptom(s) would best describe a bacterial sore throat?
- Tonsillar exudate, cough, headache
 - Substantial tonsillar exudate, swollen cervical glands and high-grade fever
 - Tonsillar exudate, swollen cervical glands, cough and headache
 - Substantial tonsillar exudate, and swollen cervical glands
 - Tonsillar exudate, swollen cervical glands and high-grade fever
- 2.15** Based on epidemiology, what would be the most likely condition for a 55-year-old man with a productive cough and a history of smoking?
- Acute bronchitis
 - Chronic bronchitis
 - Viral cough
 - Asthma
 - Postnasal drip
- Questions 2.16 to 2.21 concern the following conditions:
- Pneumonia
 - Heart failure
 - Tuberculosis (TB)
 - Chronic bronchitis
 - Laryngotracheobronchitis
- Select, from A to E, which of the above conditions:
- 2.16** Is characterized by night sweats?
- 2.17** Has initially a nonproductive painful cough that progresses to a productive cough?
- 2.18** Is closely associated with a history of smoking?
- 2.19** Is associated with a high-grade fever?

2.20 Has cough that is worst in the morning?

2.21 Has a cough has a barklike quality?

Questions 2.22 to 2.25 concern the following medications:

- A. Acrivastine
- B. Loratadine
- C. Chlorphenamine
- D. Cetirizine
- E. Antazoline

Select, from A to E, which of the above medicines:

2.22 Causes least sedation when orally administered

2.23 Is most likely to cause sedation?

2.24 Is most suitable for a pregnant woman with nasal congestion?

2.25 Can be given to children from the age of 1 year old?

Answers

2.1 Answer: e

Rationale: Only tuberculosis (e) from the listed conditions is more associated with ethnicity.

2.2 Answer: b

Rationale: Chronic bronchitis (a), bronchiectasis (c), and tuberculosis (e) are associated with productive coughs; Pneumonia (d) can start with a nonproductive cough but becomes productive; asthma (b) invariably has a nonproductive cough.

2.3 Answer: e

Rationale: Conditional referrals are important for safety netting purposes. Acute cough is defined as 3 weeks or less, so in this case giving 14 days as the referral point is correct as the person has had the cough for just 7 days.

2.4 Answer: d

Rationale: For all patients, regardless of age and gender, viral infection (d) is the most common presentation.

2.5 Answer: c

Rationale: Dyspnoea, difficulty in breathing, could be seen in all the listed conditions. However, in a community pharmacy context, people with conditions other than heart failure (c) will be less associated with dyspnoea. Other symptoms such as shortness of breath and fatigue will be more frequently seen.

2.6 Answer: d

Rationale: Based on evidence, topical sympathomimetics (d) have the strongest evidence of efficacy. The added problem here is can they be given to this patient group? Manufacturer data states no adverse effects recorded and states it to be used with caution.

2.7 Answer: b

Rationale: Guaifenesin (d) is for productive coughs; Pholcodine (a) and dextromethorphan (c) are suitable for nonproductive coughs but current advice is to avoid them where possible; likewise, although chemically inert, glycerine (e) is not advocated.

2.8 Answer: b

Rationale: Chronic bronchitis (c) tends not to have nasal congestion; pneumonia (d) after this time should present with productive cough; pneumothorax (e) is very sudden in

onset and will not have this history. This leaves UACS (a) and acute bronchitis (b) as viable options. In this case, acute bronchitis is more likely to have shortness of breath as a symptom.

2.9 Answer: a

Rationale: Viral infections are self-limiting, and no treatment is necessary, so (a) would be a suitable recommendation. A demulcent could be tried. Because they are diabetic, a sugar-free alternative would be useful, but it is unlikely that a few days' treatment with a demulcent containing sugar will affect their diabetic control. If a demulcent containing sugar is recommended, the person could be told to monitor their blood sugar level more regularly. Cough suppressants and antihistamines have no evidence of efficacy and should not be recommended. An expectorant is only suitable for productive coughs.

2.10 Answer: a

Rationale: Sputum colour can be useful in helping narrow down the differential diagnosis. Viral and bacterial infection can range from sputum with no colour to yellow, green or brown. Given that viral infection is much more prevalent than bacterial infection, this is the most likely condition in this scenario.

2.11 Answer: b

Rationale: Nasal congestion and sore throat are hallmark symptoms of the common cold. However, loss of smell in association with these symptoms can suggest sinusitis.

2.12 Answer: b

Rationale: The symptom cluster of rhinorrhoea, cough, malaise, fever, headache and hoarseness are suggestive of viral infection. Absence of cough can indicate a bacterial infection and is therefore worthy of referral.

2.13 Answer: e

Rationale: Options a, b, and c all suggest referral but the symptom cluster does sound like normal symptoms of a cold and could be treated. This leaves d and e as possible correct answers. Vitamin C (d) has no evidence of efficacy, so e is the most suitable answer.

2.14 Answer: b

Rationale: A bacterial cause is hard to establish but a symptom cluster of option b is the best descriptor.

2.15 Answer: c

Rationale: A viral cause (c) should always be considered most likely although because this person is middle aged and has a history of smoking, bronchitis (a or b) is also likely and should be considered as the next most likely cause.

2.16 Answer: C

Rationale: Associated symptoms with cough are useful in formulating a differential diagnosis. Pneumonia (A) shows signs of infection, heart failure (B) shortness of breath, chronic bronchitis (D) wheeze and breathlessness and croup (E) breathlessness. None show night sweats.

2.17 Answer: A

Rationale: Most coughs are productive or nonproductive from the outset. Heart failure (B), TB (C) and chronic bronchitis (D) are productive; croup (E) is nonproductive. Only pneumonia (A) from the listed conditions tends to change from nonproductive to productive.

2.18 Answer: D

Rationale: Croup (E) is a childhood condition; pneumonia (A) and TB (C) are infections; heart failure (B) is associated with old age. Chronic bronchitis (D) has a strong association with smoking.

2.19 Answer: A

Rationale: Fever tends to suggest infection. From the above, only two conditions are infectious in origin, pneumonia (A) and TB (C). Of these, pneumonia often presents with a high fever.

2.20 Answer: D

Rationale: Some coughs can exhibit worse symptoms at certain times of the day. From the listed conditions, this is true of chronic bronchitis (D) and croup (E). Croup shows worsening symptoms in the evening.

2.21 Answer: E

Rationale: The sound of the cough is not normally helpful in establishing a diagnosis. However, for croup (E) the noise of the cough is characteristic and helpful in establishing the diagnosis

2.22 Answer: B

Rationale: Antazoline (E) is only available via the ocular route; chlorphenamine (C) is a first-generation antihistamine and causes sedation; this leaves the three second-generation antihistamines as options. All are less sedating than first-generation antihistamines but none are truly nonsedating. Of the three, loratadine (B) appears, from trial data, to be the least sedating.

2.23 Answer: C

Rationale: As per the answer for question 2.22, chlorphenamine (C) is the correct option.

2.24 Answer: C

Rationale: Manufacturers advise against the use of second-generation antihistamines (options A, B and D). Antazoline (E) would not be used in nasal congestion.

2.25 Answer: C

Rationale: Acrivastine (A) and antazoline (E) are licensed for use in those from 12 years of age and loratadine (B) and cetirizine (D) from 2 years.

Self-assessment questions

The following questions are intended to supplement the text. Two levels of questions are provided: multiple choice questions and case studies. The multiple choice questions are designed to test knowledge and application of knowledge, and the case studies allow this knowledge to be put in context in patient scenarios.

Multiple choice questions

- 2.1** Which respiratory condition is characterized by shortness of breath and bronchoconstriction?
- Acute bronchitis
 - Asthma
 - Chronic bronchitis
 - Heart failure
 - Pneumonia
- 2.2** What course of action would be most appropriate if a baby was suffering with croup-like symptoms?
- Give the infant a cough suppressant
 - Give the infant an antihistamine
 - Put the infant into a steamy room
 - Seek medical help if symptoms persist for more than 48 hours
 - Take the infant to casualty
- 2.3** Which patient group is most at risk of pneumothorax?
- Children
 - Elderly men
 - Elderly women
 - Young men
 - Young women
- 2.4** Which one of the following medicines can cause rebound congestion with overuse?
- Chlorphenamine tablets
 - Codeine linctus
 - Guaifenesin cough mixture
 - Oxymetazoline nasal spray
 - Pseudoephedrine tablets
- 2.5** Which medicine is the drug of choice for nasal congestion caused by allergic rhinitis?
- Acrivastine
 - Chlorphenamine
 - Loratadine
 - Nasal beclometasone
 - Nasal decongestant
- 2.6** Which patient group is most likely to suffer from infectious mononucleosis?
- Adolescents
 - Adults
 - Infants
 - Children
 - The elderly
- 2.7** What symptoms are commonly associated with acute rhinosinusitis?
- Dull, diffuse bilateral pain that is often worse on bending down
 - Dull, diffuse bilateral pain that often eases on bending down
 - Dull, localized unilateral pain that is often worse on bending down
 - Dull, localized unilateral pain that often eases on bending down
 - Sharp, localized bilateral pain that often eases on bending down
- 2.8** The most likely cause of acute cough in children is:
- Asthma
 - Bacterial infection
 - Croup
 - Postnasal drip
 - Viral infection
- 2.9** Presenting symptoms of shortness of breath and dyspnoea are two symptoms most associated with?
- Asthma
 - Chronic bronchitis
 - Heart Failure
 - Pneumonia
 - Tuberculosis
- 2.10** In which group of patients should chlorphenamine be used with caution or avoided?
- People with asthma
 - People with epilepsy

- c. People with hypertension
- d. People with glaucoma
- e. People with GORD

2.11 Based on epidemiology, what would be the most likely condition for a 55-year-old man with productive cough with a history of smoking?

- a. Acute bronchitis
- b. Asthma
- c. Chronic bronchitis
- d. Postnasal drip
- e. Viral cough

2.12 In which patient group should flurbiprofen lozenges be avoided?

- a. Asthmatics
- b. Patients with peptic ulcers
- c. Hypertensive patients
- d. Patients with moderate renal impairment
- e. Patients with mild hepatic impairment

2.13 Which of the following medicines should only be given short-term for the relief of hayfever?

- a. Acrivastine
- b. Beclometasone
- c. Sodium cromoglicate
- d. Naphazoline
- e. Fluticasone

2.14 Stephanie Bridges, who is 28 years old, asks for a cough medicine for her chesty cough. From the following symptoms, which one is most likely to make you refer the patient?

- a. Associated frontal headaches
- b. Cough present for 10 days
- c. Failure of symptoms to respond to guaifenesin

- d. Occasional episodes of shortness of breath
- e. Sputum that is green in colour

Questions 2.15 to 2.17 concern the following conditions:

- A. Acute bronchitis
- B. Chronic bronchitis
- C. Heart failure
- D. Pneumonia
- E. Tuberculosis

Select in which of the above conditions (A to E):

2.15 Shortness of breath is often the main presenting symptom

2.16 Cigarette smoking is the main cause of the condition

2.17 A higher prevalence is seen in ethnic groups

Questions 2.18 to 2.20 concern the following medicines:

- A. Beclometasone
- B. Benzydamine
- C. Codeine
- D. Pholcodine
- E. Pseudoephedrine

Select, from A to E, which of the above medicines:

2.18 Should be ideally avoided by patients taking beta-blockers?

2.19 Is associated with illicit drug manufacture?

2.20 Can reduce breast milk production?

Answers

2.1 Answer: b

Rationale: Shortness of breath is rarely seen in acute bronchitis (a). All other options can show breathlessness but chronic bronchitis (c), heart failure (d) and pneumonia (e) do not normally exhibit bronchoconstriction.

2.2 Answer: d

Rationale: Traditionally people advocated putting the child in a steamy room (c) but this is now not recommended. Treatment with cough remedies (a) and (b) will be ineffective. Symptoms, although distressing, rarely warrant direct referral to an emergency department (e).

2.3 Answer: d

Rationale: Epidemiological data show that young men (d) are more prone to pneumothorax but it is unknown why.

2.4 Answer: d

Rationale: Sympathomimetics are known to have this effect (options d and e) but it only occurs with topical formulations d.

2.5 Answer: d

Rationale: All options will have a beneficial effect on symptoms; however, nasal decongestants (e) should be only used short-term. Antihistamines are effective but less so than corticosteroids in treating nasal symptoms.

2.6 Answer: a

Rationale: Glandular fever is most commonly seen in young adults as transmission is primarily through saliva (e.g. kissing).

2.7 Answer: c

Rationale: Pain is dull, thus eliminating option e. It starts as unilateral pain (generally when someone would present to the pharmacy) and so options a and b can also be eliminated. Pain is worsened on bending down so option c is correct.

2.8 Answer: e

Rationale: All possibilities can be seen in children. Croup (c) is specific to children but relatively uncommon. Asthma (a) has higher prevalence rates in children than adults but

again is not very common. Postnasal drip (d) is usually a consequence of infection, of which viral (e) is by far the most common cause of cough.

2.9 Answer: c

Rationale: Dyspnoea (laboured breathing) is a relatively uncommon symptom associated with cough. Breathlessness can be seen in pneumonia, heart failure, chronic bronchitis and asthma. Although shortness of breath as well is most seen with asthma and heart failure, but cough would be expected to be a presenting symptom in asthma.

2.10 Answer: d

Rationale: Antihistamines have an anticholinergic effect and therefore need to be used with caution in glaucoma more than the other conditions listed.

2.11 Answer: e

Rationale: Smoking history will mean that chronic bronchitis (c) is a possibility in this age group but viral cough will still be the commonest cause of cough.

2.12 Answer: b

Rationale: Dosing adjustments are required in severe renal and liver impairment only and severe heart failure as well as in patients with active or history of recurrent peptic ulceration.

2.13 Answer: d

Rationale: Nasal steroids (b and e) need to be used regularly as does cromoglicate (c) to have any beneficial effect. Acrivastine (a) can be given intermittently or long term, but naphazoline (d), because of rebound effects, is limited to short-term use only.

2.14 Answer: d

Rationale: Associated headaches with cough (a) is a relatively common symptom; duration (b) is classed as acute until 3 weeks has elapsed; failure to respond to treatment (c) doesn't necessarily require referral, but reassessment of symptoms would be advisable; sputum colour (e) unless suggestive of haemoptysis is not a referral point. However, shortness of breath (d) needs further evaluation.

2.15 Answer: C

Rationale: Heart failure is insidious in onset and does not usually present with cough as the first symptom if identified whilst still mild. The other conditions will generally present with cough as a major presenting symptom.

2.16 Answer: B

Rationale: Pneumonia (d) and tuberculosis (e) are bacterial in origin; heart failure (c) is due to left ventricular failure; acute bronchitis (a) is usually viral in origin. Chronic bronchitis (b) is associated strongly with a smoking history.

2.17 Answer: E

Rationale: Ethnicity does not usually effect prevalence of conditions associated with cough although a notable exception is tuberculosis with the majority of cases seen in people from the Indian subcontinent.

2.18 Answer: E

Rationale: Pseudoephedrine has direct and indirect sympathomimetic activity and can increase systolic blood pressure but is much less potent than ephedrine.

2.19 Answer: E

Rationale: Pseudoephedrine is structurally related to methamphetamine (crystal meth) and has been used as a base to manufacture it.

2.20 Answer: E

Rationale: None of the medicines listed in their respective SmPCs state they cause a reduction in breast milk, but there are a number of reports and research papers that have linked sympathomimetics to causing a reduction in breast milk production.

Case study

CASE STUDY 2.1

Mr RT has asked to speak to the pharmacist because he has a troublesome cough.

- a. Discuss the appropriately worded questions you will need to ask Mr RT to determine the cause of the cough.

Questions should fall broadly into two groups, those that relate to the presenting complaint (e.g., nature, duration, onset, periodicity, sputum colour [if applicable], associated symptoms, and aggravating and alleviating symptoms) and those that look at the medical, family, and social history of the patient (e.g., current medication regimen [recent changes to medication or dosage adjustment], self-medication, general well-being of the patient, smoking status).

Discussion with Mr RT indicates he has a productive cough that appeared a few days ago and the sputum is white. His nose is 'a bit blocked'. He has a headache and does not have any chest pain or shortness of breath. Before you can make a recommendation for the symptoms, you identify that he is taking the following medications:

- *Manerix 150 mg bd; he has taken this for over 6 months.*
 - *Trusopt td; he has used this for 2 years.*
 - *Paracetamol 2 qd prn for lower back pain.*
- b. Describe the products available to treat Mr RT's symptoms, and indicate which you consider would be the most beneficial.

Information related to products to treat a productive cough with nasal congestion should be sought.

This involves expectorant medication and sympathomimetics. Mr RT's current drug regimen will have to be taken into consideration and checks for interactions and suitability made. For example, Mr RT is taking Manerix; therefore, sympathomimetics should be avoided.

A few weeks later Mr RT returns to the pharmacy and complains that he is still having trouble clearing his blocked nose. A friend at work recommended Otrivine Nasal Spray.

- c. The use of local decongestants is associated with the phenomenon known as *rhinitis medicamentosa*. Explain what this is and what advice you would give to Mr RT.

Rhinitis medicamentosa relates to the problem of overly long use of topical sympathomimetics. Prolonged use (normally more than 5–7 days continuous use) results in vascular engorgement of the nose on withdrawal of the medication. Patients often believe mistakenly that symptoms have returned and begin to use the medication again, thus perpetuating the problem. This cycle of overuse has to be broken and explained to patients so that they understand why they have continued nasal congestion. Strategies to relieve the problem are, if appropriate, a switch to systemically administered decongestants or, if this is not appropriate, withdrawal of the medication. In Mr RT's case, he should be advised not to take the nasal spray because of the risk of a drug interaction between the spray and Manerix.

Case study

CASE STUDY 2.1

Mr CJ has asked to purchase some chlorphenamine for his hay fever.

- a. What appropriately worded questions will you need to ask Mr CJ to determine whether chlorphenamine is appropriate for him?

First, establish if his self-diagnosis is correct.

Questions that relate to the presenting complaint:

- *Duration of symptoms; what the symptoms are; has he had the symptoms before, and, if so, how often; do the symptoms occur at any particular time of the year, or when he comes in contact with anything in particular, such as cats?*

Questions that help to confirm diagnosis:

- *Family history of allergies; personal past history of dermatitis and/or asthma?*

Questions that relate to appropriateness of product requested:

- *How severe are the symptoms (e.g., is it disturbing his daily activities or sleep); has he used the chlorphenamine before and did it work; has he tried anything else for it?*
- *Current medicine regimen; occupation.*

Discussion with Mr CJ indicates he has had nasal itching and has been blowing his nose frequently for the last week or so; he has been kept awake with nasal congestion, sometimes making it difficult to concentrate the next day. He also states that his eyes have been itchy and red. This has occurred every April or May for the last couple of years. He tells you the symptoms last year lasted for about 2 months, and he tried a steroid nasal spray but gave up after a couple of days because it did not seem to help. So, he has been using chlorphenamine for the last couple of days, and although it has helped him with his sleep, he still finds it difficult to concentrate at work. Mr CJ reports he used to have asthma as a child but does not have symptoms any more. He is taking the following medicines:

- *Esomeprazole, 20 mg daily; he has taken this for over 12 months for reflux.*
- *Citalopram, 20 mg daily; he has taken this for 5 years for depression.*

- b. Based on this presentation and history, what is the most likely diagnosis, and why?

Mr CJ appears to be suffering from intermittent allergic rhinitis. This is supported by having had asthma as child, suggesting that he is possibly suffering from atopy. Given that it is disturbing his daily activities, the allergic rhinitis would be considered moderate to severe. No obvious cause can be determined but tree pollens are common in the spring and can cause hay fever-like symptoms.

- c. What would you recommend for Mr CJ, and why?

Given the severity of the symptoms, the presence of some congestion, and the usual duration of the symptoms (up to 8 weeks), intranasal corticosteroids would be the best option. Although Mr CJ has tried this in the past, he does not appear to have given them a very long trial because it may take several days for corticosteroids to have their maximal effect. If Mr CJ insists on using an oral antihistamine, a less sedating antihistamine such as loratadine should probably be used, given that he has complained of difficulty in concentrating, which could be next-day sedation, with the use of chlorphenamine. Also, loratadine provides 24-hour coverage, whereas chlorphenamine only lasts about 6 hours. If his eye symptoms persist, he could use eye drops. If the symptoms do not improve in 2 weeks of using a steroid spray or 5 to 7 days using loratadine, he should return to see you or visit his physician.

- d. What else could you recommend Mr CJ to try to limit his symptoms?

Allergen avoidance, although difficult, can be tried but you have not established the cause.

CASE STUDY 2.2

A female patient, who is approximately 30 years old, presents to the pharmacist complaining of a bothersome sore throat. The following information is obtained from the patient.

Information gathering	Data generated
Presenting complaint	
Symptoms you have	Pain when trying to swallow
How long you have had the symptoms?	Had for the last 2 days
Any other symptoms?	Headache
Additional questions asked	Increased temperature? don't know Difficulty swallowing? no
Examination	Throat appears normal; no ulceration or pus obviously visible using pen torch; glands do not feel swollen; running low fever (38°C [100.4°F])

Information gathering	Data generated
Medicines (OTC, Rx)	Taking nothing currently
Previous history of presenting complaint	Had cough and cold a few months ago
Past medical history	Eczema
Social history, which may include questions relating to smoking, alcohol intake, employment, personal relationships	No questions asked in relation to social history
Family history	Not applicable

Below summarises the expected findings for questions when related to the different conditions that can be seen by community pharmacists.

Condition	Age	Tonsillar, pharyngeal exudate	Duration	Cervical glands	Cough present	Other symptoms
Viral	Any age	Possible, but generally limited	3–7 days	Normal	Common	Low-grade fever, headache
Bacterial	Schoolchild	Often present and can be substantial	3–7 days	Swollen	Rare	High-grade fever, possible rash
Glandular fever	Adolescent	Unlikely	>14 days	Swollen	No	Lethargy
Trauma	Any age	Unlikely	Varies, depending on cause	Normal	No	None
Carcinoma	Older people	None	>14 days	Normal	No	Dysphagia, ear pain
Medications	Adults	None	Depends	Normal	No	

When this information is compared to our patient's symptoms, and linking this with known epidemiology on sore throat (see Table 2.7), it should be possible to make a differential diagnosis.

CASE STUDY 2.2 (Continued)

Condition	Age	Tonsillar, pharyngeal exudate	Duration	Cervical glands swollen	Cough present	Absence of dysphagia	Systemic upset present
Viral	✓	✓?	✓	✓	X	✓	✓
Bacterial	X	X	✓	X	X?	✓	✓?
Glandular fever	X	✓	X	X	✓	✓	X
Trauma	✓	✓	✓?	✓	✓	✓	X
Carcinoma	X	✓	X	✓	✓	X	X
Medications	N/A	N/A	N/A	N/A	N/A	N/A	N/A

We see that her symptoms most closely match viral infection or trauma (✓ represents symptom match). Coupled with the knowledge that the most likely cause of sore throat seen by pharmacists is viral, then the cause of her sore throat is almost certainly viral in origin.

To confirm this, the pharmacist could ask if any trauma had been experienced, because this is also a plausible option given her responses. If the answer is no (as would be expected), then this helps confirm your diagnosis.

To 'safety net', it is worth making sure that the person has none of the referral signs or symptoms (see Trigger points for referral, earlier), which is the case with this patient.

CASE STUDY 2.2

Mr MB, a man in his early 20s, asks for a 'strong' cough syrup for himself.

a. Based on epidemiology, what cause of coughs are those you need to consider on *initial* questioning?

- Viral cough
- Acute bronchitis
- Postnasal drip

b. What questions should you now ask Mr MB?

Questions relating to the presenting complaint:

- *What are the symptoms?*
 - Establish a symptom profile from which the hypothesis of most likely problem – acute viral cough – can be tested.
- *How long have you had the symptoms?*
 - Expectation that all likely causes listed above will be acute in nature, although postnasal drip can persist. If duration suggested chronic cough, this would likely result in referral. Pneumothorax, which is also an acute presentation, is a possibility but is very rare.

Mr MB said that he needed something strong to get rid of the cough that started a couple of months ago. He described the cough as a tickly dry cough that starts in the evening. Mr MB thinks that he must have caught a really strong bug because he is not getting any better, and the cough seems to be getting worse. He had the same cough last winter but it went away once the weather got warmer. Occasionally, he has a coughing fit so bad that it stops him from going for his usual run in the evening. Mr MB visited a pharmacy when he first started having this particular cough and purchased Nurofen Cold & Flu (ibuprofen 200 mg, pseudoephedrine, 30 mg).

Questions that help confirm the diagnosis:

- *Family history of atopy*
 - Information received means your thinking should now have ruled out all acute conditions and you should be looking at a more chronic problem. For his age group, the most likely condition to

cause chronic cough (and matches his symptom profile) is asthma. Often, the patient will have a personal or family history of atopy.

Questions that relate to safety netting:

- *Do you take any other medicines?*
- *Have you tried anything else for it?*
 - Knowing about any medical history will do two things. First, this would potentially support your atopy theory and, second, also inform your thinking about his management. It is worth finding out if he has tried other products because he seems to have had symptoms for some time. This will help establish their appropriateness because it appears that the product he has been using is not suitable for the symptoms experienced.

c. Based on this information, what is the most likely diagnosis now, and why?

There are enough signs and symptoms to suggest that Mr MB may be suffering from asthma. The coughing appears to start at night, provoked by a drop in temperature. The cough has also been going for several weeks and therefore is less likely to be associated with an upper airways condition. A positive atopy history would support your thinking.

d. What would you recommend for Mr MB for his cough, and why?

An antitussive or cough suppressant should be avoided because some active ingredients (e.g., pholcodine, dextromethorphan) could theoretically increase the risk of respiratory depression in patients with asthma.

Mr MB should be referred to his physician for further assessment.

e. Should he continue taking the medicines he has been taking?

Mr MB should stop taking the Nurofen Cold & Flu. The active ingredients would not help with the coughing, and the ibuprofen could cause a worsening of the symptoms.

CASE STUDY 2.3

Mr JL, an Asian man in his early 60s who is slightly overweight, wants something for his persistent cough. He has tried some OTC products from the supermarket, but they did not work. The following information is gained from the patient.

Information gathering	Data generated
Presenting complaint	
Description of symptoms	Cough with a little bit of phlegm
How long patient has had symptoms	Weeks; has been there in the background, not really bothered by it but doesn't seem to want to leave; saw his GP about 6 weeks ago and was given antibiotics; seemed to help, but the cough came back again
Nature of sputum	Not a lot there, really; seems green, brown
Onset, timing	Not noticed it being better or worse at any time
Other symptoms	Generally felt off colour for a while
Additional questions	No noticeable blood in sputum; no weight loss
Previous history of presenting complaint	Gets coughs and colds periodically but not constantly
Drugs (OTC, Rx)	Pantoprazole, 1 od, levothyroxine, 100 µg, 1 od
<i>Past medical history</i>	GORD, hypothyroidism
<i>Social history</i> , which may include questions relating to smoking, alcohol intake, employment, personal relationships	Drinks most nights plus smokes 20 to 40 cigarettes a day; currently unemployed, lives on his own
<i>Family history</i>	None

CASE STUDY 2.3 (Continued)

Below summarizes the expected findings for questions related to the different conditions that can be seen by community pharmacists.

Condition	Acute or chronic	Sputum	Sputum colour	Age	Systemic symptoms	Worse
Viral	Acute	Sometimes	White to green or yellow	Any	Yes	PM
Postnasal drip	Acute	No	N/A	Adult	No	None
Allergy	Either	No	N/A	Any	No	PM
Acute bronchitis	Acute	Sometimes	White to green or yellow	Adult	Yes	None
Croup	Acute	No	N/A	Young child	No	PM
Chronic bronchitis	Chronic	Yes	Mucopurulent	>40 years	No	AM
Asthma	Chronic	Sometimes	Yellow	Any	No	PM
Pneumonia	Acute	Yes	Rust tinged	>50 years	Yes	PM
Medication	Either	No	N/A	Adult	No	None
Heart failure	Chronic	Yes	Pink tinged	Older adult	No	PM
Bronchiectasis	Chronic	Yes	Mucopurulent	Adult	No	AM AND PM
Tuberculosis	Chronic	Yes	Blood present	Any	Yes	None
Cancer	Chronic	Yes	Dark red	>50 years	No	None
Pneumothorax	Acute	No	N/A	Young adult	No	None
Lung abscess	Chronic	No	N/A	Older adult	Yes	None
Nocardiosis	Chronic	Yes	Mucopurulent	Adult	Yes	None

When this information is compared with our patient's symptoms and linking this with known epidemiology on cough (see [Table 2.1](#)), it should be possible to make a differential diagnosis.

CASE STUDY 2.3 (Continued)

Condition	Acute or chronic	Sputum	Sputum colour (productive only)	Age	Systemic symptoms
Viral	X	✓?	X?	✓	✓
Postnasal drip	X	X	N/A	✓	X
Allergy	X?	X	N/A	✓	X
Acute bronchitis	X	✓	X?	✓	✓
Croup	X	X	N/A	X	X
Chronic bronchitis	✓	✓	✓	✓	X
Asthma	✓	✓?	✓?	✓	X
Pneumonia	X	✓	✓?	✓	✓
Medication	X?	X	N/A	N/A	N/A
Heart failure	✓	✓	X	X	X
Bronchiectasis	✓	✓	✓?	✓	X
Tuberculosis	✓	✓	✓?	✓	✓
Carcinoma	✓	✓	✓?	✓	X
Pneumothorax	X	X	N/A	X	X
Lung abscess	✓	X	N/A	✓	✓
Nocardiosis	✓	✓	✓?	✓	✓

We see that his symptoms most closely match chronic bronchitis, tuberculosis or nocardiosis (✓ represents 'symptom match') even though viral causes are the most common in all age groups.

Based on epidemiology, nocardiosis seems highly unlikely, so is it chronic bronchitis or tuberculosis? The man does smoke heavily, and this fits with chronic bronchitis, but he says that he has not had a repeated history of cough. The patient has felt unwell for 'a while' and this suggests systemic involvement. Although rare, tuberculosis appears to be a possibility, and it would seem sensible to refer him to his GP because of the long-standing nature of the symptoms, general malaise, and ethnic background.

CASE STUDY 2.3

Mrs CD, a woman in her 40s, says she has caught the 'flu' from her husband. She feels tired and has a headache. She took some of her husband's Lemsip but it hasn't really helped. Mrs CD is worried about spreading it to her kids.

a. What questions should you ask Mrs CD?

Questions relating to the presenting complaint:

- Describe the symptoms,
 - Don't rely on her self-diagnosis. Ask her to tell you about how she feels and what symptoms she is experiencing. People are likely to have the common cold much more frequently than flu. However, the severity of the common cold can vary from nuisance value to debilitating, so establishing the exact nature and severity of the symptoms is important.

Questions that help to confirm diagnosis:

- How severe are the symptoms: have you been bed-ridden? Can you function generally OK?
- How quickly did the symptoms come on?
 - Both these questions help establish the difference between true flu and a severe common cold. With flu, you would expect the person to be unable to carry out regular daily functions and to have had a sudden onset of symptoms.

Questions relating to patient management:

- Do you take any other medicines?
- History of allergies?

Mrs CD has a headache, which feels worse when she sneezes or bends over. She has to constantly blow her nose, and it feels blocked. She started experiencing these symptoms 2 days ago. She has had no fever and does not have any allergies. Mrs CD also takes the following medications:

- Ramipril, 10 mg, one daily
- Atorvastatin, 20 mg, one daily
- Esomeprazole, 20 mg, one daily

b. Based on this presentation and history, what is the most likely diagnosis, and why?

Based on the presenting symptoms, Mrs CD most likely has a common cold. It is usually self-limiting; most colds resolve in 1 week but symptoms can sometimes last 14 days or more. Her headache is probably due to rhinosinusitis because she is experiencing congestion and facial pain.

c. What would you recommend for Mrs CD, and why?

Mrs CD could get some relief from nasal congestion by using a sympathomimetic such as pseudoephedrine. However, systemic sympathomimetics could alter the control of blood pressure (although unlikely). From her medication history, Mrs CD appears to have hypertension. A topical sympathomimetic, such as an oxymetazoline nasal spray, could be recommended as a safer route of administration. However, Mrs CD should be advised that it should only be used for no more than 3 to 5 days to prevent rebound congestion.

Paracetamol can be recommended to Mrs CD for symptomatic relief of pain related to rhinosinusitis. Ibuprofen would be best avoided because this could affect her hypertension, but she also appears to have some gastrointestinal issue such as gastro-oesophageal reflux disease (GORD) or peptic ulcer, given the use of esomeprazole.

d. Mrs CD says that her neighbour said to give her children vitamin C each day to help avoid her cold. What do you advise, and what could she do to reduce the risk of the kids catching her cold?

There is no good evidence for vitamin C in preventing the common cold. To limit the viral spread, Mrs CD should use disposable tissues rather than handkerchiefs and wash her hands frequently. She should avoid sharing hand towels with the rest of her family.

Ophthalmology

In this chapter

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Background

The eye is one of the most important and complex organs of the body. Due to its complicated and intricate anatomy, many things can and do go wrong with the eye, and these manifest as ocular symptoms to the patient.

It is the pharmacist's role to differentiate between minor self-limiting and serious sight-threatening conditions. Pharmacists can also play a role in health promotion towards eye care, especially in those patients who present with repeat medication for degenerative conditions, such as glaucoma and age-related macular degeneration. Checking patient adherence, ability to administer eye drops and ointments correctly and, potentially, identify any deterioration of the patient's condition should be built into routine counselling.

General overview of eye anatomy

A basic understanding of eye anatomy is useful because knowing which structures are affected will shape the management and treatment of the presenting complaint. Fig. 3.1 highlights the principal eye structures.

The eyelids

The eyelids act as protection from excessive light and foreign bodies, as well as spreading lubricating secretions over the eyeballs. They consist mainly of voluntary muscle with a border of thick connective tissue known as the tarsal plate.

This plate is felt as a ridge when everting the eyelid. Eyelashes also help protect the eye. At the base of the eyelash, sebaceous ciliary glands release lubricating fluid. It is these glands that if infected, can cause styes.

The lacrimal apparatus

The function of the lacrimal apparatus is to drain lacrimal fluid from the orbit and are located at the upper outer margin of the eye orbit (between the corner of the eye and the bridge of the nose). Blockage of the lacrimal duct can mean that tears are not drained, leading to increased intraocular pressure and glaucoma.

The conjunctiva

This is a transparent, thin continuous mucous membrane that covers the inside of the eyelids (palpebral conjunctiva) and the sclera (bulbar conjunctiva). It acts as a protective layer for the eye. Dilation and congestion of blood vessels of the bulbar conjunctiva via infection, allergy or irritants causes *red eye*.

The sclera and cornea

The sclera encircles the eye, apart from a small window at the very front of the eye where the cornea is located. The sclera is often referred to as the white of the eye and gives shape and rigidity to the eyeball. The transparent cornea allows light to enter the eye and, because of its curved nature, helps converge light onto the retina; it is responsible for approximately 75% of light refraction.

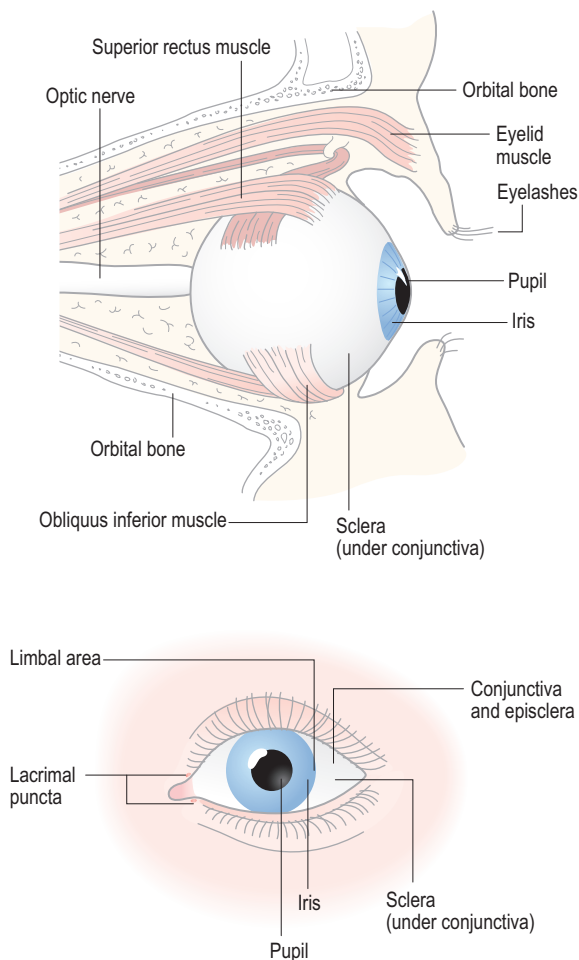


Fig. 3.1 Anatomy of the eye. *Above, side view; below, front view.*

The iris and pupil

The iris is the coloured part of the eye; its main function is to regulate the amount of light entering the eyeball. It is an incomplete circle, with a hole in the middle, which forms the pupil. It is suspended between the cornea and lens and is attached to the ciliary processes.

The lens

The lens sits behind the pupil and iris and is held in position by fibres that attach to the ciliary processes. It is responsible for fine-focusing light onto the retina and possesses the ability to vary its focusing power. However, this variable focus power is lost with increasing age as the lens grows harder and less elastic. This is why many people require reading glasses as they get older.

The retina

The retina is the light-sensitive layer of the eye and the start of the visual pathway. The functioning of the retina can be compromised by many factors, such as an underlying disease state (e.g., age-related macular degeneration), and foreign bodies causing retinal damage and detachment.

Interior of the eyeball

The lens divides the interior of the eyeball into the anterior cavity and vitreous chamber. The anterior cavity consists of the anterior (front) and posterior (back) chambers. Both are filled with a watery solution (aqueous humor) that bathes the lens and cornea. This is manufactured behind the iris by the ciliary processes and travels through the posterior chamber and pupil before draining at the anterior chamber angle (where the iris meets the cornea). Intraocular pressure is produced mainly by this aqueous humor.

History taking and the eye examination

History

A detailed history should be sought from the patient when attempting to decide on the cause of the presenting complaint. Pay attention to changes in vision, the severity and nature of discomfort, and the presence of discharge. Do not forget to ask about any family history of eye disease (e.g., glaucoma) and the person's previous eye and medication history. Answers to these questions should enable the pharmacist to build up a picture of the problem and arrive at a differential diagnosis.

The history gained should then be supplemented by performing an eye examination. A great deal of information can be learnt from a close inspection of the eye. For example, you can check the size of the pupils, their comparative size and reaction to light, the colour of the sclera, the nature of any discharge, and whether there is any eyelid involvement. It is impossible for you to agree with a patient's self-diagnosis or to differentially diagnose any form of conjunctivitis from behind a counter. Pharmacists owe it to their patients to perform a simple eye examination.

The eye examination

Before performing an eye examination, it is important to fully explain to the patient what you are about to do and to gain their consent. There are three basic steps that must

be undertaken; the order is unimportant as long as they are all performed:

1. Inspect the eye.
2. Check for visual acuity.
3. Check pupil reactions.

Points 2 and 3 help assess for possible sinister pathology, whereas point 1 will establish the distribution and extent of redness. Before any examination takes place, wash your hands and sit down with the patient so that you are at each other's eye level.

1. Inspect the eye

To allow a full assessment of the distribution and severity of the affected eye(s), it is necessary to view all aspects of the sclera. This is done by basic manipulation of the eyelids:

To examine the lower part of the sclera, you need to gently pull down the lower lid and ask the patient to look upwards and to both the left and the right.

To examine the upper part of the sclera, you need to gently lift up the upper lid and ask the patient to look downwards and to both the left and the right.

If only one eye is affected, you should perform these procedures on both the good and the bad eyes so that you have a comparison between normal and abnormal.

2. Check for visual acuity

Visual acuity can be assessed by asking the patient to read small print with the affected eye while blocking off the good eye. Printed material should be held at a minimum of arm's length and the person asked to read the text. A reduction in visual acuity requires referral.

3. Check pupil size, shape and reactions

Assess the pupil for size and shape. Pupils should be round and equal in size. Pupil reflexes should be normal in those conditions which are within the remit of community pharmacy management. A light source (a pen torch is adequate) needs to be shone into the eye. The patient should look directly at you while you bring in the light source from the side of their face. The light should be shone onto the pupil for less than 1 second to evoke a pupil reaction. Direct and consensual responses should be checked. Normal reflexes and pupil constriction would be expected.

It is also possible that while examining the eye, the pharmacist may encounter non-red eye-related pathology. For example, pinguecula (yellowish, slightly raised thickening of the conjunctiva on the sclera close to the edge of the cornea), pterygium (raised, triangular or wedge-shaped benign growth of conjunctiva tissue) and xanthelasma (yellowish deposit of cholesterol under the skin on or around the eyelids). These are best referred to the optician for fuller evaluation.

Red eye

Background

Conjunctivitis simply means inflammation of the conjunctiva; it is characterized by varying degrees of ocular redness, irritation, itching and discharge. Redness of the eye and inflammation of the conjunctiva has been reported as being the most common ophthalmic problem encountered in the Western world.

Because conjunctivitis (bacterial, viral and allergic forms) is the most common ocular condition encountered by community pharmacists, this section will focus on recognizing the different types of conjunctivitis and differentially diagnosing them from more serious ocular disorders.

Prevalence and epidemiology

The exact prevalence of conjunctivitis is not known, although statistics from general practice show that eye problems account for up to 5% of their workload; one small UK community pharmacy-based study found that on average, pharmacies see two cases of red eye per week. Conjunctivitis seems to affect sexes equally and may present in any age of patient, although bacterial conjunctivitis is more common in children and viral conjunctivitis more common in adults. All three types of conjunctivitis are essentially self-limiting, although viral conjunctivitis can be recurrent and persist for many weeks.

Aetiology

Pathogens that cause bacterial conjunctivitis vary between adults and children. In adults, *Staphylococcus* species are most common (>50% of cases), followed by *Streptococcus pneumoniae* (20%), *Moraxella* species (5%) and *Haemophilus influenzae* (5%). In children, *Streptococcus*, *Moraxella* and *Haemophilus* are most common. The adenovirus is most commonly implicated in viral conjunctivitis, and pollen usually causes seasonal allergic conjunctivitis.

Arriving at a differential diagnosis

Red eye is a presenting complaint of both serious and non-serious causes of eye pathology. Community pharmacists must be able to differentiate between conditions that can be managed and those that need referral. Table 3.1 depicts the conditions that may be seen by the pharmacist.

Redness of the eye can occur alone or present with accompanying symptoms of pain, discomfort, discharge and loss of visual acuity. Along with an examination of the eye, a number of eye-specific questions should always be asked of the patient to establish a differential diagnosis (Table 3.2).

Table 3.1
Causes of red eye and their relative incidence in community pharmacy

Incidence	Cause
Most likely	Bacterial or allergic conjunctivitis
Likely	Viral conjunctivitis, subconjunctival haemorrhage
Unlikely	Episcleritis, scleritis, keratitis, uveitis, neonatal conjunctivitis
Very unlikely	Acute closed-angle glaucoma

Clinical features of conjunctivitis

The overwhelming majority of patients presenting to the pharmacy with red eye will have some form of conjunctivitis. Each of the three common types of conjunctivitis has similar but varying symptoms; each presents with the main symptoms of redness, discharge and discomfort. [Table 3.3](#) and [Figs 3.2 to 3.4](#) highlight the similarities and differences in the classic presentations of the three conditions.



Table 3.2
Specific questions to ask the patient: Red eye

Question	Relevance
Uni or bilateral eye involvement	A foreign body or trauma is usually unilateral, whereas conjunctivitis may start as unilateral and then become bilateral.
Discharge present	Most commonly seen in conjunctivitis. Can vary from watery to mucopurulent, dependent on the type. Mucopurulent discharge is more suggestive of bacterial conjunctivitis, especially if the eyes are glued together in the absence of itching.
Danger symptoms	The most important associated sinister symptoms are reduced visual acuity or a deep aching pain within the eye. This is generally associated with conditions requiring referral (e.g., scleritis, keratitis, uveitis, acute glaucoma).
Location of redness	Redness concentrated near or around the coloured part of the eye (limbal area) can indicate sinister pathology (e.g., uveitis). Generalized redness and redness towards the fornices (corner of the eyes) is more indicative of conjunctivitis. Localized scleral redness can indicate scleritis or episcleritis.
Duration	Any ocular redness, apart from subconjunctival haemorrhage, and allergic conjunctivitis that lasts more than 1 week is unusual.
Photophobia	Photophobia is usually associated with sinister eye pathology (e.g., keratitis and uveitis)
Other symptoms	Signs and symptoms of an upper respiratory tract infection point towards a viral cause of conjunctivitis. Vomiting suggests glaucoma.

Table 3.3
Symptoms that help distinguish between the different types of conjunctivitis

	Bacterial	Viral	Allergic
Eyes affected	Normally both; occasionally unilateral	Both, but one eye is often affected first	Both
Discharge	Purulent	Watery	Watery
Pain	Gritty feeling	Gritty feeling	Itching
Distribution of redness	Generalized and diffuse	Generalized	Generalized, but greatest in fornices
Associated symptoms	None commonly	Cough and cold symptoms	Rhinitis (may also have family history of atopy)

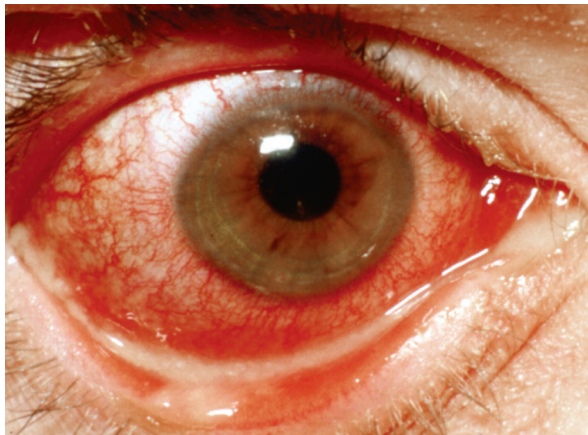


Fig. 3.2 Bacterial conjunctivitis. From Palay, D. A., & Krachmer, J. H. (2005). *Primary care ophthalmology* (2nd ed.). Elsevier Mosby.



Fig. 3.3 Viral conjunctivitis. From Sowka, J. W., Gurwood, A. S., & Kabat, A. *Handbook of ocular disease management* (4th ed.). Jobson Publishing.

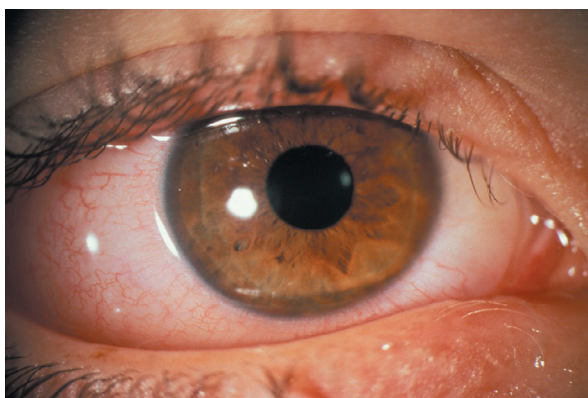


Fig. 3.4 Allergic conjunctivitis. From Krachmer, J. H., Mannis, M. J., & Holland, E. J. (Eds). (2005). *Cornea: Volume 1 fundamentals, diagnosis and management* (3rd ed.). Elsevier Mosby.

Conditions to eliminate

Likely causes

Subconjunctival haemorrhage

The rupture of a blood vessel under the conjunctiva causes subconjunctival haemorrhage. A segment of or even the whole eye will appear bright red (Fig. 3.5). It occurs spontaneously but can be precipitated by coughing, straining or lifting. The suddenness of symptoms and the brightness of the blood invariably mean that patients present very soon after they have noticed the problem. There is no pain, and the patient should be reassured that symptoms will resolve in 10 to 14 days without treatment. However, a patient with a history of trauma should be referred to exclude ocular injury.

Unlikely causes

Episcleritis

The episclera lies just beneath the conjunctiva and adjacent to the sclera. If this becomes inflamed the eye appears red, which is segmental, affecting only part of the eye (Fig. 3.6). The condition affects only one eye in the majority of cases and is usually painless; however, a dull ache might be present. It is more commonly seen in young women and is usually self-limiting, resolving in 2 to 3 weeks, but it can take 6 to 8 weeks before symptoms disappear.

Scleritis

Inflammation of the sclera is much less common than episcleritis. It is often associated with connective tissue disorders and autoimmune diseases. For example, in 20% of cases the patient has rheumatoid arthritis. It presents similarly to episcleritis, but pain (generally severe) is a predominant feature, as is blurred vision. Eye movement



Fig. 3.5 Subconjunctival haemorrhage.



Fig. 3.6 Episcleritis. From Kanski, J. J. (2007). *Clinical ophthalmology: A systematic approach* (6th ed.). Butterworth Heinemann.

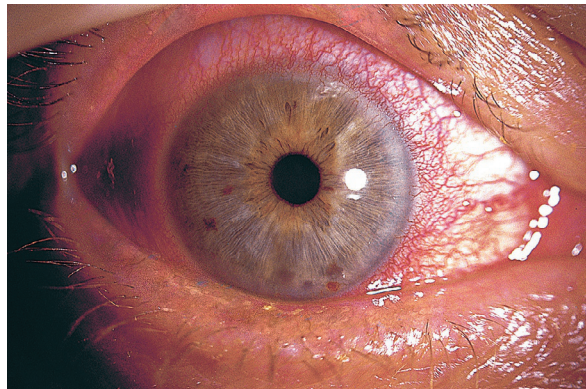


Fig. 3.7 Uveitis. From Kanski, J. J. (2006). *Clinical diagnosis in ophthalmology*. Elsevier Mosby.

can worsen pain. Scleritis also tends to affect older people (mean presentation age is in the early 50s).

Discharge is rare or absent in both episcleritis and scleritis.

Keratitis (corneal ulcer)

Keratitis has generally an infectious cause, although keratitis from other causes does occur (e.g., administration of long-term steroid drops), but is rare. Incidence is increasing in the Western world and is linked to greater usage of contact lenses. A compromised corneal epithelium, often caused from abrasion by a foreign body, is required to allow infiltration by invading pathogens. *Acanthamoeba* infection is commonly implicated in contact lens wearers.

Pain, which can be very severe, is a prominent feature. The patient usually also complains of photophobia, a worsening of redness around the iris (limbal redness), a watery discharge and lid oedema. The physical examination shows a loss of visual acuity often accompanied by a small pupil. Immediate referral is needed because loss of sight is possible if left untreated.

Uveitis (iritis)

Uveitis describes inflammation involving the uveal tract (iris, ciliary body and choroids). It is most commonly seen in individuals between 20 and 50 years of age. The likely cause is an antigen-antibody reaction, which can occur as part of a systemic disease, such as rheumatoid arthritis or ulcerative colitis. Photophobia and pain are prominent features, along with redness. The pain may be exacerbated when reading or performing close work. Usually, only one eye is affected, and the redness is often localized to the limbal area (known as the *ciliary flush*). On examination, the pupil will appear irregularly shaped, constricted or fixed (Fig. 3.7). Immediate referral is needed.

Neonatal conjunctivitis

Bilateral red eye within the first month of birth is associated with maternal chlamydial infection. The baby will present with purulent or mucoid discharge and diffuse redness. It is usually a mild infection but requires referral to the doctor for confirmation of the diagnosis.

Very unlikely causes

Acute closed-angle glaucoma

There are two main types of glaucoma:

- Simple chronic open-angle glaucoma, which does not cause pain
- Acute closed-angle glaucoma, which can present with a painful red eye

The latter requires immediate referral to an emergency department because it is a sight-threatening condition. It is due to inadequate drainage of aqueous fluid from the anterior chamber of the eye, which results in a rapid increase in intraocular pressure. The onset can be very quick and characteristically occurs in the evening. Severe unilateral eye pain associated with a headache on the same side as the painful eye is the major presenting symptom. The eye appears red and may be cloudy (Fig. 3.8). Vision is blurred and/or decreased, and the patient might also notice haloes around lights. Vomiting is often experienced due to the rapid rise in intraocular pressure. The pupil appears fixed in a vertically oval shape. It classically occurs in older, far-sighted patients. Because it is such a painful condition, patients are unlikely to present to the community pharmacist.

Fig. 3.9 can be used to help differentiate between serious and nonserious red eye conditions.

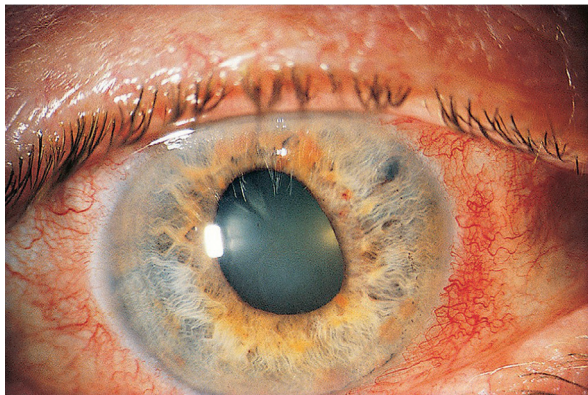


Fig. 3.8 Acute-angle glaucoma. From Batterbury, M., Bowling, B., & Murphy, C. (2010). *Ophthalmology: An illustrated colour text* (3rd ed.). Elsevier Churchill Livingstone.

! TRIGGER POINTS indicative of referral: Red eye

Symptoms and signs	Possible danger and reason for referral	Urgency of referral
Clouding of the cornea Associated vomiting	Suggests glaucoma	Immediately to emergency department
Redness caused by a foreign body	Requires removal of body (but outside the remit of community pharmacist)	Urgent same-day referral to an optician
Irregular-shaped pupil or abnormal pupil reaction to light Photophobia True eye pain Distortion of vision Redness localized around the limbal area	Suggest sinister pathology	

Evidence base for over-the-counter medication

Bacterial conjunctivitis

Bacterial conjunctivitis is regarded as self-limiting – 65% of people will have a clinical cure in 2 to 5 days, with no treatment – yet antibiotics are routinely given by medical practitioners (and pharmacists) because they are considered clinically desirable to speed recovery and reduce relapse.

Propamidine and dibromopropamidine isethionate have been used for decades to treat conjunctivitis, and are active against a wide range of organisms, including those responsible for bacterial conjunctivitis. However, clinical trials are lacking to substantiate their effectiveness, and a further possible limitation is the licensed dosage regimen (four times a day for drops). This has been reported to be too infrequent to achieve a sufficient concentration to kill or stop the growth of the infecting pathogen.

Chloramphenicol has proven efficacy and can be used in all causes of bacterial conjunctivitis but its routine use has been called in to question. Rose et al (2005) questioned whether antibiotics were needed in children as no significant difference was seen in the cure rate after 7 days; 86% of the children were clinically cured in the antibiotic group compared with 83% in the placebo group. The authors concluded that antibiotics were not needed in children. However, the most recent Cochrane review (Sheikh et al., 2012) concluded that:

Although acute bacterial conjunctivitis is frequently self limiting, the findings from this updated systematic review (previous review 2006) suggest that the use of antibiotic eye drops is associated with modestly improved rates of clinical and microbiological remission in comparison to the use of placebo. Use of antibiotic eye drops should therefore be considered in order to speed the resolution of symptoms and infection.

Summary of advice for patients

Despite the findings from the 2012 Cochrane review, anti-infectives are not always necessary; self-help measures should be recommended and include the following:

- Bathe the eyelids with lukewarm water to remove any discharge.
- Use tissues to wipe the eyes and throw away immediately.
- Wash hands regularly and avoid sharing pillows and towels.

Viral conjunctivitis

Currently, there are no specific over-the-counter (OTC) preparations available to treat viral conjunctivitis. However, symptoms may be eased by bathing the eyelids to remove any discharge and using lubricant eye drops. Viral causes are highly contagious, and the pharmacist should instruct the patient to follow strict hygiene measures (e.g., not sharing towels, washing hands frequently), which will help control the spread of the virus. A patient will remain infectious until the redness and weeping resolve (usually in 10–12 days). Public Health England currently does not recommend an exclusion period from school or nursery.

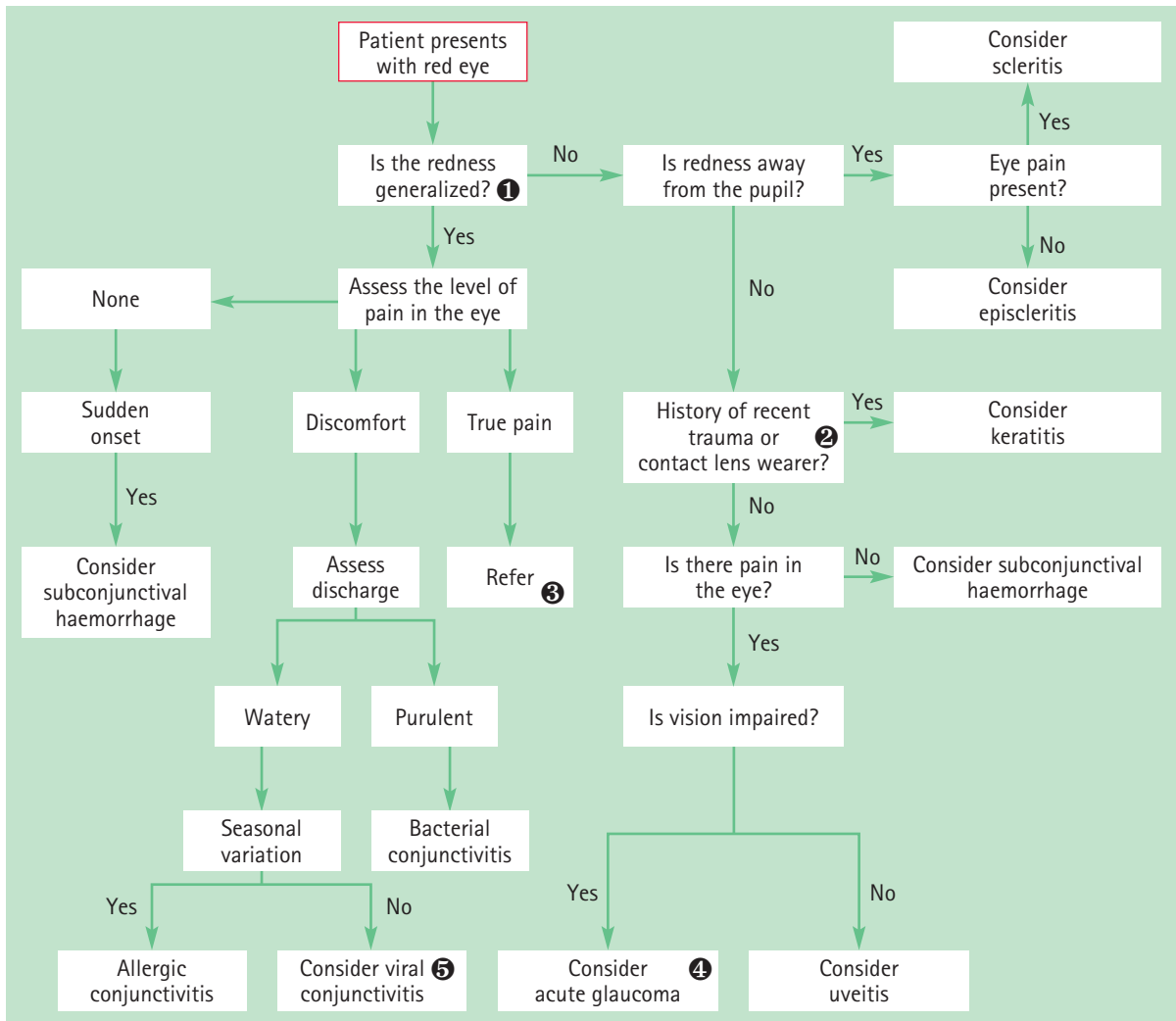


Fig. 3.9 Primer for differential diagnosis of red eye.

1 Generalized redness. Most episodes of conjunctivitis will show generalized redness, although the intensity of redness tends to be worse towards the corners of the eye or away from the pupil. Occasionally, severe conjunctivitis can have marked redness throughout the eye; these cases are best referred.

2 Contact lens wearers. Contact lens wearers are more predisposed to keratitis because the space between the contact lens and cornea can act as an incubator for bacteria and enhance mechanical abrasion. This is especially true if patients sleep with their lenses in because contact time for abrasion to occur is prolonged.

3 True pain. It is important to distinguish true pain from ocular irritation. Red eye caused by conjunctivitis causes discomfort, often described as gritty or a foreign body

sensation. It does not normally cause true eye pain. True pain would indicate more serious ocular pathology, such as scleritis, uveitis or keratitis. It is important to encourage the patient to describe the sensation carefully to enable an accurate assessment of the type of pain experienced.

4 Glaucoma. This is more common in people older than 50 years and long-sighted people. Dim light can precipitate an attack. It is a medical emergency and immediate referral is needed.

5 Viral conjunctivitis. Associated symptoms of an upper respiratory tract infection might be present (e.g., cough and cold). Viral conjunctivitis often occurs in epidemics, and it is not unusual to see a number of cases in a very short space of time.

Allergic conjunctivitis

Avoidance of the allergen will, in theory, result in the control of symptoms. However, total avoidance is almost impossible, and the use of prophylactic medication is advocated. The evidence base for ocular mast cell stabilizers, sympathomimetics and oral antihistamines is discussed in Chapter 2 in the rhinitis section.

Practical prescribing and product selection

Prescribing information relating to medication for red eye reviewed in the section 'Evidence base for over-the-counter medication' is discussed and summarized in Table 3.4; useful tips relating to treatment are given in 'Hints and Tips' in Box 3.1.



Table 3.4
Practical prescribing: Summary of medicines for red eye

Name of medicine	Use in children	Side effects: Very common ($\geq 1/10$) or common ($\geq 1/100$)	Drug interactions of note	Patients for whom care is exercised	Pregnancy and breastfeeding
<i>Allergic conjunctivitis</i>					
Mast cell stabilizers (e.g., sodium cromoglicate)	>6 years	Local irritation, blurred vision	None	None	OK
Antihistamines (e.g., antazoline) ^a	>12 years	Local irritation, bitter taste	Avoid concomitant use with monoamine oxidase inhibitors (MAOIs) and moclobemide due to risk of hypertensive crisis	Avoid in glaucoma	OK
Sympathomimetics (e.g., naphazoline)	>12 years	Local irritation	Avoid concomitant use with MAOIs and moclobemide due to risk of hypertensive crisis	None	Not adequately studied but not yet shown to be a risk; probably OK
<i>Bacterial conjunctivitis</i>					
Chloramphenicol	>2 years	Local burning and stinging	None	Avoid if there is a family history of blood and bone marrow problems	In pregnancy, ideally avoid; OK in breastfeeding
Propamide and dibromopropamide isethionate	>12 years	Blurred vision	None	None	OK

^aOnly available in combination with naphazoline.

HINTS AND TIPS BOX 3.1: EYE DROPS

Contact lens wearers	Patients who wear soft contact lenses should be advised to stop wearing them while treatment continues and for 48 hours afterwards. This is because preservatives in the eye drops can damage lenses
Chloramphenicol drops	These must be stored in the refrigerator. If they are put into the eye cold, it will be uncomfortable. Patients should be told to remove them from the refrigerator prior to use to allow them to warm up to room temperature
Administration of eye drops	Wash your hands Tilt your head backwards until you can see the ceiling Pull down the lower eyelid by pinching outwards to form a small pocket, and look upwards Hold the dropper in the other hand as near as possible to the eyelid without touching it Place one drop inside the lower eyelid, and then close your eye Wipe away any excess drops from the eyelid and lashes with the clean tissue Repeat steps 2–6 if more than one drop needs to be administered
Administration of eye ointment	Repeat eye drop steps 1 and 2 Pull down the lower eyelid Place a thin line of ointment along the inside of the lower eyelid Close your eye, and move the eyeball from side to side Wipe away any excess ointment from the eyelids and lashes using a clean tissue After using ointment, your vision may be blurred but will soon be cleared by blinking

Products for bacterial conjunctivitis***Chloramphenicol***

Chloramphenicol drops and ointment (e.g., Golden Eye Antibiotic Drops and Ointment, Optrex Infected Eye Drops and Ointment, Boots Infected Eyes) are licensed for use in children older than 2 years. The recommended dosage for the drops is one drop every 2 hours for the first 48 hours and then reducing to four times a day for a maximum of 5 days of treatment. The ointment, if used in conjunction with the drops, should only be applied at night; approximately 1 cm of ointment should be applied to the inside of the eyelid, after which blinking several times will spread the ointment. If used alone, the ointment should be used three or four times a day. These can be used in most patient groups, although they should be avoided in patients with a family history of blood dyscrasias. For use in pregnancy, a lack of manufacturer data means that they are not recommended, so hygiene measures should be adopted. If absolutely necessary, they can be used in breastfeeding women.

Propamidine isethionate and dibromopropamidine isethionate

Propamidine isethionate 1% (Brolene and GoldenEye drops) and dibromopropamidine isethionate 0.15% (GoldenEye ointment) are only licensed for adults and children older than 12 years. The dosage for eye drops is one or two drops up to

four times daily, whereas the ointment should be applied once or twice daily. If there has been no significant improvement after 2 days, the person should be re-assessed. Blurring of vision may occur when first used but is transient. The manufacturers state that safety for use in pregnancy has not been established, but there appear to be no reports of teratogenic effects and therefore could be used in pregnancy if deemed appropriate. These are free from drug interactions and can be given to all patient groups, including to women who are breastfeeding.

Products for allergic conjunctivitis***Mast cell stabilizer (sodium cromoglicate)***

As this is a prophylactic agent it needs to be given continuously while the patient is exposed to the allergen. The dose is one or two drops administered in each eye four times a day for children aged 6 years of age and older. Clinical experience has shown it to be safe in pregnancy, and expert opinion considers sodium cromoglicate to be safe in breastfeeding. It has no drug-drug interactions and can be given to all patient groups. Instillation of the drops may cause a transient blurring of vision.

Sympathomimetics

These agents can be used to reduce redness of the eye. Products contain a combination of sympathomimetic and antihistamine (e.g., antazoline-xylometazoline [Otrivine-Antistin])

or sympathomimetic alone (e.g., Naphazoline 0.01%). They are useful in reducing redness in the eye but will not treat the underlying pathology that is causing the eye to be red. They should be limited to short-term use to avoid rebound effects. Like all sympathomimetics, they can interact with monoamine oxidase inhibitors (MAOIs) and should not be used by patients receiving such treatment or within 14 days of ceasing therapy.

Otrivine-Antistin

Used in adults and children older than 12 years, the dosage is one or two drops two or three times a day. Patients with narrow angle glaucoma should avoid this product due to the potential of the antihistamine component to increase intra-ocular pressure. Local transient irritation and a bitter taste after application have been reported.

Naphazoline

The use of products containing naphazoline (e.g., Murine Irritation and Redness Relief Eye Drops and Murine Bright and Moist Eyes; Optrex Bloodshot Eyes Eye Drops and Optrex Brightening Eye Drops) is restricted to adults and children older than 12 years. One or two drops should be administered into the eye three or four times a day.

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Websites

- Eyecare Trust: <http://www.eyecaretrust.org.uk>
- International Glaucoma Association: <http://www.glaucoma-association.com>
- The Royal College of Ophthalmologists: <https://www.rcophth.ac.uk>
- Uveitis Information Group: <http://www.uveitis.net>
- American College of Optometrist Clinical Guidelines: <https://www.college-optometrists.org/guidance/clinical-management-guidelines.html>.

Eyelid disorders

Background

A number of disorders can afflict the eyelids, ranging from mild dermatitis to malignant tumours. In the context of community pharmacy consultations, the most common presenting conditions will be blepharitis, hordeola (styes), and chalazion (Table 3.5).

Prevalence and epidemiology

Data on the incidence or prevalence of eyelid disorders is limited; however, clinical practice guidelines suggest that blepharitis, and hordeola (styes), are frequently encountered. For example, blepharitis has been reported to account for 5% of primary care ophthalmic consultations.

Aetiology

Blepharitis has staphylococcal, seborrhoeic, or meibomian gland dysfunction aetiologies. Further classification of blepharitis is sometimes used based on its anatomical location. For example, anterior blepharitis refers to staphylococcal

Table 3.5
Causes of eyelid disorders and their relative incidence in community pharmacy

Incidence	Cause
Most likely	Blepharitis, hordeola
Likely	Contact or irritant dermatitis
Unlikely	Chalazion, ectropion, entropion, dacryocystitis
Very unlikely	Orbital cellulitis, carcinoma

and seborrhoeic causes because they primarily affect the bases of the eyelashes. Posterior blepharitis refers to meibomian gland dysfunction because these are situated on the posterior lid. Patients will, however, show overlapping signs and symptoms that suggest mixed aetiology. Furthermore, it appears that many blepharitis sufferers also have dry eye syndrome, but the exact relationship between the two conditions is unclear.

Styes are caused by bacterial infection (staphylococcal in 90%–95% of cases) and can be internal or external. External styes occur on the outside surface of the eyelid and are due to an infected gland, the Zeis gland (a type of sebaceous gland) or the gland of Moll (a type of sweat gland), both of which are located near the base of the eyelashes. An internal hordeolum is a secondary infection of the meibomian gland in the tarsal plate. Occasionally, internal styes can evolve into a chalazion, a granulomatous inflammation that develops into a painless lump.

Arriving at a differential diagnosis

Blepharitis and hordeola are the most likely presentations and should be relatively straightforward to recognize as long as a careful history, eye examination and appropriate questioning are undertaken (Table 3.6).

Clinical features of blepharitis

Typically, blepharitis is bilateral with, symptoms ranging from irritation, itching, and burning of the lid margins. Lid margins may appear red and raw, accompanied by

excessive tearing and crusty debris or skin flakes around the eyelashes. Symptoms also tend to be worse in the mornings, and patients might complain of eyelids being stuck together (Fig. 3.10). Symptoms are often intermittent, with exacerbations and remissions occurring over long periods. The mean age of occurrence is 50 years of age. In chronic cases, madarosis (missing lashes) and trichiasis (inturned lash) can occur. This latter symptom can lead to further local irritation and result in conjunctivitis. A seborrhoeic aetiology is likely if greasy crusting of the lashes and oily scale predominate compared with eyelash loss or misdirection, which suggests a staphylococcal cause.

Clinical features of styes

Styes typically present as acute, painful, localized eye swelling that develops over a few days. If external, the stye presents as a swollen upper or lower lid, which will be painful and sensitive to touch. A small yellow pus-filled lesion may be visible. The lesion will then spontaneously shrink and resolve or burst over the next few days (Fig. 3.11). Symptoms of internal styes are similar to those of an external stye, with pain, redness, and swelling being present, although pain is often more severe, and pus-filled lesions are not obvious due to inward growth. If the eyelid is everted, localized swelling should be visible.

Conditions to eliminate

Likely causes

Contact or irritant dermatitis

Many products – especially cosmetics – can be sensitizing and result in itching and flaking skin that mimics blepharitis.



Table 3.6
Specific questions to ask the patient:
The eyelid

Question	Relevance
Duration	A long-standing history of sore eyes is indicative of blepharitis, or dry eye syndrome.
Lid involvement	If most of the lid margin is inflamed and red, then this suggests blepharitis. Hordeola tend to show localized lid involvement.
Eye involvement	Conjunctivitis is a common complication in blepharitis.
Other coexisting conditions	Patients who suffer from blepharitis often have a coexisting skin condition, such as seborrhoeic dermatitis or rosacea.

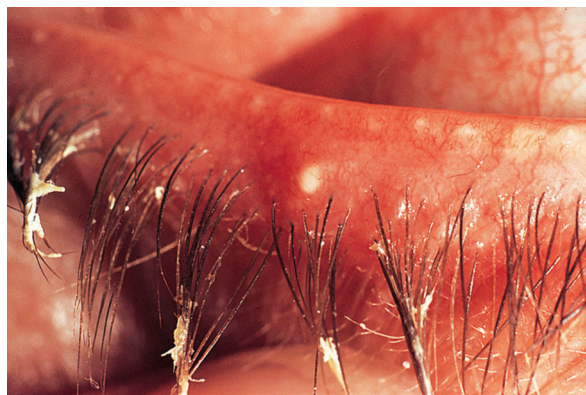


Fig. 3.10 Blepharitis. From Kanski, J. K. (2007). *Clinical ophthalmology: A systematic approach* (6th ed.). Butterworth Heinemann.



Fig. 3.11 External sty. From Kanski J. J. (2007). *Clinical ophthalmology: A systematic approach* (6th ed.). Butterworth Heinemann.

The patient should be questioned about recent use of such products to allow dermatitis to be eliminated. For further information on dermatitis, see [Chapter 8](#).

Blepharitis unresponsive to therapy

If the patient fails to respond to OTC treatment, or the condition recurs, it is possible that another cause, such as rosacea, might be responsible for the symptoms. If OTC treatment has failed, then medical referral is needed as topical antibiotics are probably needed.

Unlikely causes

Chalazion

A chalazion forms when the meibomian gland becomes blocked. It develops over a number of weeks and initially can cause discomfort but becomes painless. A lump should be clearly visible if the eyelid is everted. A chalazion is self-limiting, although it might take a few weeks to resolve completely. No treatment is needed unless the patient complains that it is particularly bothersome and is affecting vision. Referral in these cases is needed for surgical removal.

Entropion

Entropion is defined as an inversion of the eyelid margin. It can be unilateral or bilateral, with the lower eyelid more frequently affected. The in-turning of the eyelid causes the eyelashes to be pushed against the cornea, resulting in ocular irritation and conjunctival redness ([Fig. 3.12](#)). It is most often seen in older adults due to aging changes making the musculature more lax. Referral is needed for surgical repair to correct the problem. Taping down the lower lid to draw the eyelid margin away from the eye is sometimes employed as a temporary solution.



Fig. 3.12 Entropion. From Palay D., & Krachmer, J. (2005). *Primary care ophthalmology* (2nd ed.). Elsevier Mosby.

Ectropion

Ectropion is the converse of entropion; the eyelid turns outward, exposing the conjunctiva and cornea to the atmosphere ([Fig. 3.13](#)). Patients will often present complaining of a continually watering eye. Paradoxically, this can lead to dryness of the eye because the eye is not receiving adequate lubrication. Ectropion is seen with advancing age and often is noted in people who suffer from Bell's palsy.

Dacryocystitis

This is an infection of the lacrimal sac caused by a blocked nasolacrimal duct. Symptoms are sudden in onset and cause pain, tenderness, and swelling over the lacrimal sac. Fever can also be present.



Fig. 3.13 Ectropion. From Kanski, J. J. (2007). *Clinical ophthalmology: A systematic approach*, (6th ed.). Butterworth Heinemann.

Very unlikely causes

Orbital cellulitis

Inflammation of the skin surrounding the orbit of the eye is usually a complication from a sinus infection, although in extreme cases of stye, the infection can spread to involve the entire lid and even the periorbital tissues. The patient will present with unilateral swollen eyelids, be unwell, and might show restricted eye movements. This has to be referred immediately because blindness is a potential complication.

Basal cell carcinoma

This is the most common form of eyelid malignancy and accounts for over 90% of cases. The lesion is usually nodular, with a reddish hue (due to permanent capillary dilation), and most frequently affects the lower lid margin. No pain or discomfort is present. Long-term exposure to the sun is the main cause. For further information on sun-induced skin damage, see [Chapter 8](#).

! TRIGGER POINTS indicative of referral: Blepharitis and styes

Symptoms/signs	Possible danger/ reason for referral	Urgency of referral
Chalazion that becomes bothersome to the patient	May need surgical intervention; assessment from doctor required	Nonurgent but as soon as practicable
Inward or outward turning of the lower eyelid	Requires medical intervention	
Patient with swollen eyelids and associated feelings of being unwell	Suggests orbital cellulitis	Immediate to emergency department
Middle-aged/elderly patient with painless nodular lesion on or near eyelid	Suggests sinister pathology, possibly carcinoma	Urgent

Evidence base for over-the-counter medication

OTC medication is generally not required for blepharitis or styes. No specific products are available, and both conditions can respond well to conservative treatment.

Practical prescribing and product selection

Blepharitis

The mainstay of treatment for blepharitis is improved lid hygiene. The eyelids should be cleaned using a diluted mixture of baby shampoo (1:10) with warm water and applied to the eyelids using a cotton bud. This should be done twice daily initially and can be reduced to once daily if symptoms improve. In addition, a warm compress should be applied to closed eyelids for 5–10 minutes once or twice daily. Because blepharitis can cause dry eye, prescribing an ocular lubricant (e.g., hypromellose, carbomer) can be tried and, if there are signs of staphylococcal infection, a topical antibiotic such as fusidic acid gel or even systemic treatment with oxytetracycline should be considered.

Styes

Although styes are caused by bacterial pathogens, the use of antibiotic therapy is not usually needed. Topical application of ocular antibiotics does not result in speedier symptom resolution, but it might prevent a subsequent staphylococcal infection from a lash lower down. A warm compress applied for 5–10 minutes three or four times a day can bring an external stye to a head and, once it bursts, the pain will subside, and the symptoms will resolve. The use of dibromopropamide has been advocated in the treatment of styes but is of unproven benefit.

Further reading

- Lindsley, K., Matsumura, S., Hafez, E., & Akpek, E. K. (2012). Interventions for chronic blepharitis. *Cochrane Database of Systematic Reviews*, 5:CD005556.
- Shields, S. R. (2000). Managing eye disease in primary care. *Postgraduate Medicine*, 108, 83–86, 91–96

Dry eye disease (keratoconjunctivitis sicca)

Background

Dry eye is a frequent cause of eye irritation, causing varying degrees of discomfort. The condition is chronic, with no cure.

Prevalence and epidemiology

The exact prevalence of dry eye is unclear due to a lack of consistency in its definition coupled with few population-based studies, which used differing criteria for diagnosis. However what is clear is that dry eye syndrome is common.

Almost 3% of older adults will develop dry eye each year, and its prevalence increases with increasing age. It is also more common in women than in men.

Aetiology

Dry eye disease is a multifactorial ocular surface disease. It is caused by tear film instability that leads to a loss of homeostasis of the tear film. Environmental and patient factors can result in the instability of the tear film increasing electrolyte concentrations, resulting in dry eye.

Arriving at a differential diagnosis

There are a number of conditions that can cause dry eye (Table 3.7) with dry eye syndrome accounting for most dry eye cases. From a community pharmacist’s perspective, many patients will want to buy artificial tears. Good practice would dictate that the pharmacist enquire whether the patient has been instructed from their doctor or optician to buy these products or whether this is a self-diagnosis. If it is a self-diagnosis, the pharmacist should eliminate underlying pathology and ask a number of eye-specific questions to determine whether the self-diagnosis is correct (Table 3.8).

Clinical features of dry eye

This usually affects both eyes; symptoms reported are eyes that burn, feel tired, itchy, irritated, or gritty, with symptoms worsening throughout the day. The conjunctiva is not red unless irritated (e.g., eye rubbing or allergy). Decreased tear production results in irritation and burning. Typically, symptoms fluctuate in intensity and are intermittent, with symptom severity not always correlating with clinical signs.

Incidence	Cause
Most likely	Dry eye syndrome
Likely	Blepharitis, Sjögren syndrome, medicine-induced dry eye
Unlikely	Ectropion, rosacea
Very unlikely	Bell's palsy



Table 3.8 Specific questions to ask the patient: Dry eye

Question	Relevance
Have you had daily, persistent, troublesome dry eyes for more than 3 months?	A positive response to at least one of these questions would indicate dry eye syndrome
Do you have a recurrent sensation of sand or gravel in the eyes?	
Aggravating factors	Dry eyes are worsened by dry air, wind, dust, and smoke
Associated symptoms	Normally no other symptoms are present in dry eye. If the patient complains of a dry mouth, check for medication causes. If medication is not implicated, then symptoms could be due to an autoimmune disease.
Amount of tears produced	If the patient complains of watery eyes but states that the eyes are dry and sore, check for ectropion

Conditions to eliminate

Likely causes

Blepharitis

Chronic disease of eyelashes, eyelids, or margins of the eyelids can lead to irritation of the conjunctiva. See earlier in this chapter for more information on blepharitis.

Sjögren's syndrome

This syndrome has an unknown aetiology but is associated with rheumatic conditions. It occurs in the same patient population as dry eye syndrome and has very similar symptoms, although symptoms tend to be more severe. It is also associated with dryness of other mucous membranes, especially the mouth. Tiredness is also common.

Medicine-induced dry eye

A number of medicines can exacerbate or produce side effects of dry eyes as a result of decreased tear production (Table 3.9). If medication is suspected, the pharmacist should contact the patient’s doctor to discuss possible alternative therapies to alleviate the problem.



Table 3.9
Medications that can cause dry eye

Diuretics
Drugs that have an anticholinergic effect (e.g., tricyclic antidepressants [TCAs], antihistamines)
Isotretinoin
Hormone replacement therapy (HRT), particularly oestrogen alone
Androgen antagonists
Cardiac arrhythmic drugs, beta blockers
Selective serotonin reuptake inhibitors (SSRIs)

Unlikely causes

Ectropion

Sometimes the lower eyelid turns outward. This overexposes the conjunctiva to the atmosphere, leading to eye dryness. For further information, see page 67.

Rosacea

Rosacea is a disease of the skin characterized by facial skin findings, including erythema, telangiectasia, papules, and pustules that mimic acne vulgaris, although many patients also suffer from marginal blepharitis and dry eyes.

Very unlikely causes

Bell's palsy

Bell's palsy is characterized by unilateral facial paralysis, often with a sudden onset. A complication of Bell's palsy is that the patient might be unable to close one eye or blink, leading to decreased tear film and dry eye.



TRIGGER POINTS indicative of referral: Dry Eye

Symptoms/signs	Possible danger/ reason for referral	Urgency of referral
Associated dryness of mouth and other mucous membranes	Sjögren's syndrome?	As soon as practicable
Outward turning lower eyelid	Requires medical intervention	

Evidence base for over-the-counter medication

Dry eyes are managed by the instillation of artificial tears and lubricating ointments. Products in the UK consist of

hypromellose, polyvinyl alcohol, carmellose, carbomer 980, sodium hyaluronate, and wool fats.

Despite a lack of published trial data, hypromellose products have been in use for over 50 years. They possess film-forming and emollient properties, but unfortunately do not have ideal wetting characteristics, which results in up to hourly administration to provide adequate relief.

This disadvantage of frequent installation has led to the development of other products. Polyvinyl alcohol 1.4% acts as a viscosity enhancer. At this concentration, the product has the same surface tension as normal tears, lending optimal wetting characteristics and hence less frequent dosing, typically four times a day. Similar to hypromellose, there is a lack of published data confirming efficacy.

Carbomer has been shown to be more efficacious than placebo and as safe as, but better tolerated, than polyvinyl alcohol (Brodwall et al., 1997). In a comparison study between two proprietary brands, Viscotears and GelTears, both were found to be equally effective, although neither was significantly better than the other (Bron et al., 1998). Sodium hyaluronate has been subject to a number of trials that have shown a reduction in symptom severity. It has also been compared with carbomer products and carboxymethylcellulose and found to be equally effective.

Summary

Evidence of superior efficacy among any of the ophthalmic lubricants is lacking. Choice is based on patient acceptability and adherence as well as sensitivity/allergy to preservatives contained in the product. Hypromellose is often used as first-line treatment for most cases of acute dry eye.

Practical prescribing and product selection

Prescribing information relating to medications for dry eye is discussed and summarized in Table 3.10, and useful tips on medication are given in 'Hints and Tips' in Box 3.2.

The dosage of all products marketed for dry eye is largely dependent on the patient's need for lubrication, and is therefore given on an as-needed basis. All products are pharmacologically inert and none are known to interact with any medicine, only cause minimal and transient side effects and can be given to all patient groups.

Hypromellose and carmellose

Hypromellose 0.3% is widely available, but is also available at higher concentrations (e.g., Isopto Plain 0.5%); carmellose is available as multiple brands at 0.5% or 1.0% concentration. All might require hourly or even half-hourly dosing initially, which should reduce as symptoms improve.



Table 3.10
Practical prescribing: Summary of medicines for dry eye

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients for whom care is exercised	Pregnancy and breastfeeding
Hypromellose, carmellose	Dry eye in children rare; therefore, should be referred	Transient stinging and/or burning reported; blurred vision after instillation of carbomer and polyvinyl alcohol	None	None	OK
Carbomer 940					
Polyvinyl alcohol		None reported			
Wool fats					
Hyaluronate					

HINTS AND TIPS BOX 3.2: DRY EYE

Preservatives in eye drops Many eye drops contain benzalkonium chloride, which by itself can cause eye irritation. If symptoms persist, or are worsened by the eye drops, it may be worth trying a preservative-free formulation or single-dose unit preparations

Polyvinyl alcohol

Three proprietary products are available – Liquifilm Tears, Refresh Ophthalmic, and Sno Tears. Liquifilm is also available as a unit dose preservative-free formulation.

Carbomer

Manufacturers recommend that adults and older adults use one drop three or four times a day or as required, depending on patient need. Due to the products' viscosity properties, carbomer (e.g., Artelac Nighttime, Clinitas Hydrate, GelTears, Liquivisc, Viscotears) should be used last if other eye drops need to be instilled. Manufacturers advise avoidance in pregnancy and lactation due to insufficient data. Clinical experience, however, has shown that carbomer can be used safely in these patient groups.

Lubricants

Wool fats

These products contain a mixture of white soft paraffin, liquid paraffin, and wool fat (e.g., Lacri-Lube). They are useful

at bedtime when prolonged lubrication is needed, but because they blur vision, they are unsuitable for use during the day.

Sodium hyaluronate

The dosage for all products containing sodium hyaluronate (e.g., Biotrue, Clinitas Soothe, Murine Professional Advanced Dry Eye Relief, Optrex Night Restore Gel Drops) is on an as-needed basis.

References

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Further reading

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with moderate to severe dry eye syndrome. *Ophthalmology, 104*, 1402–1408.

- Vitali, C., Bombardieri, S., Jonsson, R., et al. (2002). Classification criteria for Sjogren's syndrome: A revised version of the European criteria proposed by the American-European Consensus Group. *Annals of the Rheumatic Diseases, 61*, 554–558.

Website

Sjögren's Syndrome Foundation: <http://www.sjogrens.org/home>

Self-assessment questions

The following questions are intended to supplement the text. Two levels of questions are provided, multiple-choice questions and case studies. The multiple-choice questions are designed to test knowledge and the application of knowledge, and the case studies allow this to be put in context in patient scenarios.

Multiple choice questions

- 3.1** A middle-aged woman presents to the pharmacy suffering from a red left eye. The redness appeared quite quickly, and she has no other symptoms. Based on this information, what is the most likely diagnosis?
- Bacterial conjunctivitis
 - Allergic conjunctivitis
 - Episcleritis
 - Subconjunctival haemorrhage
 - Keratitis
- 3.2** A man in his late 40s presents to the pharmacy suffering from a red right eye. The redness appeared a day or so ago, and he says the feeling is uncomfortable. He says he has not noticed any discharge, but mentions his eye is watering more than usual. Based on this information, what is the most likely diagnosis?
- Scleritis
 - Uveitis
 - Keratitis
 - Viral conjunctivitis
 - Glaucoma
- 3.3** A woman in her late 30s presents with a red left eye. She says the eye has been red for a little while (at least 2 weeks), but that it has not been bothering her; however, she would like to get rid of the redness before attending a work party. What is the most likely diagnosis?
- Allergic conjunctivitis
 - Episcleritis
 - Scleritis
 - Blepharitis
 - Subconjunctival haemorrhage
- 3.4** Red eye is a common presenting symptom. Based solely on epidemiology, which of the conditions listed below is *least* likely to be seen in a community pharmacy?
- Viral conjunctivitis
 - Scleritis
 - Glaucoma
 - Subconjunctival haemorrhage
 - Episcleritis
- 3.5** Mr Simmonds, a 54-year-old, presents with a red right eye. He has had the symptoms for a week or so. He is complaining of photophobia and takes methotrexate for rheumatoid arthritis. What is the most likely diagnosis?
- Scleritis
 - Episcleritis
 - Uveitis
 - Glaucoma
 - Keratitis
- 3.6** Priya Patel, a 27-year-old woman, presents with bilateral red eye of 3 days' duration. She complains also of slight discharge. Visual examination reveals nothing untoward. Your differential diagnosis is conjunctivitis. Which of the following symptoms help(s) differentiate allergic conjunctivitis from bacterial and viral conjunctivitis?
- She also has nasal congestion.
 - Redness is distributed throughout the conjunctiva.
 - She complains of itching eyes.
 - Discharge is mucopurulent.
 - Symptoms were sudden in onset.
- 3.7** A patient presents with the following symptoms. There is a bright red patch in the eye, which appeared overnight. There is no recent history of trauma to the eye. There is no pain or discomfort and no discharge from the eye. Vision is normal, and there is no evidence of photophobia. What is the most likely diagnosis for this set of symptoms?
- Subconjunctival haemorrhage
 - Uveitis
 - Episcleritis
 - Keratitis
 - Viral conjunctivitis

- 3.8** A middle-aged woman presents with a history of a red left eye for the last 24 hours. Which of the following symptoms should alert you to potential sinister pathology?
- Discomfort in the eye
 - Generalized scleral redness
 - Irregular pupil
 - Redness located in the fornix
 - Mucopurulent discharge
- 3.9** A mother of a young girl (8 years old) asks you to look at her daughter's sore left eye. On examination, you notice that her eyelid is slightly swollen, and her eye is a little red and tender to the touch. What is the most likely diagnosis?
- Blepharitis
 - Bacterial conjunctivitis
 - Stye
 - Chalazion
 - Entropion
- 3.10** Mr Singh, a 76-year-old man, asks to speak with the pharmacist. He has a sore right eye. He says that his eye is watering and irritated. The symptoms have been present for quite some time. Eye examination is normal. Based on this information, what is the most likely diagnosis?
- Blepharitis
 - Conjunctivitis
 - Dry eye syndrome
 - Entropion
 - Stye
- 3.11** Mrs Bradley comes into your pharmacy to ask about treatment for an infected eye. For OTC treatment of acute bacterial conjunctivitis, which one of the following regimens should be recommended for chloramphenicol eye drops, 0.5%?
- Apply one drop four times a day. Duration of treatment is 7 days.
 - Apply one drop every 2 hours for 2 days and then four times a day thereafter. Duration of treatment is 5 days.
 - Apply two drops four times a day. Duration of treatment is 5 days.
 - Apply one drop every 4 hours for 3 days and then four times a day. Duration of treatment is 7 days.
 - Apply one drop every 4 hours for 2 days and then four times a day. Duration of treatment is 5 days.
- 3.12** Mrs Sykes, a 52-year-old woman, presents with a bright red left eye that she noticed the previous day. Which of the symptom clusters would you most likely think warrants referral to an optician?
- Slight eye discomfort but no discharge, with vision unaffected
 - Slight pain with little discharge and vision unaffected
 - Slight pain with little discharge and blurred vision due to tearing
 - Slight pain with mucopurulent discharge and vision unaffected
 - Moderate pain with slight discharge and vision unaffected
- 3.13** Mr X presents one evening to the pharmacy with symptoms of blurred vision and eye pain. Which one of the following is the most likely diagnosis?
- Episcleritis
 - Glaucoma
 - Keratitis
 - Uveitis
 - Viral conjunctivitis
- 3.14** Mrs Beattie, a 65-year-old woman, asks to speak with the pharmacist. She says that both her eyes are sore and feel itchy and watery. The symptoms have been present for quite some time. Eye examination is normal. Based on this information, what is the most likely diagnosis?
- Blepharitis
 - Dry eye syndrome
 - Conjunctivitis
 - Stye
 - Entropion
- 3.15** Mrs Jenkins asks for your advice. She tells you that she was gardening 2 days ago when a branch went into her right eye. Since then, she has experienced severe pain, with watery discharge. On inspecting her eye, you see redness around the iris and a small pupil. Which of the following conditions is this most likely to be?
- Subconjunctival haemorrhage
 - Uveitis
 - Keratitis
 - Viral conjunctivitis
 - Episcleritis
- Questions 3.16 to 3.20 concern the following conditions:
- Allergic conjunctivitis
 - Bacterial conjunctivitis
 - Viral conjunctivitis
 - Subconjunctival haemorrhage
 - Episcleritis

Select, from A to E, which of these conditions:

- 3.16 Shows redness greatest in the fornices
- 3.17 Is bilateral, and discomfort is described as itching?
- 3.18 Is usually sudden in onset unilateral and painless?
- 3.19 Affects women more than men
- 3.20 Is associated with other symptoms such as cough?

Questions 3.21 to 3.25 concern the following symptoms:

- A. Painful upper eyelid
- B. Painless lump on the upper eyelid
- C. Unilateral swollen eyelid
- D. Burning of lid margins

- E. In-turning eyelid
- F. Out-turning eyelid
- G. Pain and swelling over the lacrimal sac

Select, from A to G, which of these symptoms is most closely associated with which condition:

- 3.21 Stye
- 3.22 Orbital cellulitis
- 3.23 Blepharitis
- 3.24 Carcinoma
- 3.25 Entropion

Answers

3.1 Answer: d

Rationale: Bacterial (a) and allergic (b) conjunctivitis are bilateral; the other three are unilateral, but keratitis (e) is painful. This leaves a choice between episcleritis (c) and subconjunctival haemorrhage (d). Given that symptoms appeared quickly, d is the most likely.

3.2 Answer: d

Rationale: All options, other than d, will present with true eye pain rather than discomfort.

3.3 Answer: b

Rationale: Because the eye is not causing any discomfort, then the options listed that are plausible are episcleritis (b) and subconjunctival haemorrhage (e). Based on duration, b is more likely than e.

3.4 Answer: c

Rationale: Sinister causes of red eye are relatively uncommon. Options a (viral conjunctivitis), d (subconjunctival haemorrhage) and e (episcleritis) are likely to be seen routinely by community pharmacists. This leaves a choice between b (scleritis) and c (glaucoma) as the right answer. Scleritis is rare but an acute presentation of glaucoma constitutes the most unusual case that a pharmacist would see.

3.5 Answer: c

Rationale: Photophobia is a symptom of few ocular conditions seen by a pharmacist. From the list below, this only occurs in uveitis (c) and keratitis (e). However, there is an association with keratitis and autoimmune disease. Therefore, uveitis (c) is most likely in this case.

3.6 Answer: c

Rationale: Nasal congestion (a) is not associated with allergic conjunctivitis but could be seen in viral; redness distribution (b) can be helpful but generalized redness is associated with bacterial and viral causes; discharge (d) can suggest bacterial conjunctivitis but is not useful for confirming allergic conjunctivitis; sudden-onset conjunctivitis (e) is more useful in bacterial and viral causes.

3.7 Answer: a

Rationale: Painless red eye, from the options listed, can only be subconjunctival haemorrhage (a) or episcleritis (c). Because this was sudden in onset, the cause is likely to be option a.

3.8 Answer: c

Rationale: All acute self-limiting causes of red eye will have normal pupil reactions and shape. Therefore, option c is the correct answer.

3.9 Answer: c

Rationale: The most likely condition in this age group is either bacterial conjunctivitis (b) or stye (c). Because she has local pain associated with her eyelid, stye is the most likely condition based on the symptoms listed.

3.10 Answer: c

Rationale: Entropion (d), blepharitis (a), and dry eye syndrome (c) can all cause excessive tearing. However, an eye examination would generally show other symptoms of redness and skin flaking in blepharitis. As eye examination is normal this tends to rule out entropion. Dry eye syndrome seems the most likely diagnosis. Supporting this is that Mr Singh's age also fits with this diagnosis.

3.11 Answer: b

Rationale: The dosing schedule for option b is in accordance with product licence for chloramphenicol.

3.12 Answer: b

Rationale: True eye pain should be referred for further evaluation but pain is subjective. Slight eye pain is, in most cases, manageable in the pharmacy. In this case, only option e warrants referral.

3.13 Answer: c

Rationale: Viral conjunctivitis (e) and episcleritis (a) can be discounted because neither are painful or cause blurred vision. All others will cause pain but keratitis (c) and uveitis (d) are least associated with blurred vision compared to glaucoma, which also occurs frequently in the evening.

3.14 Answer: b

Rationale: Bilateral presentation will rule out stye (d) and entropion (e). No signs of conjunctival redness would also rule out conjunctivitis (c). The description could be either blepharitis (a) or dry eye syndrome (b). Because the eye examination is normal, this points to b more than a because one would expect to see skin debris and/or lash deformities in blepharitis.

3.15 Answer: c

Rationale: Subconjunctival haemorrhage (a) and episcleritis (e) are painless; viral conjunctivitis (d) causes discomfort not pain. This leaves uveitis (b) and keratitis (c) as an option, both of which cause pain. Pupil changes occur in both but uveitis shows an irregular shaped pupil compared to a small pupil in keratitis.

3.16 Answer: A

Rationale: Allergic rhinitis (A) shows redness in the fornices because pollen is washed into the corner of the eyes, causing local direct irritation; Bacterial (B) and viral (C) can show generalized redness; subconjunctival haemorrhage (D) and episcleritis (E) show segmental redness.

3.17 Answer: A

Rationale: Bilateral involvement is associated with options (A), (B) and (C), the three forms of conjunctivitis commonly seen in community pharmacy. Bacterial (B) and viral (C) are described as discomfort rather than itching

3.18 Answer: D

Rationale: From 3.17, then only subconjunctival haemorrhage (D) and episcleritis (E) should be considered. Both tend to be painless but subconjunctival haemorrhage is associated with an abrupt onset.

3.19 Answer: E

Rationale: All forms of conjunctivitis (A–C) and subconjunctival haemorrhage show no gender differences.

3.20 Answer: C

Rationale: Bacterial conjunctivitis (B), subconjunctival haemorrhage (D) and episcleritis (E) have no other

associated symptoms. Allergic conjunctivitis (A) and viral conjunctivitis (C) can show other symptoms; allergic conjunctivitis can have nasal symptoms but not cough.

3.21 Answer: A

Rationale: Styes tend to cause localized pain. Given the options, (B) and (D) through (G) can be excluded, leaving painful upper eyelid (A) and unilateral swollen eyelid C as possible viable options. Based on the information given, A is a better fit than (C).

3.22 Answer: C

Rationale: Orbital cellulitis causes swelling and, based on this symptom, only (C) is a viable option.

3.23 Answer: D

Rationale: Blepharitis involves the lid margins rather than the eyelids themselves. Based on this, the only viable option is D.

3.24 Answer: B

Rationale: Carcinomas affecting the eyes/eyelids tend to be slow-growing, insidious, and painless. This means that options (A), (C), (D) and (G) can be excluded. Options (E) and (F) can also be excluded because they are a consequence of eyelid pathology but not tumour growth.

3.25 Answer: E

Rationale: Physical changes are not seen with entropion so options (A) to (D) and (G) can be ruled out. Option (F) is the opposite manifestation of lid pathology.

Self-assessment questions

The following questions are intended to supplement the text. Two levels of questions are provided: multiple choice questions and case studies. The multiple choice questions are designed to test knowledge and application of knowledge, and the case studies allow this knowledge to be put in context in patient scenarios.

Multiple choice questions

- 3.1** Which of the following would be the most appropriate course of action for a patient with a chalazion?
- Application of Golden Eye ointment twice a day
 - Bathing with salt water three times a day
 - Instillation of Brolene eye drops four times a day
 - No treatment
 - Referral to the GP
- 3.2** Basal cell carcinoma usually affects?
- The eye only
 - The lower lid margin
 - The lower lid margin and eye itself
 - The upper eye lid
 - Upper and lower eyelids equally
- 3.3** How can visual acuity be assessed in the community pharmacy?
- By checking for accommodation
 - By checking pupil reaction to light
 - By observing lateral eye movements
 - Getting the patient to read print from a book
 - Getting the patient to walk in a straight line
- 3.4** Which one of the following medicines can cause dry eyes?
- Atenolol
 - Codeine
 - Isotretinoin
 - Pantoprazole
 - Pseudoephedrine
- 3.5** Symptoms of eye pain in a patient with a history of rheumatoid arthritis suggests:
- Episcleritis
 - Glaucoma
 - Keratitis
 - Uveitis
 - Viral conjunctivitis
- 3.6** In which of the following conditions is severe eye pain experienced with limbal flush?
- Ectropion
 - Entropion
 - Keratitis
 - Scleritis
 - Subconjunctival haemorrhage
- 3.7** What viral pathogen is responsible for the majority of viral conjunctivitis cases?
- The adenovirus
 - The Epstein–Barr virus
 - The Norwalk-like virus
 - The rhinovirus
 - The rotavirus
- 3.8** Subconjunctival haemorrhage is associated with?
- A segment or whole eye appearing bright red and no pain
 - A segment or whole eye appearing bright red and with pain
 - A segment of the eye only that appears bright red and with pain
 - A segment of the eye only that appears pale red and no pain
 - Redness associated as ciliary flush
- Questions 3.9 to 3.11 concern the following symptoms:**
- A clear, watery discharge
 - Haloed seen around bright lights
 - Soreness of the surface of the eye
 - A small, hard lump under the skin of the upper lid
 - Grittiness and burning of the eyes in an elderly patient

Select from A to E, which of the above statements relate to the following conditions:

3.9 Acute closed-angle glaucoma

3.10 Chalazion

3.11 Allergic conjunctivitis

Questions 3.12 to 3.14 concern the following OTC medications:

a. Carbomer 940

b. Dibromopropamide isethionate

c. Hypromellose

d. Naphazoline

e. Sodium cromoglicate

Select, from a to e, which of the above medicines:

3.12 Is used to treat allergic conjunctivitis?

3.13 Can cause rebound conjunctivitis?

3.14 May require hourly administration?

Questions 3.15 to 3.17: for each of these questions *one or more* of the responses is (are) correct. Decide which of the responses is (are) correct. Then choose:

a. If a, b and c are correct

b. If a and b only are correct

c. If b and c only are correct

d. If a only is correct

e. If c only is correct

Directions summarized

A	B	C	D	E
a, b and c	a and b only	b and c only	a only	c only

3.15 Which condition(s) are associated with autoimmune disease?

- a. Scleritis
- b. Keratitis
- c. Glaucoma

3.16 Subconjunctival haemorrhage is characterized by:

- a. Eye that is red and bloodshot
- b. No pain
- c. Onset is sudden

3.17 Patients with dry eye syndrome can present with:

- a. Itchy/sore eyes
- b. Associated red eye
- c. A long-standing history of dry eye

Questions 3.18 to 3.20: these questions consist of a statement in the left-hand column followed by a statement in the right-hand column. You need to:

- Decide whether the first statement is true or false
- Decide whether the second statement is true or false

Then choose:

- A. If both statements are true and the second statement is a correct explanation of the first statement
- B. If both statements are true but the second statement is NOT a correct explanation of the first statement
- C. If the first statement is true but the second statement is false
- D. If the first statement is false but the second statement is true
- E. If both statements are false

Directions summarized

	1st statement	2nd statement	
A	True	True	2nd explanation is a correct explanation of the first
B	True	True	2nd statement is not a correct explanation of the first
C	True	False	
D	False	True	
E	False	False	

First statement

Second statement

3.18 Conjunctivitis is caused by infection only

Inflammation of the conjunctiva tends to be away from the pupil

3.19 Ectropion should be referred

It requires surgical intervention

3.20 Blepharitis can cause red eye

Skin flaking results in direct conjunctival irritation

Answers

3.1 Answer: d

Rationale: A chalazion is generally a self-limiting lump under the eyelid and requires no therapeutic intervention, thus eliminating options a, b and c. Referral (e) could be made, but in the first instance reassurance and taking a wait and see approach is advocated.

3.2 Answer: b

Rationale: These can appear anywhere and so all options are plausible; however, it is the lower lid margin (b) that is most commonly implicated.

3.3 Answer: d

Rationale: Visual acuity is acuteness or clearness of vision and is measured by the ability to identify letters or numbers on a standardized Snellen eye chart from a specific viewing distance. Use of such charts is not possible in a pharmacy but reading print from a book is a good substitute.

3.4 Answer: c

Rationale: Only pseudoephedrine (e) is not associated with ADRs associated with the eye. Blurred vision has been reported with codeine (b) and pantoprazole (d) but not dry eye. Atenolol (a) has rare reports of dry eye but with isotretinoin (c) dry eye is very common.

3.5 Answer: d

Rationale: Eye pain is not seen in episcleritis (a) and viral conjunctivitis (e) and can be discounted. The other three conditions all cause true eye pain, but only uveitis (d) is associated with autoimmune disorders.

3.6 Answer: c

Rationale: As in 3.5 identifying conditions with true pain is important, and relates to options c and d. Redness in keratitis (d) is toward the coloured part of the eye and referred to as limbal flush.

3.7 Answer: a

Rationale: The Epstein-Barr virus (b) causes glandular fever; Norwalk-like virus (c) and rotavirus (e) are associated with diarrhoeal disease; rhinovirus (d) causes colds.

3.8 Answer: a

Rationale: Subconjunctival haemorrhage is characterized by a bright red injection of blood in to part or whole of the sclera where no pain is present. The best description of this is answer a.

3.9 Answer: B

Rationale: Glaucoma is not associated with discharge (A); true pain is experienced not soreness (C); symptoms are acute and no abnormalities seen (D); and although seen in an elderly population (E) like (C) pain is experienced not discomfort.

3.10 Answer: D

Rationale: Chalazion does not affect the conjunctiva so is not associated with discharge (A), soreness (C), or grittiness (E); It causes no visual disturbances (B).

3.11 Answer: A

Rationale: Allergic conjunctivitis does not affect vision (B) nor have any associated growths (D). It could fit with the other three options but soreness (C) and grittiness (E) are more commonly seen with bacterial conjunctivitis.

3.12 Answer: e

Rationale: Carbomer (a) and Hypromellose (c) are used to treat dry eyes; naphazoline (d) helps reduce eye redness; Options b and e are used to treat conjunctivitis; b is for bacterial and e is for allergic forms.

3.13 Answer: d

Rationale: Carbomer (a) and Hypromellose (c) are pharmacologically inert and have no side effects. b and e only cause transient side effects such as stinging.

3.14 Answer: c

Rationale: Due to its poor wetting characteristics Hypromellose needs very frequent application.

3.15 Answer: d

Rationale: All three listed eye conditions cause severe pain and require referral. However only scleritis (d) is associated with autoimmune problems. Keratitis is

commonly seen due to direct trauma/abrasion and glaucoma is due to rapid rise in intraocular pressure often resulting from poor drainage of aqueous humour.

3.16 Answer: A

Rationale: Characteristically subconjunctival haemorrhage is seen as redness of the eye with sudden onset and no pain, thus all statements are correct.

3.17 Answer: A

Rationale: In dry eye syndrome the patient has a long-standing history of dry eyes that are described as sore or itchy and which can also cause redness – so like 3.16 all statements are correct.

3.18 Answer: D (False/True)

Rationale: Conjunctivitis is commonly has an infective cause but notably it is also caused by allergens; redness

associated with all forms of conjunctivitis is less prominently seen near the coloured part of the eye.

3.19 Answer: B (True/True – statement 2 is not a correct explanation of statement 1)

Rationale: Ectropion cannot be managed over-the-counter and can only be corrected through surgical intervention, although this does not explain statement one.

3.20 Answer: A (True/True – statement 2 is a correct explanation of statement 1)

Rationale: Blepharitis is associated with red eye and is caused by skin flaking, irritating the conjunctiva.

Case studies

CASE STUDY 3.1

Mrs JR, a 32-year-old-woman, asks you for something to treat her sore eye. She does not wear contact lenses.

- a. What are your initial thoughts on the problem based solely on the information given?

Epidemiology of eye problems dictates that Mrs JR is likely to have some form of conjunctivitis or possibly an eyelid or eye/lash problem.

- b. Working from this hypothesis, what would you do next?

Ideally, you should look at the eyes to see if there is an obvious cause for the discomfort. A basic inspection (without performing a specific eye examination) should reveal any eyelid or eyelash problems and scleral redness.

This basic observation reveals no obvious lid or lash involvement but generalized redness in the left eye, which is mirrored in the right eye but not as pronounced.

- c. What are your thoughts now on the differential diagnosis?

It appears we are dealing with red eye and almost certainly some form of conjunctivitis.

The pharmacy is busy and the consultation room is occupied, meaning that you cannot perform a full eye examination. You have to rely on questioning only to arrive at a differential diagnosis.

- d. What questions would you ask Mrs JR to help you differentiate between the different forms of conjunctivitis?

Discriminatory questions are required that allow you to match the patient's symptoms with the presentations of the various forms of conjunctivitis.

1. Nature of soreness

Allergic = itch; bacterial and viral = discomfort

2. If discharge present, what is it like?

Allergic and viral = watery;

bacterial = mucopurulent

3. Is redness particularly worse anywhere in the sclera?

Allergy is associated with redness in the fornices

By asking such questions you should be able to build up a picture of the symptoms that should more strongly point to one form of conjunctivitis and, thus, be your differential diagnosis.

Case studies

CASE STUDY 3.1

Ms BB, a 26-year-old woman, asks you for something for her sore eyelids.

- a. What questions would you ask Ms BB, and what observations would you make of her eyes to help you diagnose her eye condition?

Questions that relate to the presenting illness:

Does it affect one or both eyelids; what are the exact symptoms; are there any other ocular symptoms; does she use anything on the eyelids (e.g., cosmetics, cleansers) and, if so, has she changed them recently; how long has she had it; has she had these symptoms before?

Questions to help with diagnosis:

Does she have a history of skin diseases such as seborrhoeic dermatitis or rosacea?

Questions about patient management:

What medical conditions does she have; what medications does she take; does she wear contact lenses; has she tried anything to treat it?

Observations you would make:

Look at the appearance of the eyelids to check for swelling, lumps on the eyelid, the presence of secretions, discharge or debris on the eyelid or lashes; any loss of eyelashes; and the presence of conjunctivitis.

Ms BB tells you that her eyelids have been itching for a couple of weeks, but it comes and goes. She tells

you that occasionally in the morning her eyelids are stuck together. Ms BB has suffered from quite bad scalp dermatitis on and off for a number of years, for which she sees a dermatologist, and wondered if it was related because she has noticed the same flakes on her eyelashes. She tells you that she does use mascara but has used the same brand for 10 years and never had this problem before. You examine her eyelid, and it appears to be red around the margins, with some yellow flakes at the base of the eyelashes. Ms BB does wear contact lenses, but has no other medical conditions, and only takes the oral contraceptive pill. She has not tried anything so far; she has just been rubbing her eyes a lot, which makes them sore.

- b. What do you think Ms BB has, and why?

The presentation is consistent with blepharitis. It only appears to affect the lid margins, and it is across the entire margin rather than a single red lump. The presence of yellow flakes is also suggestive of blepharitis.

- c. What would you recommend for Ms BB?

She could try bathing the eyelid with a mild shampoo, such as baby shampoo. She should dilute the shampoo in a container and then use a cotton bud to wipe down from the base of the lid to the end of the lashes. She should do this for both the upper and lower lids. She could also try a warm compress on the eye. If this does not resolve in a couple of weeks, she should seek help from her doctor for alternative treatments.

CASE STUDY 3.2

A man in his early 30s presents at lunchtime to the pharmacy with a bright red eye. He wants to ease the redness. The following questions are asked, and responses received.

The following summarizes the expected findings for questions when related to the different conditions that can be seen by community pharmacists.

Information gathering	Data generated
Presenting complaint	
On examination	Right eye only and redness fully injected. No visible signs of any capillaries. Visual acuity OK. Pupil reactions normal.
Type and severity of pain	None
Discharge	None
Other symptoms	None
How long had the symptoms	Since mid-morning
Previous history of presenting complaint	No
Past medical history	Takes blood pressure medicines but cannot remember their names
Drugs (OTC, Rx)	Rennies for indigestion now and then
Social history, which may include questions relating to smoking, alcohol intake, employment, personal relationships	Not relevant in this case to ask
Family history	No history of eye problems in the family (parents)

CASE STUDY 3.2 (Continued)

	Discharge	Pain	Visual disturbance	Pupil reflex	Eyes affected	Redness
Conjunctivitis—bacterial	Yes, often mucopurulent	Sore, gritty	No	OK	One or both	Generalized redness
Conjunctivitis—viral	Yes, sometimes watery	Sore, gritty	No	OK	One or both	Generalized redness
Conjunctivitis—allergic	Yes, watery	Very itchy	No	OK	Both	Worse in fornices
Subconjunctival haemorrhage	No	No	No	OK	Either	Segmental
Episcleritis	No	Little or none	No	OK	One	Segmental
Scleritis	No	Yes	No	OK	One	Segmental
Keratitis	Watery	Yes, severe	Photophobia	Abnormal	One	Around iris
Uveitis	No	Painful	Photophobia	Abnormal	One	Around iris
Glaucoma	No	Yes, severe	Blurred	Abnormal	One	Haloes (vomiting)

When this information is compared to our patient's symptoms, and linking this with known epidemiology on red eye (see Table 3.1), it should be possible to make a differential diagnosis.

His symptoms most closely match subconjunctival haemorrhage or episcleritis (✓ represents symptom match). By looking at the presenting history, subconjunctival

haemorrhage is most likely because it has a very sudden onset. Additionally, episcleritis is more common in women and not seen as an 'injection' of bright red blood in the eye.

To 'safety net': it is worth making sure the person has none of the referral signs or symptoms (see 'Trigger points for referral', page 61), which is the case with this patient.

	Discharge absent	Absence of true pain	Visual disturbance	Pupil reflex normal	Eyes affected	Redness
Conjunctivitis—bacterial	✗	✓	✓	✓	✓	✓
Conjunctivitis—viral	✗	✓	✓	✓	✓	✓
Conjunctivitis—allergic	✗	✓	✓	✓	✓	✓
Subconjunctival haemorrhage	✓	✓	✓	✓	✓	✓
Episcleritis	✓	✓	✓	✓	✓	✓
Scleritis	✓	✗	✓	✓	✓	✓
Keratitis	✗	✗	✗	✗	✓	✗
Uveitis	✓	✗	✗	✗	✓	✗
Glaucoma	✓	✗	✗	✗	✓	✗

CASE STUDY 3.2

Ms YL requests some eye drops. She says that her eyes feel tired and irritated.

- a. What questions would you ask Ms YL, and what observations would you make of her eyes to help you diagnose her eye condition?

Questions that relate to the presenting illness:

- Explore fully the symptoms described.
- Does it affect one or both eyes?
 - Most problems will affect both eyes but there are notable exceptions, such as episcleritis, scleritis and keratitis.
- How long has she had it?
 - Limited value in differentiating ocular conditions but useful to understand where in the symptom presentation the person has come to seek help.
- Does she have any other symptoms (e.g., nasal or sinus symptoms, itch, pain, discharge, photophobia)?
 - Knowing associated symptoms helps allow discrimination and confirmation of conditions with similar ocular symptoms, such as true pain (e.g., scleritis, keratitis) versus discomfort (e.g., conjunctivitis).
- Has there been any change in her vision?
 - This should also be picked up through observation and examination and will always be a referral point because changes in vision suggest a sinister pathology.
- Does she work with a computer or spend a long time in activities such as reading?

Questions about patient management:

- Does she wear contact lenses?
 - This possibly could be contributing to symptoms and the risk of developing keratitis but also some drops should be avoided with soft contact lenses.
- What medical conditions does she have; does she take any medications?
 - Potentially underlying medical conditions can contribute to eye irritation. Knowledge of previous medication tried (especially if appropriate) may shape your recommendations.

Observations you would make to help with differential diagnosis:

- Redness of the conjunctiva, including location and spread.
- Presence of discharge.
- Determining if the cornea looks clear or cloudy (referral point).
- Checking for visual acuity and pupil reaction (abnormal would require referral).

Ms YL tells you that her eyes often feel gritty and tired later in the day. Occasionally, she feels a burning sensation in her eyes as well. She does not have any other symptoms and has not tried anything to treat it. She spends most of her day working on a computer. She has had the symptoms before, and a colleague had some eye drops that he suggested she try. She has been using them for 2 weeks and they gave her some relief. She is unsure of the name. She does not have any other medical conditions and does not take any medications. She does not use contact lenses.

From observation, there was slight general redness in both eyes, but no indication of infection.

- b. What do you think Ms YL has?

The presentation is consistent with dry eye. The use of a computer for many hours in the day could also contribute to the symptoms of irritation and tiredness.

- c. What would you recommend for Ms YL?

Dry eyes are managed by instilling artificial tears and lubricating ointments. There is no evidence of any difference in efficacy for any of the ophthalmic lubricants. Hence, the choice would be based on Ms YL's preference in terms of frequency and/or method of administration and cost. She should be advised not to share eye drops with others because that could lead to spread of infections.

CASE STUDY 3.3

A mother asks for your advice for her 14-year-old daughter. Emma has a sore and red eye. Questioning reveals the following:

- *Emma has had the symptoms for 2 to 3 days.*
- *The redness is located away from the coloured part of the eye.*
- *There is a slight discharge, although Emma has not noticed much colour in the discharge.*
- *Her eye feels slightly gritty.*
- *Her other eye is a little red but not as red as the problem eye.*
- *She is complaining of slight headaches around her eyes.*
- *She has taken nothing for the problem and only takes erythromycin for acne from the GP.*
- *She has not had these types of symptoms before.*

- a. Using the tabulated information on condition presentation of red eye from Case Study 3.2, what do you think is the cause of her symptoms?

A differential diagnosis of bacterial or viral conjunctivitis is most likely. It can be difficult to be definitive because some of her symptoms overlap between the two conditions.

- b. What action are you going to take?

We know that bacterial conjunctivitis will clear without intervention in most cases, and viral conjunctivitis is self-limiting, but hygiene measures are important to control the spread of infection. In this case, the person could be told to practice good hygiene measures and, if these fail to control symptoms, the patient could be offered an antibacterial eye drop.

To 'safety net': it is worth making a conditional referral to her GP if symptoms fail to improve in 3 to 5 days because this implies a viral cause.

CASE STUDY 3.3

Mr DD has brought his 5-year-old son BJ into the pharmacy, asking if someone could have a look at his eyes.

- a. What questions would you ask Mr DD and his son, and what observations would you make of BJ's eyes?

Questions that relate to the presenting illness:

- Before asking specific questions, get a description of the symptoms from Mr DD and then go on to ask more specific questions:
- How long has he had symptoms?
 - In this context, how helpful is this? This is probably of little help, because a 5-year-old is very unlikely to have symptoms that are other than acute, except for hay fever-type symptoms.
- Does he have any other symptoms (e.g., nasal or sinus symptoms, itch, true pain, discharge, photophobia)?
- Has BJ had these types of symptoms before?
 - As above, one would expect no history of ongoing eye problems.

Mr DD says that BJ woke up this morning with his eyelids 'glued together'. Both eyes are affected, and BJ hasn't mentioned any other symptoms. Mr DD said that he washed away the yellow discharge this morning with water and has not used anything else to treat BJ's eyes.

Observations you would make to help with differential diagnosis.

Redness of the conjunctiva, including location and spread in both eyes.

Presence of discharge.

Checking for visual acuity and pupil reaction.

Redness is generalized in both eyes. No obvious discharge is present on examination, and both visual acuity and pupil reaction are normal.

Questions about patient and management:

Standard questions such as 'does BJ have any medical conditions?' and 'does he take any medication?' are of very limited use in this context and are unlikely to shape any action you take.

From your observations, you notice redness towards the fornices of BJ's eyes. There is discharge around the eyes. BJ has no visual changes and his eyes are not affected by bright light.

- b. What do you think BJ has, and why?

The presence of purulent discharge, redness of conjunctiva and lack of other symptoms is consistent with symptoms of bacterial conjunctivitis.

- c. What would you recommend for BJ?

Bacterial conjunctivitis is regarded as self-limiting and resolves in most cases within 5 days without treatment. Use of antibiotic eye drops could be considered to speed resolution of the infection by a day or so. The parent should continue with self-help measures such as bathing BJ's eyelids with lukewarm water to remove discharge and using tissues to wipe the eyes, which are thrown away immediately.

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Ear conditions

In this chapter

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History taking and physical examination 83

Earwax (cerumen) impaction 84

Otitis externa 88

Self-assessment questions 91

Background

Community pharmacists can offer help to patients with conditions that affect the external and middle ears. However, for full assessment of middle ear problems, pharmacists should perform an ear examination using an otoscope. This will currently require most pharmacists to gain further training on their use.

General overview of ear anatomy

The external ear consists of the pinna (Fig. 4.1) and external auditory meatus (EAM—ear canal). Their function is to collect and transmit sound to the tympanic membrane (eardrum).

The pinna chiefly consists of cartilage and has a firm elastic consistency. The EAM opens behind the tragus and curves inwards, approximately 3 cm; the inner two-thirds is bony, and the outer third cartilaginous. The skin lining the cartilaginous outer portion has a well-developed subcutaneous layer that contains hair follicles and ceruminous (secretes cerumen) and sebaceous glands. The combination of hairs and cerumen helps prevent particulate matter and foreign bodies from entering the ear.

The two portions of the meatus have slightly different directions; the outer cartilaginous portion is upwards and backwards, whereas the inner bony portion is forwards and downwards. This is important to know when examining the ear.

History taking and physical examination

A thorough and accurate history, coupled with a physical examination of the ear, should be undertaken because certain symptoms can help decide from which structure of the ear the problem originates (Table 4.1) and the likely causes (Table 4.2).

Physical examination

After taking a history of the presenting complaint, the ear should be examined. Before performing an examination, explain to the patient what you want to do, and gain their consent.

1. First, wash your hands.
2. Next, inspect the external ear for redness, swelling and discharge.
3. Then, apply pressure to the mastoid area, which is directly behind the pinna (if the area is tender, this suggests mastoiditis, a rare complication of otitis media (OM)).
4. Next, move the pinna up and down and manipulate the tragus. If either is tender on movement, this would suggest external ear involvement.
5. You should finally examine the EAM. This is best performed using an otoscope.
 - a. Select correct size speculum for the ear canal.
 - b. Straighten the ear canal. Because of the shape of the EAM, the pinna needs to be manipulated to obtain the best view of the ear canal (Fig. 4.2).

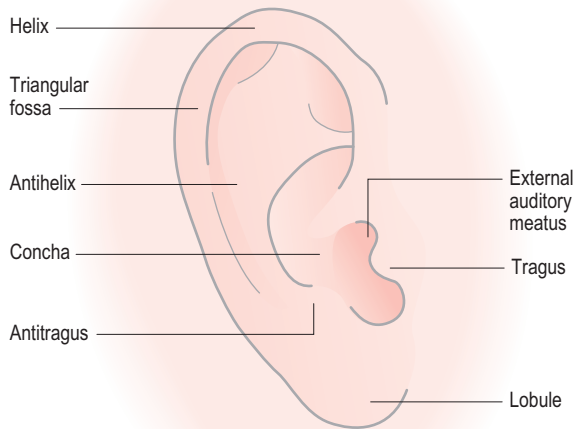


Fig. 4.1 The pinna.

Symptom	External ear	Middle ear	Inner ear
Itch	✓		
Pain	✓	✓	
Discharge	✓	✓	
Deafness	✓	✓	✓
Dizziness			✓
Tinnitus			✓

Data from C Acomb, *Pharmaceutical Journal*, August 1991.

- Brace your hand against the patient's face (to accommodate unexpected movement).
- Insert the otoscope.
- Visualize eardrum looking for discharge, redness, or swelling.
- Remove the otoscope and dispose of speculum in readiness for the next examination

A video showing this procedure is available on *Student Consult*.

Table 4.2
Signs and symptoms of ear pain and possible causes

Signs and symptoms	Possible causes
Redness and swelling	Perichondritis, haematoma
Discharge	Otitis externa or media. If discharge is mucinous, it would have originated from the middle ear because the external auditory meatus (EAM) has no mucous glands.
Pain in mastoid area	Otitis media, mastoiditis
Pain when pressing tragus or moving pinna	Otitis externa

Earwax (cerumen) impaction

Background

Earwax performs a number of important functions, including mechanical protection of the tympanic membrane, trapping dirt, repelling water and contributing to a slightly acidic medium, which has been reported to exert protection against bacterial and fungal infections. Cerumen varies in its composition between individuals but can be broadly divided into two types: a wet or sticky type of wax, which is common in children and those of white and African American ethnicity; or dry, which is common in Asian populations.

Prevalence and epidemiology

The exact prevalence rates of earwax impaction are not clear but studies have shown that 3% to 6% of the general population suffer from impacted wax. Earwax removal is the most common ear, nose and throat (ENT) procedure performed in primary care, with approximately 4 million ears irrigated annually in the UK. A number of patient groups appear to be more prone to earwax impaction than the general population; for example, patients with congenital anomalies (narrowed ear canal), patients with learning difficulties and those fitted with a hearing aid. Older adults are more susceptible to impaction due to the decrease in cerumen-producing glands, resulting in drier and harder earwax.

Aetiology

The skin of the tympanic membrane is unusual. It is not simply shed, like skin from the rest of the body, but is migratory.

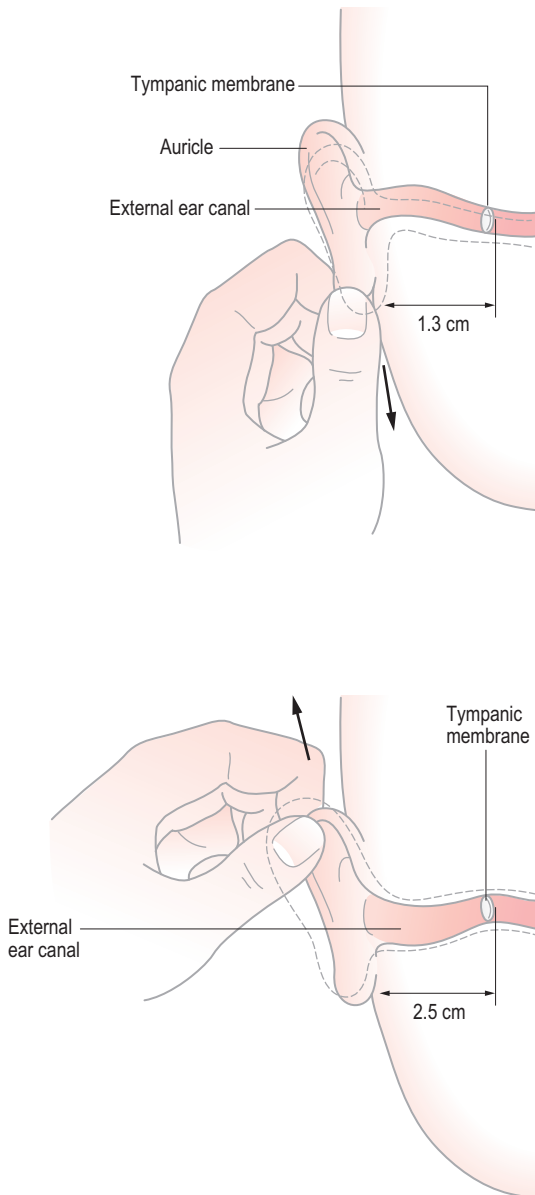


Fig. 4.2 Inspection of the external auditory meatus. Above, in children; below, in adults.

This is because the auditory canal is the body's only 'dead end' and abrasion of the stratum corneum cannot occur. Skin therefore moves outwards away from the eardrum and out along the ear canal. This means that the ears are largely self-cleaning because the ear canal naturally sheds wax from the ear. However, this normal function can be interrupted, usually by misguided attempts to clean ears. Wax therefore becomes trapped, hampering its outward migration.



Table 4.3
Specific questions to ask the patient: Earwax

Question	Relevance
Course of symptoms	The patient usually has a history of gradual hearing loss with earwax impaction.
Associated symptoms	Dizziness and tinnitus indicate an inner ear problem and should be referred. Earwax impaction rarely causes tinnitus, vertigo or true pain.
History of trauma	Check whether the person has recently tried to clean the ears. This often leads to wax impaction.
Use of medicines	If a patient has used an appropriate OTC medication correctly, this would necessitate referral for further investigation and possibly ear irrigation.

Arriving at a differential diagnosis

Careful questioning, along with inspection of the EAM, should mean that wax impaction is readily distinguished from other conditions (Table 4.3).

Clinical features of earwax impaction

The key features of earwax impaction are a history of gradual hearing loss (most common symptom) and ear discomfort (to variable degrees). Itching, tinnitus and dizziness occur infrequently. Otoscopic examination should reveal excessive wax.

Conditions to eliminate

Trauma of the ear canal

It is common practice for people to use all manner of implements to try and clean the ear canal of wax (e.g. cotton buds, hairgrips and pens). Inspection of the ear canal might reveal laceration of the ear canal, and the patient may experience greater conductive deafness because of the wax becoming further impacted. Trauma might also lead to discharge from the ear canal; these cases are probably best referred.

Foreign bodies

Symptoms can mimic earwax impaction but, over time, discharge and pain are observed. Children are the most likely age group to present with a foreign body in the ear canal.

Otoscopic examination should reveal the object. For removal of the object, the person needs to be referred to a doctor.

Polyp of the ear canal

This is a rare cause of gradual hearing loss, with most patients experiencing a persistent or recurring watery, often smelly, discharge from the ear. Some people may experience slight discomfort in their ear.

TRIGGER POINTS indicative of referral: Earwax

Symptoms/signs	Possible danger/ reason for referral	Urgency of referral
Dizziness or tinnitus	Suggests inner ear problem; requires further investigation	As soon as practicable
Fever and general malaise in children	Middle ear infection?	
Associated trauma-related conductive deafness	Requires further investigation by a doctor	
Foreign body in the EAM		
Over-the-counter (OTC) medication failure		

Evidence base for over-the-counter medication

Cerumenolytics have been used for many years to help soften, dislodge, and remove impacted earwax. A Cochrane

Review identified 10 studies with a total of 623 participants (900 ears) that examined oil- and water-based treatments and other active comparators (e.g. saline, water). They compared these treatments with each other and to no treatment (Aaron et al., 2018). The authors found only one study that showed a significant increase in the proportion of patients with complete clearance of earwax (22%) compared with placebo (5%). However, comparisons of active treatments with water or saline, or with each other, failed to demonstrate any significant differences. The authors concluded that although active treatment may result in a greater likelihood of complete clearance compared with no treatment at all, there is no evidence that one active treatment is better than another, nor is there any evidence that commercially produced treatments are better than saline or water alone. However, there is also a lack of data showing that saline or water is better than no treatment.

Summary

The evidence from limited trial data suggests simple remedies, such as water, appear to be equally as effective as marketed earwax products. Additionally, trial data do not clearly point to one particular cerumenolytic having superior efficacy.

Practical prescribing and product selection

Prescribing information relating to earwax medicines reviewed in the section 'Evidence base for over-the-counter medication' is discussed and summarized in [Table 4.4](#), and useful tips relating to patients presenting with earwax are given in 'Hints and Tips' in [Box 4.1](#).

Cerumenolytics

Agents used to soften earwax are very safe. They can be given to all patient groups, do not interact with any



Table 4.4
Practical prescribing: Summary of medicines for earwax

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy & breastfeeding
Oil-based products	>1 year (Earex olive oil drops)	None	None	None	OK
Peroxide-based products		Irritation			
Docusate		Irritation			
Sodium bicarbonate		None			

HINTS AND TIPS BOX 4.1: EARWAX

Peanut allergy	Peanut allergy affects approximately 1 in 200 people, and patients should be warned about preparations that contain <i>Arachis</i> or almond oil.
Hypersensitivity reactions to ear drops	Local reactions to the active ingredient or constituents have been reported. If a person has had a previous reaction using ear drops, care must be exercised.
Administration of ear drops	<ol style="list-style-type: none"> 1. Hold the bottle in your hands for a few minutes before administration to warm the solution. This makes insertion more comfortable. 2. Have the patient lie on a bed with the affected ear pointing towards the ceiling, or tilt the head to one side, with the affected ear pointing towards the ceiling. 3. With one hand, straighten the patient's ear canal. Adults pull the pinna up and back, and children pull the pinna down and back. 4. Holding the dropper in the other hand, hold it as near as possible to the patient's ear canal without touching it, and place the correct number of drops into the ear canal. 5. The patient's head should be kept in the same position for several minutes. 6. Once the patient's head is returned to the normal position, any excess solution should be wiped away with a clean tissue.

medicines, and can be used in children. They have very few side effects, which if experienced, would appear to be limited to local irritation when first administered. They might, for a short while, increase deafness and the patient should be warned about this possibility.

Oil-based products***Cerumol ear drops (Arachis – peanut oil, 57.3%)***

The standard dose for adults and children is five drops into the affected ear twice a day, repeated for up to 3 days. In between administration, a plug of cotton wool, moistened with Cerumol or smeared with petroleum jelly, should then be applied to retain the liquid.

Olive oil drops (Cerumol Extra Virgin Olive Oil Drops, Earex olive Oil drops, Otex olive oil drops)

For adults and children, two to three drops should be instilled twice a day for up to 7 days. Like Cerumol, a cotton wool plug should be gently placed in the ear to retain the liquid.

Peroxide-based products (Exterol, Earex Advance & Otex range)

For adults and children, up to five drops should be instilled once or twice daily for at least 3 to 4 days. Unlike other products, the patient should be advised not to plug the ear but retain the drops in the ear for several minutes by keeping the head tilted and then wipe away any surplus. Patients

might experience mild temporary effervescence in the ear as the urea – hydrogen peroxide complex liberates oxygen.

Water-based products (e.g. sodium bicarbonate)

This is only available as a nonproprietary product and should be instilled two to three times a day for up to 3 days.

Docusate (Waxsol, Molcer)

The manufacturers of both products recommend that adults and children use enough ear drops sufficient to fill the affected ear, place a small plug of cotton wool in the ear and repeat for two consecutive nights.

Reference

Aaron, K., Cooper, T. E., Warner, L., & Burton, M. J. (2018). Ear drops for the removal of earwax. *Cochrane Database System Review*, 7:CD012171.

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Burton, M. J., & Doree, C. (2009). Ear drops for the removal of earwax. *Cochrane Database System Review*, 1:CD004326.
 Corbridge, R. J. (1998). *Essential ENT Practice*. London: Arnold.
 Rodgers, R. (2004). Hearing loss and wax occlusion in older people. *Practice Nursing*, 15:290–204.

Website

British Tinnitus Association: <http://www.tinnitus.org.uk>

Otitis externa

Background

Otitis externa refers to generalized inflammation throughout the EAM and is generally caused by bacterial infection. It usually occurs as an acute episode but may become chronic (>3 months).

Prevalence and epidemiology

The lifetime prevalence of acute otitis externa is 10%, and a family doctor will see approximately 16 new cases per year. It occurs in all age groups but is most common in those aged 7 to 12 years.

It is more common in hot and humid climates and, in the West, the number of episodes increases in the summer months. People who swim are five times more likely than nonswimmers to develop it, and it is reported to be slightly more common in women.

Aetiology

Primary infection, contact sensitivity, or a combination of both cause otitis externa. Changes to microflora result from excessive moisture leading to skin maceration and skin cerumen breakdown that changes the microflora of the ear canal. Pathogens implicated with acute otitis externa include *Pseudomonas aeruginosa*, *Staphylococcus* spp. and *Streptococcus pyogenes*. Fungal overgrowth with *Aspergillus* spp. is also seen, especially after prolonged antibiotic treatment.

Certain local or general factors can precipitate otitis externa. Local causes include trauma or discharge from the middle ear; general causes include seborrhoeic dermatitis, psoriasis, and skin infections.

Arriving at a differential diagnosis

In common with earwax impaction, otitis externa is easily recognized, provided that a careful history and ear examination has been conducted. However, other otological conditions can present with similar symptoms of pain and discharge (Table 4.5).

It is therefore important to differentiate between otitis externa and conditions that require referral. Table 4.6 highlights some of the questions that should be asked of the patient to establish a differential diagnosis.

Clinical features of otitis externa

Otitis externa is characterised by itching and irritation, which, depending on the severity, can become intense. This

Table 4.5
Causes of ear canal symptoms and their relative incidence in a community pharmacy

Incidence	Cause
Most likely	Otitis media
Likely	Otitis externa caused by infection or trauma
Unlikely	Dermatitis (contact, allergic, seborrhoeic or atopic)
Very unlikely	Perichondritis, malignancy



Table 4.6
Specific questions to ask the patient: Otitis externa

Question	Relevance
Symptom presentation	Principal symptoms of acute otitis externa are itch, irritation and pain.
Discharge	Otitis media is the most common cause of ear discharge and is usually mucopurulent. If discharge is present with otitis externa, discharge would not be mucopurulent.
Systemic symptoms	Otitis externa should not present with any systemic symptoms Fever and cold symptoms are often present in otitis media In all forms of dermatitis, systemic symptoms should not be present

provokes the patient to scratch the skin of the EAM, resulting in trauma and pain. Patients might not present until pain becomes a prominent feature. However, there should be a period when irritation is the only symptom apparent. Chewing and manipulation of the tragus and pinna can exacerbate pain. Otorrhoea (ear discharge) follows, and the skin of the EAM can become oedematous, leading to conductive hearing loss. On examination, the ear canal or external ear, or both, appear red, swollen or eczematous (Fig. 4.3).

Conditions to eliminate

Likely causes

Acute otitis media

Acute otitis media is most common in children up to the age of 4 years old. In young children, it is often manifested as



Fig. 4.3 Otitis externa. From Milford, C., & Rowlands, A. (1999). *Shared care for ENT*. Isis Medical Media; Martin Dunitz Publishers, with permission of Taylor & Francis Books UK.

irritability or crying, with characteristic ear tugging/rubbing. Systemic symptoms, such as fever and loss of appetite, can also be present. In older children, ear pain/ earache is the predominant feature and tends to be throbbing.

An examination of the ear should reveal a red-yellow and bulging tympanic membrane, with a loss of normal landmarks. Over three-quarters of episodes resolve within 3 days (but it can last up to 1 week) without treatment; current UK guidelines do not advocate the routine use of antibiotics. Patients should be managed with analgesia (paracetamol or ibuprofen) unless they are systemically unwell. These cases should be referred for consideration of antibiotics (a 5- to 7-day course of amoxicillin).

Children may go on to have persistent otitis media. This is known as *chronic suppurative otitis media* or *otitis media with effusion* (glue ear). Suppurative otitis media is characterized by ear discharge (through perforation in the tympanic membrane) lasting more than 2 weeks that is not associated with pain or fever. Glue ear is symptomless, apart from impaired hearing, but can have a negative impact on a child's language and educational development if unresolved.

Unlikely causes

Dermatitis

Allergic, contact, seborrhoeic and atopic forms of dermatitis can occur on the external ear and could be mistaken for otitis

externa. Itch is a prominent symptom, but there should be no ear pain or discharge associated with dermatitis. In addition, in the seborrhoeic and atopic forms, skin involvement elsewhere should be present.

Very unlikely causes

Perichondritis

In severe cases of otitis externa, inflammation can spread from the outer ear canal to the pinna, resulting in perichondritis (Fig. 4.4). Referral is needed because systemic antibiotics are required.

Trauma

Recent trauma (e.g. blow to the head) can cause an auricular haematoma. This is best known as a *cauliflower ear* and requires nonurgent referral.



Fig. 4.4 Perichondritis. Courtesy Dr Joydeep Som. From Belleza, W. G., & Kalman, S. (2006). *Emergencies in the outpatient setting: Part 1. Medical Clinics of North America*, 90(2), 329–353., Elsevier, with permission.

Malignant tumours

Basal and squamous cell carcinomas are typically slow growing and are associated with increasing age. Any older patient presenting with an ulcerative or crusting lesion needs referral.

! TRIGGER POINTS indicative of referral: Otitis externa

Symptoms/signs	Possible danger/reason for referral	Urgency of referral
Generalized inflammation of the pinna Mucopurulent discharge Systemically unwell	Possibly indicates perichondritis Otitis media?	Same-day referral
Impaired hearing in children not associated with earwax	Development of glue ear?	As soon as practicable
Slow-growing growths on the pinna in older adults	Possibly indicate malignancy	

Evidence base for over-the-counter medication

OTC treatment of otitis externa is currently very limited. Inflammation of the EAM would respond to corticosteroids and antimicrobial ear drops; however, all such ear drops or sprays are currently only available on prescription. This limits OTC options to oral antihistamines, to try and combat itching and irritation, or analgesia to control pain.

In addition, acetic acid is available OTC (EarCalm Spray, 2% acetic acid) and is indicated for the treatment of

superficial infections of the EAM. A Cochrane review (Kaushik et al., 2010) concluded that acetic acid was as effective as antibiotics and steroids for up to a 1-week treatment, and current (March 2020) UK guidelines (Clinical Knowledge Summaries) advocate its use for mild cases. The British National Formulary (BNF) 78 also states 'that in severe cases an anti-inflammatory preparation with or without an anti-infective drug is required'.

Practical prescribing and product selection

Prescribing information relating to acetic acid is discussed below and summarized in Table 4.7. Pain associated with otitis media can be managed with simple analgesics, such as paracetamol and ibuprofen.

Acetic acid (EarCalm Spray)

This can be given to adults and children older than 12 years. The dosage is one spray (60 mg) into the affected ear at least three times a day. The maximum dosage frequency is one spray every 2 to 3 hours. Treatment should be continued until 2 days after symptoms have disappeared but, if symptoms do not improve or worsen within 48 hours, the patient should be referred. The spray should not be used for more than 7 days.

References

Kaushik, V., Malik, T., & Saeed, S. R. (2010). Interventions for acute otitis externa. *Cochrane Database System Review*, 1:CD004740. <https://doi.org/10.1002/14651858.CD004740.pub2>.

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Rosenfeld, R. M., Brown, L., Cannon, C. R., et al. (2006). Clinical practice guideline: Acute otitis externa. *Otolaryngology Head and Neck Surgery*, 134:S4–S23.



Table 4.7
Practical prescribing: Summary of medicines for otitis externa

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
Acetic acid	>12 years	Transient stinging or burning sensation	None	None	OK

Self-assessment questions

The following questions are intended to supplement the text. Two levels of questions are provided, multiple choice questions and case studies. The multiple-choice questions are designed to test factual recall, and the case studies allow knowledge to be applied to a practice setting.

Multiple-choice questions

- 4.1** Which of these anatomical features is responsible for most sound collection?
- Tympanic membrane
 - The pinna
 - Tragus
 - Antihelix
 - Helix
- 4.2** Which anatomical feature appears to bulge in the presence of infection?
- Mastoid area
 - The pinna
 - Tympanic membrane
 - Eustachian tube
 - The EAM
- 4.3** Which of the listed products has the most evidence of efficacy in treating earwax?
- Oil-based products (e.g. Cerumol)
 - Peroxide-based products (e.g. Otex)
 - Water-based products (e.g. sodium bicarbonate)
 - Saline
 - All products are comparable
- 4.4** From the list of symptoms below, which are most closely associated with outer ear problems?
- Itch and pain
 - Pain and discharge
 - Discharge and deafness
 - Deafness and dizziness
 - Dizziness and tinnitus
- 4.5** Tenderness associated with manipulation of the tragus suggests what?
- Middle ear problem
 - Inner ear problem
 - Outer ear problem
 - Perichondritis
 - Mastoiditis
- 4.6** Which of the listed patient groups is most susceptible to suffer from earwax impaction?
- Young children
 - Young adults
 - Middle-aged adults
 - Older adults
 - All groups are equally susceptible
- 4.7** A patient presents with a left ear problem. Which of the following symptoms would most strongly suggest a referral to the general practitioner (GP)?
- Redness in the outer ear
 - Pain
 - Hearing loss
 - Mucopurulent discharge
 - Swollen ear canal
- 4.8** Mrs Brown brings in her 8-year-old son who has been complaining of ear pain that he has had for the last 24 hours. He is generally well and otoscopic investigation reveals a red-yellow and bulging tympanic membrane. What course of action are you going to take?
- Tell Mrs Brown her son has otitis media, and the symptoms will resolve on their own. No further action is required.
 - Tell Mrs Brown her son has otitis media, and the symptoms will resolve on their own. The pain can be managed with simple analgesia.
 - Tell Mrs Brown her son has otitis media and the symptoms will resolve on their own. However, it would be best to get him checked out by the GP.
 - Tell Mrs Brown her son has otitis media, and the symptoms will NOT resolve on their own. He needs antibiotics and must see the doctor.
 - Tell Mrs Brown her son has otitis media, and the symptoms will resolve on their own. The pain can be managed with ear drops.
- 4.9** Manufacturers of earwax products recommend plugging the ear with cotton wool except for which of the following?

- a. Cerumol
- b. Earex
- c. Earex Advance
- d. Molcer
- e. Waxsol

4.10 Which patient group is most susceptible to otitis externa?

- a. Infants
- b. Children younger than 5 years
- c. Older adults
- d. Young adolescents
- e. People in their 30s

4.11 Mr Burnett, a 48-year-old man, enters the pharmacy and wants some advice about a sore ear that he has experienced for the last 3 days. He describes having some local itching and pain. What is the most likely diagnosis?

- a. Local inflammation of the pinna
- b. Otitis externa
- c. Perichondritis
- d. Otitis media
- e. Ménière's disease

4.12 Otitis media is more prevalent in which age group?

- a. 0 to 4 years
- b. 4 to 6 years
- c. 7 to 9 years
- d. 10 to 12 years
- e. Older than 12 years

4.13 If a patient complains of tinnitus and deafness, what is the most likely part of the ear that is affected?

- a. Outer ear
- b. Middle ear
- c. Inner ear
- d. Either middle or outer ear
- e. Inner and middle ear

4.14 Which patient group is predisposed to otitis externa?

- a. Patients with seborrhoeic dermatitis
- b. Patients with acne vulgaris
- c. Patients with tinea corporis
- d. Patients with discoid eczema
- e. Patients with lichen planus

4.15 Symptoms suggestive of a middle ear problem are?

- a. Itch, pain and discharge
- b. Pain, discharge and deafness
- c. Deafness, dizziness and tinnitus
- d. Pain only
- e. Itch only

4.16 The best way to view the EAM of an adult is to?

- a. Pull the pinna up and back to straighten the EAM
- b. Pull the pinna down and back to straighten the EAM
- c. Pull the pinna up and forward to straighten the EAM
- d. Pull the pinna down and forward to straighten the EAM
- e. Pull the pinna back to straighten the EAM

Questions 4.17 to 4.25 concern the following signs and symptoms:

- A. Itch
- B. Discharge
- C. Deafness
- D. Earache
- E. Localized ear swelling
- F. Lesions slow to heal
- G. Localized ear tenderness
- H. Dizziness

Select from A to E which of the above is most associated with the following conditions:

4.17 Otitis media

4.18 Earwax

4.19 Perichondritis

4.20 Otitis externa

4.21 Polyp

4.22 Malignancy

4.23 Mastoiditis

4.24 Foreign body

4.25 Glue ear

Answers

4.1 Answer: b

Rationale: Structures c to e (tragus, antihelix and helix) help with sound collection; the tympanic membrane (a) receives sound rather than collects it.

4.2 Answer: c

Rationale: Pressure increases from a buildup of fluid will cause structures to bulge. This can only happen where fluid cannot escape, which is the tympanic membrane (c).

4.3 Answer: e

Rationale: Using drops of any sort appears to be better than no treatment, but it is uncertain if one type of drop is any better than another.

4.4 Answer: a

Rationale: Symptoms associated with the different ear structures do overlap. However, itching is only associated with external ear problems. Pain and discharge are associated with external or middle ear problems. Deafness can be associated with external, middle and inner ear problems. Only inner ear problems are associated with dizziness and tinnitus.

4.5 Answer: c

Rationale: The tragus is the small cartilaginous area that sits in front of the outer ear canal. Tenderness here is strongly associated with an outer ear problem. The mastoid area is situated behind the ear (pinna) and perichondritis is an inflammation of the whole pinna.

4.6 Answer: d

Rationale: Older adults are more susceptible to impaction due to the decrease in cerumen producing glands resulting in drier and harder earwax.

4.7 Answer: d

Rationale: Symptoms a to c and e are all associated with otitis externa. Discharge is also associated with otitis externa but is generally not mucopurulent in nature. This is much more commonly seen in otitis media.

4.8 Answer: b

Rationale: Patients should be managed with analgesia (paracetamol or ibuprofen) unless they are systemically unwell or are younger than 2 years and have discharge. These cases should be referred for GP consideration of antibiotics.

4.9 Answer: c

Rationale: Hydrogen peroxide causes effervescence, and this should not be contained with a plug. Earex Advance is the only product from the list that contains this ingredient.

4.10 Answer: b

Rationale: Epidemiological data suggest that young children are most affected, so the answer is b.

4.11 Answer: b

Rationale: Perichondritis (c) should exhibit outer ear structure swelling; Otitis media (d) presents with pain but no itching; Ménière disease (e) exhibits dizziness. This leaves a and b as the more likely options. Local inflammation (a) is unlikely to present with itching.

4.12 Answer: a

Rationale: Epidemiological data suggest that young children are most affected, so the answer is a.

4.13 Answer: c

Rationale: Tinnitus is a symptom most closely associated with the inner ear, so option c or e is correct. Middle ear problems are not associated with tinnitus so option e is incorrect.

4.14 Answer: a

Rationale: People suffering from seborrhoeic dermatitis (a) can experience inflammation in the ear canals and thus develop otitis externa.

4.15 Answer: b

Rationale: Dizziness (c) or itch (a) and (e) should not occur; it is unusual for sole symptoms of pain (d) to be present.

4.16 Answer: a

Rationale: Due to the shape of the EAM, an upward movement is needed, so options b, d and e are wrong. It also needs to be moved backwards, so option c is also wrong.

4.17 Answer: D

Rationale: Otitis media is a middle ear infection, and therefore localized ear swelling (E) and localized ear tenderness (G) can be ruled out, as can lesions (F); dizziness is associated with the inner ear (H) and itch (A) and deafness (C) with the outer ear. This leaves discharge (C) and ear tugging (D) as the only two options remaining. Both are associated with middle ear problems but earache is the common presentation before discharge may be seen.

4.18 Answer: C

Rationale: Earwax is associated with the outer ear, and therefore symptoms involving the middle or outer ear can be discounted, although outer and middle ear symptoms can overlap. Certainly dizziness (H) and earache (D) can be excluded. Like 4.17, ear swelling (E), tenderness (G) and lesions (F) can be ruled out. This leaves options of itch (A), discharge (B) or deafness (C). Itch (A) is a symptom of otitis externa, and discharge (B) is a symptom of otitis media (B). Deafness (C) is the correct answer.

4.19 Answer: E

Rationale: Perichondritis affects the outer structure of the ear and thus almost all options can be excluded except for ear swelling (E) and tenderness (G). Whilst tenderness maybe present, this is due to marked ear swelling.

4.20 Answer: A

Rationale: See answer 4.18.

4.21 Answer: C

Rationale: Growths in the ear canal are normally benign, can reduce the amount of sound reaching the tympanic membrane and cause gradual hearing loss.

4.22 Answer: F

Rationale: Ear malignancies are usually located on the outer structures of the ear and are observed as some form of growing lesion. Internal malignancies are also possible and may cause the other symptoms listed.

4.23 Answer: G

Rationale: The mastoid area is located behind the pinna and thus, like 4.19, only two options are feasible. In this case, localized tenderness (G) will be present.

4.24 Answer: B

Rationale: A blockage of the EAM by a foreign body will cause local inflammation and discharge.

4.25 Answer: C

Rationale: This is a chronic problem affecting the middle ear that tends to be symptomless, apart from varying degrees of deafness.

Self-assessment questions

The following questions are intended to supplement the text. Two levels of questions are provided: multiple choice questions and case studies. The multiple choice questions are designed to test knowledge and application of knowledge, and the case studies allow this knowledge to be put in context in patient scenarios.

Multiple choice questions

- 4.1** Which of the following OTC treatments would you recommend for otitis media?
- Acetic acid
 - Emollient
 - Hydrocortisone
 - Local analgesia
 - Sodium bicarbonate
- 4.2** Ear wax problems tend to be more common in the elderly population because of?
- Decreased cerumen production
 - The skin migrates at a slower rate
 - Decreased oestrogen concentrations cause less wax to be produced
 - The use of hearing aids
 - Greater immobility
- 4.3** Which of the following contains peanut oil?
- Cerumol
 - Earcalm
 - Exterol
 - Molcer
 - Otex
- 4.4** Which group of symptoms are most closely associated with otitis externa?
- Itch and irritation
 - Itch, irritation and deafness
 - Itch, irritation and pain
 - Itch, irritation and deafness that can lead to pain
 - Deafness only
- 4.5** For the following statements which is false when performing an ear examination?
- The ear canal needs to be straightened before insertion of the otoscope
 - The outer ear should be inspected
 - The hand needs to be braced against the side of the patient's head
 - A speculum of any size can be used to view the ear canal
 - The 'good' ear should be viewed first
- 4.6** Which fungal pathogen is most implicated in causing otitis externa?
- Pseudomonas aeruginosa*
 - Staphylococcus* spp.
 - Streptococcus pyogenes*
 - Aspergillus* spp.
 - Candida albicans*
- Questions 4.7 to 4.9 concern the following OTC medications:
- Arachis oil ear drops
 - Docusate ear drops
 - Hydrogen peroxide ear drops
 - Olive oil drops
 - Sodium bicarbonate ear drops
- Select, from a to e, which statement relates to one of the above medicines:
- 4.7** The ear should not be plugged after using the drops
- 4.8** Avoided in patients with peanut allergy
- 4.9** Can cause effervescence after administration
- Questions 4.10 to 4.14: for each of these questions *one or more* of the responses is (are) correct. Decide which of the responses is (are) correct. Then choose:
- If a, b and c are correct
 - If a and b only are correct
 - If b and c only are correct
 - If a only is correct
 - If c only is correct
- Directions summarized**
- | A | B | C | D | E |
|------------|--------------|--------------|--------|--------|
| a, b and c | a and b only | b and c only | a only | c only |

4.10 Which statements are associated with the EAM:

- The outer third consists mainly of cartilage
- To inspect the EAM of a child the pinna should be pulled down and back
- To inspect the EAM of an adult the pinna should be pulled down and back

4.11 Conductive deafness can be caused by:

- Insertion of a foreign body into the EAM
- Blockage of the eustachian tube
- Poor ear-cleaning technique

4.12 The principal symptoms associated with otitis externa are?

- Intense ear pain
- Mucopurulent discharge
- Itch

4.13 Which of the following signs or symptoms would warrant referral to a doctor?

- Tinnitus
- Bulging tympanic membrane
- Conductive deafness

4.14 Which are the principal symptoms of otitis media in young children?

- Irritability
- Throbbing ear pain
- Deafness

Questions 4.15 to 4.20: these questions consist of a statement in the left-hand column followed by a statement in the right-hand column. You need to:

- Decide whether the first statement is true or false
- Decide whether the second statement is true or false

Then choose:

- If both statements are true and the second statement is a correct explanation of the first statement
- If both statements are true but the second statement is NOT a correct explanation of the first statement
- If the first statement is true but the second statement is false
- If the first statement is false but the second statement is true
- If both statements are false

Directions summarized

	1st statement	2nd statement	
A	True	True	2nd explanation is a correct explanation of the 1st
B	True	True	2nd statement is not a correct explanation of the 1st
C	True	False	
D	False	True	
E	False	False	
	First statement	Second statement	
4.15	Ear wax removal is generally not necessary	If ear wax products are used and ineffective, then ear irrigation can be tried	
4.16	Acetic acid is effective for otitis externa	It works by killing bacteria	
4.17	Simple analgesia is recommended for otitis media	Antibiotics are now no longer recommended	
4.18	Swimmers often get otitis externa	Prolonged exposure to water predisposes people to EAM infections	
4.19	Perichondritis is a precursor to otitis externa	Topical antibiotics are ineffective	
4.20	All children with ear pain must be referred	Systemic antibiotics are needed	

Answers

4.1 Answer: d

Rationale: Middle ear infections are characterized by pain. Therefore symptomatic relief of pain (d) would be appropriate

4.2 Answer: d

Rationale: The mobility of the patient is of no relevance (e); skin migration (b) is unaltered with age; cerumen production is also not oestrogen dependant (c) and one would expect cerumen production to increase and not decrease (a). Hearing aids stimulate cerumen production and inhibits outflow.

4.3 Answer: a

Rationale: Otex (e) and Exterol (c) contain the active ingredient urea hydrogen peroxide with excipients 8-Hydroxyquinoline and glycerol. Earcalm (b) contains acetic acid with macrogol excipients. Molcer's (d) active ingredient is docusate and propylene glycol excipient.

4.4 Answer: a

Rationale: Otitis externa is classically associated with itch, so rules out option e. Pain is not common unless the ear canal has been traumatized through scratching and so options c and d are less likely. The choice is then between a and b. Deafness is generally not a symptom of otitis externa meaning that option a is the best answer.

4.5 Answer: d

Rationale: In an ear exam it is important to visually inspect the outer ear (b) to look for signs of previous ear problems (e.g. scars), topi etc; speculums (d) come in different sizes to accommodate the size of the canal (e.g. smaller speculums for children); the ear canal (a) must be straightened to allow easier insertion of the otoscope and it is important to brace the head (c) to accommodate any sudden movement.

4.6 Answer: d

Rationale: Options a to d are known to cause otitis externa, and although option e is fungal in origin it does not cause otitis externa. The only fungal pathogen listed in the options between a and d is Aspergillus (d).

4.7 Answer: c

Rationale: As hydrogen peroxide releases oxygen it is important to allow this to escape from the ear canal

4.8 Answer: a

Rationale: Arachis oil is also known as groundnut oil or peanut oil.

4.9 Answer: c

Rationale: Arachis oil (a), Docusate (b) and olive oil (d) all have agents that directly help to soften wax; sodium bicarbonate (e) also softens wax; Hydrogen peroxide works by liberating oxygen, which acts to break up the hardened wax, and thus causing effervescence.

4.10 Answer: B

Rationale: The pinna needs to be manipulated in different directions of children and adults so options B and C cannot be the same. For children to straighten the ear canal the pinna is moved down and back (B). The ear canal consists of both cartilage and bone; the inner aspect is bone and the outer cartilage.

4.11 Answer: D

Rationale: Deafness is caused through the reduction of sound waves to the middle and inner ear and thus any blockage to this process can contribute to deafness. In this case only the first statement is plausible.

4.12 Answer: e

Rationale: Ear pain is more associated with otitis media and so is discharge, although discharge can be seen in otitis externa but is secondary to itch.

4.13 Answer: B

Rationale: Tinnitus suggests an inner ear problem and is not manageable in a pharmacy. Bulging ear drum suggests a middle ear infection and whilst pain relief can be provided, antibiotics may be required and again referral to the GP would be warranted. Deafness is seen in ear wax compaction, and as a symptom is usually manageable by the pharmacy team.

4.14 Answer: B

Rationale: Deafness is not associated with middle ear infection of any age and classically ear pain is seen in older children. In young children it is often manifested as irritability or crying with characteristic ear tugging/rubbing. Fever and loss of appetite, can also be present.

4.15 Answer: B (True/True – statement 2 not correct explanation of statement 1)

Rationale: Ear wax is a naturally occurring substance and does not need to be removed unless excessive build up is observed and affects hearing, First-line treatment would be to use a product to loosen and soften wax. If this fails then ear irrigation can be performed.

4.16 Answer: E (False/False)

Rationale: Acetic acid is recommended to treat superficial infections. It does have antibacterial action but also antifungal action.

4.17 Answer: B (True/True – statement 2 not correct explanation of statement 1)

Rationale: Regular paracetamol or ibuprofen should be given to control pain symptoms (CKS, 2019) and antibiotics can be given but are generally reserved for severe infections and in those who are systemically unwell or who have high risk of complications.

4.18 Answer: A (True/True – statement 2 is a correct explanation of statement 1)

Rationale: Swimmers are predisposed to otitis externa because of skin maceration and it provides entry routes to pathogens.

4.19 Answer: E (False/False)

Rationale: Perichondritis can result because of having otitis externa, not that perichondritis will cause otitis externa. Perichondritis is a bacterial infection and responds well to antibiotics – either ciprofloxacin or clindamycin.

4.20 Answer: E (False/False)

Rationale: Ear pain is often associated with ear infection, but not all will require antibiotic treatment, and symptoms subside on their own. Antibiotics can be used but GPs are encouraged to not give antibiotics to everyone.

Case studies

CASE STUDY 4.1

Mr SW has asked to speak to the pharmacist because his ear is bothering him.

- a. Discuss the appropriately worded questions you will need to ask Mr SW to determine the diagnosis of his symptoms.

Questions to establish a differential diagnosis:

- *Nature of symptoms*
- *Progression of symptoms (check the order in which the symptoms are presented)*
- *Any precipitating factors*
- *Previous history of symptoms*
- *Severity of symptoms*
- *Whether the symptoms are getting better, worse, or staying about the same*
- *Degree of discomfort*
- *If medication has already been tried*

Symptoms reveal that Mr SW has a loss of hearing in his left ear. Symptoms started a few days ago, and his hearing is now worse. He describes it as if he has been swimming and got water in his ear. He is unaware of why he

has the symptoms; he has not had these symptoms before, and symptoms are just a bit bothersome because he is struggling to hear conversations properly at work, especially in meetings. He has not tried any medication.

- b. Based on this description, what would be your differential diagnosis?

Earwax. You ask if it is OK to look in his ear with an otoscope to confirm your differential diagnosis.

- c. How would a physical examination help confirm or refute your diagnosis?

You would be expecting to see visible earwax impaction and, if the eardrum were observable, this should be normal and show no redness, bulging or loss of landmarks.

To 'safety net': it is worth making sure the person has none of the referral signs or symptoms. (See Trigger points for referral, page 86), which is the case with this patient.)

Case studies

CASE STUDY 4.1

Mrs JJ has brought her 14-year-old son BJ into the pharmacy and wants to speak to the pharmacist because her son is complaining of an earache.

- a. What are your initial thoughts about possible diagnoses for BJ?

Earache is a common symptom that is often associated with infection. Otitis media is very common in children younger than BJ but still needs to be considered in the differential diagnosis. Otitis externa can also cause ear pain but is not normally the first symptom experienced.

- b. What questions need to be asked to allow differentiation to determine the diagnosis?

Questions related to the complaint:

Sequence of symptoms: Was ear pain the major presenting symptom, or were other symptoms present prior to pain? The former points to otitis media and the latter to otitis externa.

Systemic symptoms: Otitis externa rarely manifests with any systemic symptoms.

- c. Are there any other confirmatory questions you could ask?

Does BJ spend a lot of time in the water? Otitis externa has a close association with increased prevalence in swimmers.

- d. How would performing an otoscopic examination help?

Examination of the outer ear canal may show redness and inflammation, suggesting otitis externa, whereas otitis media would usually show changes to the eardrum, such as redness and bulging.

BJ has started swimming squads at school and has been swimming 5 days a week for the last month. He describes the pain as mainly itching and a slight aching. There has been no discharge or fever. He has asthma and uses Symbicort (budesonide + formoterol), and he has never had these symptoms before.

- e. What do you think BJ has, and why?

BJ appears to have otitis externa. He has no systemic symptoms, and pain is not prominent, so it is unlikely to be otitis media. It is most likely caused by swimming.

- f. What treatment would you recommend for BJ?

BJ could try using oral analgesics such as paracetamol for the pain. There is little evidence for any other non-prescription medicines to treat otitis externa except acetic acid, which has been shown to help in mild infection. If the pain lasts more than a couple of days, he could try using acetic acid drops.

- g. Is there anything you could recommend for BJ to prevent or reduce this in the future?

Unless BJ is training for an important swimming event, he should probably avoid swimming until the symptoms subside. Once BJ returns to swimming, he should try to avoid getting water in his ears by using earplugs and/or a swimming cap.

CASE STUDY 4.2

Mrs PR asks to speak to the pharmacist about her 7-year-old son Luke. She wants some Calpol to treat his earache.

a. How do you respond?

The pharmacist needs to determine the cause of the pain and establish the severity of the earache.

b. Based on the age of the child, what would be your initial thoughts on a differential diagnosis?

Otitis media (OM) immediately springs to mind. It is a common complaint in this age group, and earache is a predominant symptom.

c. Basing your initial thoughts on a diagnosis of otitis media, what questions would you ask to help confirm these thoughts?

- *Are there any associated symptoms?*
- *It is likely that Luke will be irritable and off-colour.*

- *Description of the pain*
- *Pain is usually described as throbbing.*

You find out that the earache has been present for a day or so, and Luke is more irritable than normal. Mrs PR says he has a temperature, but she has not actually taken it. Apart from this, Luke has no other symptoms. However, he had this problem about a year ago and was given Calpol then, which seemed to have helped.

d. What course of action are you going to take?

It appears that Luke does have a middle ear infection. Examination of the tympanic membrane would confirm this and should be conducted. Confirmation of the diagnosis would be through visible redness of the eardrum, bulging and possible loss of land marks. Giving Calpol seems reasonable, and Mrs PR could buy some for Luke.

To 'safety net'; it is worth recommending a conditional referral of 24 hours to the GP if symptoms do not subside.

CASE STUDY 4.2

Mr CC, a 55-year-old man, comes into the pharmacy wanting to buy Earex eardrops for himself because a friend had recommended it to him.

- a. Based on his age only, what conditions are most likely for him to need eardrops?

Ear wax and otitis externa are the two most likely conditions

- b. What questions you will need to ask Mr CC?

Establish what symptoms he is experiencing:

- What symptoms does he have?
- How long has he had the symptoms?
- What was the order in which the symptoms appeared?

Questions to allow differentiation:

- Is he able to hear clearly? This suggests wax if deafness is present.
- Is itch present? This suggests otitis externa.
- Does he spend a lot of time in the water? This suggests otitis externa.
- Has he recently put anything into his ear? This suggests wax impaction.
- Does he have ear pain? This suggests otitis media.

You find out that Mr CC is experiencing ear discomfort (blocked feeling) and had attempted to clean his ears

with a cotton bud. He's had the discomfort over the last week. He now feels some pain from within his ear. He does swim occasionally for exercise because his doctor has advised him to lose some weight. However, he has not gone for a swim since he had the discomfort in his ears.

You perform an otoscopic examination and find the ear drum to be normal, with no loss of landmarks, although visualization is difficult due to wax. No outer ear canal inflammation is seen.

- c. What do you think Mr CC has, and why?

It appears that wax impaction is the cause of his symptoms based on the history and examination; this may have been compounded by the use of cotton buds.

- d. What do you recommend for Mr CC, given that he takes the following medications:

- Candesartan 16 mg daily
- Atenolol 50 mg daily
- Metformin 500 mg twice a day
- Atorvastatin 40 mg daily

He could consider using the product recommended by his friend because cerumenolytics may help with wax impaction, despite evidence being poor. Current medication does not preclude using the drops. It would be useful to find out about his allergy status (peanuts) before recommending the product.

Central nervous system

In this chapter

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Background

The number of patient requests for advice and/or products to treat headache and insomnia make up a smaller proportion of pharmacist's workload than other conditions, yet sales for analgesics and hypnotics are extremely high (£535 million for pain relief and £49 million for sleep aids in 2017). The vast majority of patients will present with benign and non-serious conditions, and only in very few cases will sinister pathology be responsible.

General overview of central nervous system anatomy

The central nervous system (CNS) comprises the brain and spinal cord. Its major function is to process and integrate information arriving from sensory pathways and communicate an appropriate response back via afferent pathways. CNS anatomy is complex and outside the scope of this text. The reader is referred to any good anatomical text for a comprehensive description of CNS anatomy.

History taking

A differential diagnosis for all CNS conditions will be made solely from questions asked of the patient. It is especially important that a social and work-related history is sought, along with questions asking about the patient's presenting

symptoms because pressure and stress are implicated in conditions such as headache and insomnia.

Headache

Background

Headache is not a disease state or condition but rather a symptom, of which there are many causes. Headache can be the major presenting complaint; for example, in migraine, cluster, and tension-type headaches – or one of many symptoms; for example, in an upper respiratory tract infection. [Table 5.1](#) highlights conditions that might be seen in a community pharmacy where headache is the major presenting symptom.

Headache classification

If the pharmacist is to advise on appropriate treatment and referral, it is essential to make an accurate diagnosis. However, with so many disorders having headache as a symptom, pharmacists should endeavour to follow an agreed classification system. The International Headache Society (IHS) classification is now almost universally accepted ([Table 5.2](#); www.ichd-3.org). The system first distinguishes between primary and secondary headache disorders. This is useful to the community pharmacist because any secondary headache disorder is symptomatic of an underlying cause and would normally require referral. In the IHS system, primary headaches are classified on symptom profiles, relying on

Table 5.1
Causes of headache and their relative incidence in community pharmacy

Incidence	Cause
Most likely	Tension-type headache
Likely	Migraine, sinusitis, eye strain
Unlikely	Cluster headache, medication overuse headache, temporal arteritis, trigeminal neuralgia, depression
Very unlikely	Glaucoma, meningitis, subarachnoid haemorrhage, raised intracranial pressure

Careful questioning coupled with epidemiological data on the distribution of a particular headache disorder has within the population.

Prevalence and epidemiology

The exact prevalence of headache is not precisely known. However, virtually everyone will have suffered from a headache at some time; it is probably the most common pain syndrome experienced by people. It has been estimated that up to 80% to 90% of the population will experience one or more headaches per year. Tension-type headache has been reported to affect between 30% and 80% of people in Western countries, with age prevalence peaking between 20 to 40 years.

Table 5.2
International Headache Society classification of headache

Primary headaches	1. Migraine, including: 1.1 Migraine without aura 1.2 Migraine with aura 2. Tension-type headache, including: 2.1 Infrequent, episodic, tension-type headache 2.2 Frequent, episodic, tension-type headache 2.3 Chronic tension-type headache	3. Cluster headache and other trigeminal autonomic cephalalgias, including: 3.1 Cluster headache 4. Other primary headaches
Secondary headaches	5. Headache attributed to head and/or neck trauma, including: 5.2 Chronic posttraumatic headache 6. Headache attributed to cranial or cervical vascular disorder, including: 6.2.2 Headache attributed to subarachnoid haemorrhage 6.4.1 Headache attributed to giant cell arteritis 7. Headache attributed to nonvascular intracranial disorder, including: 7.1.1 Headache attributed to idiopathic intracranial hypertension 7.4 Headache attributed to intracranial neoplasm 8. Headache attributed to a substance or its withdrawal, including: 8.1.3 Carbon monoxide-induced headache 8.1.4 Alcohol-induced headache	8.2 Medication-overuse headache 8.2.1 Ergotamine-overuse headache 8.2.2 Triptan-overuse headache 8.2.3 Analgesic-overuse headache 9. Headache attributed to infection, including: 9.1 Headache attributed to intracranial infection 10. Headache attributed to disorder of homeostasis 11. Headache or facial pain, attributed to disorder of cranium, neck, eyes, ears, nose, sinuses, teeth, mouth or other facial or cranial structures including: 11.2.1 Cervicogenic headache 11.3.1 Headache attributed to acute glaucoma 12. Headache attributed to psychiatric disorder
Neuralgias and other headaches	13. Cranial neuralgias, central and primary facial pain, and other headaches, including: 13.1 Trigeminal neuralgia	14. Other headache, cranial neuralgia, central or primary facial pain

Adapted by the British Association of Headache (BASH) from the International Headache Society Classification Subcommittee (2013). The International Classification of Headache Disorders, 3rd ed. Cephalalgia. Hoboken, NJ: Blackwell.

Migraine affects 15% to 20% of women and is approximately two to three times more common than in men. The peak onset for a person to have their first attack is in adolescence or as a young adult (mean age of onset for men, 14 years; for women, 18 years). Conversely, cluster headache is more common in men; episodic cluster headache, which accounts for 90% of cases, is about four times more common and chronic cases 15 times more common in men than women. Age of onset is usually from 20 to 40 years.

Aetiology

Considering headache affects almost everyone, the mechanisms that cause headache are still poorly understood. Pain control systems modulate headaches of all types, independent of the cause. However, the exact aetiology of tension-type headache and migraine are still to be fully elucidated. Tension-type headache is commonly referred to as *muscle contraction headache* because electromyography has shown pericranial muscle contraction, often exacerbated by stress. However, similar muscle contraction is noted in migraine sufferers, and this theory has now fallen out of favour. Consequently, no current theory for tension-type headache is

unanimously endorsed, but recent studies suggest a neurobiological basis.

Traditionally, migraine was thought to be a result of abnormal dilation of cerebral blood vessels, but this vascular theory cannot explain all migraine symptoms. The use of 5-HT₁ agonists to reduce and stop migraine attacks suggests some neurochemical pathophysiology. Migraine is therefore probably a combination of vascular and neurochemical changes, the neurovascular hypothesis. Migraine also appears to have a genetic component, with about 70% of patients having a first-degree relative with a history of migraine.

Arriving at a differential diagnosis

Given that headache is extremely common, and most patients will self-medicate, any patient requesting advice should ideally be questioned by the pharmacist because it is likely that the headache has not responded to an over-the-counter (OTC) medication or is troublesome enough for the patient to seek advice. Arrival at an accurate diagnosis will rely exclusively on questioning; therefore, a number of headache-specific questions should be asked (Table 5.3). In addition to these symptom-specific questions, the



Table 5.3
Specific questions to ask the patient: Headache

Question	Relevance
Onset of headache	In early childhood or as a young adult, primary headache is most likely. After 50 years of age, the likelihood of a secondary cause is much greater. Headache that follows head trauma might indicate postconcussive headache or intracranial pathology.
Frequency and timing	Headache associated with the menstrual cycle or at certain times (e.g. weekend, holiday) suggests migraine. Headaches that occur episodically at the same time of day or night suggest cluster headache. Headaches that occur on most days with the same pattern suggest tension-type headache.
Location of pain (see Fig. 5.1)	Cluster headache is nearly always unilateral in the frontal and ocular areas (can also be felt in the temporal areas). Migraine headache is unilateral in 70% of patients but can change from side to side and from attack to attack. Tension-type headache is often bilateral, either in frontal or occipital areas, and described as a tight band. Very localized pain suggests an organic cause.
Severity of pain	Pain is a subjective personal experience and there are therefore no objective measures. Using a numeric pain intensity scale should allow you to assess the level of pain the person is experiencing: 0 represents no pain and 10 the worst pain possible. Dull and band-like suggests tension-type headache. Severe to intense ache or throbbing suggests haemorrhage or aneurysm. Piercing, boring, searing eye pain suggests cluster headache. Moderate to severe throbbing pain that often starts as dull ache suggests migraine.



Table 5.3
Specific questions to ask the patient: Headache (Continued)

Question	Relevance
Triggers	Pain that worsens on exertion, coughing and bending suggests a tumour. Food (in 10% of sufferers), menstruation and relaxation after stress are indicative of migraine. Lying down makes cluster headache worse.
Attack duration	Typically, migraine attacks last between a few hours and 3 days. Tension-type headaches last between a few hours and several days, such as 1 week or longer. Cluster headache will only normally last 2–3 hours.
Associated symptoms	Headache and fever at the same time imply an infectious cause. Nausea suggests migraine or more sinister pathology, such as a subarachnoid haemorrhage and space-occupying lesions. Scalp tenderness is associated with temporal arteritis.

pharmacist should also enquire about the person's social history because social factors – mainly stress – play a significant role in headache. Ask about the person's work and family status to determine whether the person is suffering from greater levels of stress than normal.

Clinical features of headache

In a community pharmacy, the overwhelming majority of patients (80%–90%) will present with a tension-type headache. A further 10% will have migraine. Very few will have other primary headache disorders, and fewer still will have a secondary headache disorder (see Tables 5.1 and 5.2).

Tension-type headache

Tension-type headaches can be classed as either episodic or chronic. Episodic tension-type headache can be further subdivided into infrequent and frequent forms. Most patients will present to the pharmacist with the infrequent episodic form; that is, they occur less than once per month. Headaches last from 30 minutes to up to 7 days in duration. Pain is bifrontal or bioccipital, generalized and nonthrobbing (Fig. 5.1). The patient might describe the pain as a tightness or a weight pressing down on the head. The pain is gradual in onset and tends to worsen progressively throughout the day. Pain is normally mild to moderate and is not aggravated by movement, although it is often worse under pressure or stress. Nausea and vomiting are not associated with tension-type headache, and it rarely causes photophobia or phonophobia. Overall, the headache has a limited impact on the individual, although he or she might have tried OTC medication without complete symptom resolution or say that the headaches are becoming more frequent.

Patients who have frequent episodic tension-type headaches suffer more frequent headaches (more than monthly episodes) and, over time, these can develop into chronic tension-type headache. Headaches occur on at least 10

episodes per month and might be daily, lasting for at least 3 months. These types of headaches can severely affect the patient's quality of life and should not be managed by the community pharmacist.

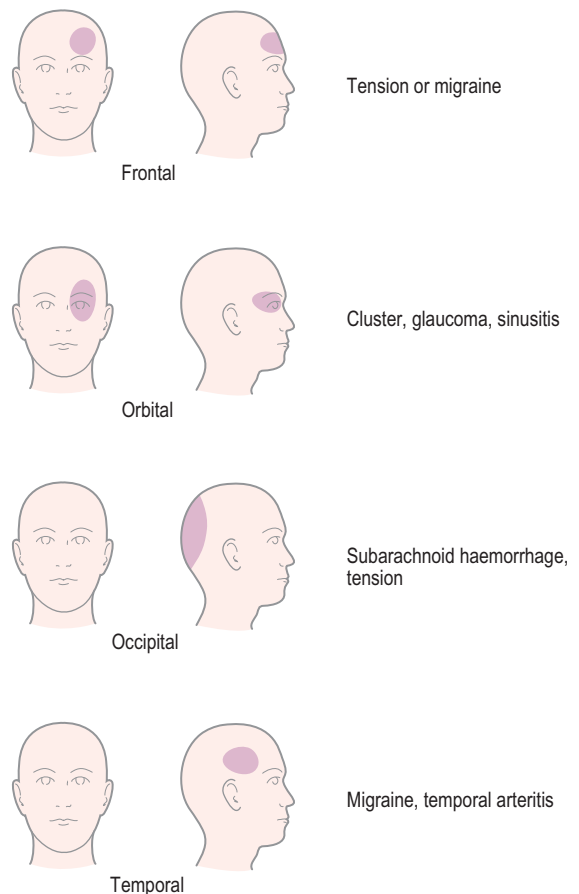


Fig. 5.1 Location of pain in headache.

Migraine

There are an estimated 5 million migraine sufferers in the UK, half of whom have not been diagnosed by their doctor. Migraines are rare over the age of 50 and anyone in this age group presenting for the first time with migraine-like symptoms should be referred to the doctor to eliminate secondary causes of headache. If this is not their first attack, they will normally have a history of recurrent and episodic attacks of headache. Attacks last anywhere from 4 to 72 hours. The average length of an attack is 24 hours. The IHS classification recognizes several subtypes of migraine, but the two major subtypes are migraine with aura (classic migraine) and migraine without aura (common migraine). A migraine attack can be divided into three phases:

- Phase one: Premonitory phase, which can occur hours or possibly a couple of days before the headache. The patient might complain of a change in mood or notice a change in behaviour. Feelings of well-being, yawning, poor concentration and food cravings have been reported. These prodromal features are highly individual but are relatively consistent to each patient. Identification of triggers is sometimes possible (Table 5.4).
- Phase two: Headache with or without aura.

Table 5.4
Triggers and strategies to reduce migraine attacks

Trigger	Strategy
Stress	Maintain regular sleep pattern. Perform regular exercise. Modify work environment. Do relaxation techniques, such as yoga.
Diet. Any food can be a potential trigger, but food that is implicated includes cheese, citrus fruit, chocolate	Maintain a food diary. If an attack occurs within 6 hours of food ingestion and is reproducible, it is likely that it is a trigger for migraine. Eat regularly and do not skip meals. NOTE: Detecting triggers is complicated because they appear to be cumulative, jointly contributing to a threshold above which attacks are initiated.

- Phase three: Resolution phase, as the headache subsides; The patient can feel lethargic, tired and drained before recovery, which might take several hours.

Headache with aura (classic migraine)

This accounts for less than 25% of migraine cases. The aura, which is fully reversible, develops over 5 to 20 minutes and can last for up to 1 hour. It can be visual (accounts for ~90% of auras experienced) or neurological. Visual auras can take many forms, such as scotomas (blind spots), fortification spectra (zigzag lines) or flashing and flickering lights. Neurological auras (pins and needles) typically start in the hand, migrating up the arm before jumping to the face and lips. Within 60 minutes of the aura ending, the headache usually occurs. Pain is unilateral, throbbing and moderate to severe. Sometimes the pain becomes more generalised and diffuse. Physical activity and movement tend to intensify the pain. Nausea affects almost all patients but less than one-third will vomit. Photophobia and phonophobia often mean that patients will seek out a dark quiet room to relieve their symptoms. The patient might also suffer from fatigue, find concentrating difficult, and be irritable.

Headache without aura (common migraine)

The remaining 75% of sufferers do not experience an aura but do suffer from all other symptoms, as described above.

Other likely causes of headache

Eye strain

People who perform prolonged close work – for example, visual display unit (VDU) operators – can suffer from frontal-aching headache. In the first case, patients should be referred to an optician for a routine eye check.

Sinusitis

The pain tends to be relatively localised, usually orbital, unilateral, and dull. For further information on the signs and symptoms of sinusitis, see under the cold section in chapter 2. A course of decongestants could be tried, but if treatment failure occurs, referral to the doctor for possible antibiotic therapy would be appropriate.

Unlikely causes

Cluster headache

Typically, the headache occurs at the same time each day with abrupt onset and lasts between 10 minutes and 3 hours, with 50% of patients experiencing nighttime symptoms. Patients are awoken 2 to 3 hours after falling asleep, with very intense, unilateral, orbital-boring pain. Additionally, conjunctival redness, lacrimation and nasal congestion (which laterally becomes watery) are observed on the pain

side of the head. Facial flushing and sweating are common. Patients tend to be restless and irritable and often pace the floor.

The condition is characterized by periods of acute attacks, typically lasting a number of weeks to a few months, with sufferers experiencing between one and three attacks per day. This is then followed by periods of remission, which can last months or years. During acute phases, alcohol can trigger an attack. Nausea is usually absent, and a family history is uncommon. Referral is required because subcutaneous sumatriptan is required.

Medication-overuse headache

Patients with long-standing symptoms of headache who regularly use medicines to treat pain can develop medication-overuse headache. Pain receptors (nociceptors) instead of being switched off when analgesics are taken, are in fact switched on. The consequence is a cycle where patients take more and more painkillers that are stronger and stronger to control the pain. Patients will experience daily or near-daily headaches described as dull and nagging. Obviously, in these cases, a medication history is essential and should prompt the pharmacist to refer the patient to the doctor. Treatment is to stop all analgesia for a number of weeks, which requires careful planning. Symptoms usually resolve within 2 months of withdrawing the medication.

Temporal arteritis (giant cell arteritis)

The temporal arteries that run vertically up the sides of the head, just in front of the ears, can become inflamed. Unilateral pain is experienced, and the person generally feels unwell, with fever, myalgia and general malaise. Scalp tenderness is seen about 50% of patients. It is most commonly seen in older white populations and is three times more common in women. Prompt treatment with oral corticosteroids is required because the retinal artery can become compromised, leading to blindness. Urgent referral is needed.

Trigeminal neuralgia

Pain follows the course of the second (maxillary; supplying the cheeks) or third (mandibular; supplying the chin, lower lip, and lower cheek) division of the nerve, leading to pain experienced in the cheek, jaws, lips or gums. Pain is short lived, usually lasting from a few seconds to a couple of minutes. Pain is severe and lancing (electric shock-like) and is almost always unilateral. The person may experience many attacks a day, although the events are episodic and may remit for weeks or months before returning. It is more common in women than in men and rarely seen before the age of 40 years.

Depression

A symptom of depression can be tension-type headaches. However, other more prominent symptoms should be present. The *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) criteria are often used to aid a diagnosis of depression. The pharmacist should check for a loss of interest or pleasure in activities, fatigue, inability to concentrate, loss of appetite, weight loss, sleep disturbances and constipation. If the patient exhibits some of these features (especially loss of interest in doing things and feeling down and hopeless), referral to the doctor is necessary. Recent changes to the patient's social circumstances might also support your differential diagnosis.

Very unlikely causes

Glaucoma

Patients experience a frontal-orbital headache, with severe pain in the eye. The eye appears red and is painful. Vision is blurred, the cornea can look cloudy and haloes might be noticed around the vision. For further information on glaucoma, see red eye in chapter 2.

Meningitis

Signs and symptoms are nonspecific in the early stages of the disease and are similar to flu, but can develop quickly to severe generalized headache associated with fever (although neonates may not have fever), an obviously ill patient, neck stiffness, nausea and vomiting. Latterly a nonblanching purpuric rash are classically associated with meningitis. However, not all patients will exhibit all symptoms, and any child that has difficulty in placing the chin on the chest and is running a temperature above 38.9°C (102°F) should be referred urgently.

Subarachnoid haemorrhage

The patient will experience an incapacitating headache with very intense severe pain, located in the occipital region. Nausea and vomiting are often present, and a decreased level of consciousness is prominent. Patients often describe the headache as the worst headache they have ever had. It is extremely unlikely that a patient would present in the pharmacy with such symptoms but, if one does, immediate referral to the Accident and Emergency Department (A&E) would be needed.

Conditions causing raised intracranial pressure

Space-occupying lesions (e.g., brain tumour, haematoma, abscess) can give rise to varied headache symptoms, ranging from severe chronic pain to intermittent moderate

pain. Pain can be localized or diffuse and tends to be more severe in the morning, with a gradual improvement over the next few hours. Coughing, sneezing, bending and lying down can worsen the pain. Nausea and vomiting are common. After a prolonged period of time, neurological symptoms, such as drowsiness, confusion, lack of concentration, difficulty with speech and paraesthesia, start to become evident.

Any patient with a recent history (lasting 2–3 months) of head trauma, headache of long-standing duration, or insidious worsening of symptoms, especially associated with decreased consciousness and vomiting, must be referred urgently for fuller evaluation.

Fig. 5.2 (and the summary table shown in Case Study 5.1) will help in the differentiation of serious and nonserious causes of headache.

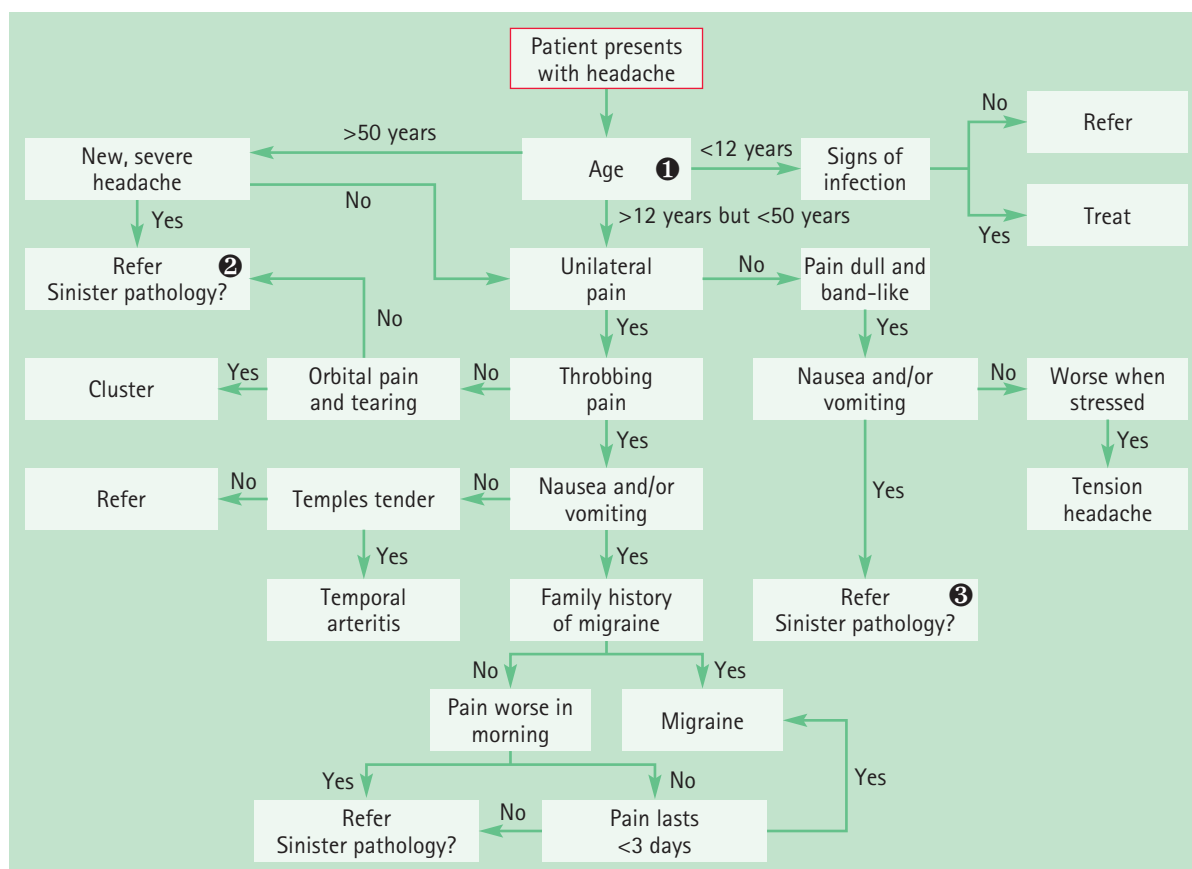


Fig. 5.2 Primer for differential diagnosis of headache.

❶ Age. Caution should be exercised in children who present with headache. Although most headaches will not have an organic cause, children younger than 12 years are probably best referred if they show no signs of a systemic infection (e.g., fever, malaise).

❷ Referral for suspected sinister pathology. With increasing age, it is more likely that a sinister cause of headache is responsible for the symptoms, especially if the patient has not

experienced similar headache symptoms before. Mass lesions (tumours and haematoma) and temporal arteritis should be considered.

❸ Referral for suspected sinister pathology. Nausea and vomiting in the absence of migraine-like symptoms should be treated seriously. Mass lesions and subarachnoid haemorrhage need to be eliminated.

! TRIGGER POINTS indicative of referral: Headache

Symptoms and signs	Possible danger and reason for referral	Urgency of referral
Headache in children <12 years old who have a stiff neck, high temperature or skin rash	Meningitis?	Immediate referral to general practitioner (GP) or A&E
Headache after recent (1–3 months) trauma or injury	Haematoma?	
Nausea and/or vomiting in the absence of migraine symptoms Neurological symptoms, if migraine is excluded, especially change in consciousness Very sudden and/or severe onset of headache	All can suggest sinister pathology and require further investigation.	
New or severe headache in patients >50 years Progressive worsening of headache symptoms over time		As soon as practicable to GP
Headache unresponsive to analgesics	Simple analgesia is effective; if this has not worked, the patient's symptoms require further investigation. Suspect medication overuse headache.	

Evidence base for over-the-counter medication

Simple analgesia (e.g., paracetamol, aspirin, ibuprofen) has shown clinical benefit in relieving migraine attacks.

A Cochrane review (Derry et al., 2013) found that a single oral dose of paracetamol, 1000 mg, was effective in relieving moderate to severe migraine symptoms, compared with placebo. Approximately 20% of patients will be pain-free in 2 hours (reduced from moderate to severe), and 60% of patients can expect a reduction in the severity of pain from moderate/severe to mild pain by 2 hours. (Note that the addition of metoclopramide saw an efficacy equivalent to a dose of 100 mg sumatriptan; such products are available OTC in other countries, such as Australia.) A further Cochrane review (Rabbie et al., 2013) investigating ibuprofen's effect on migraine concluded that it was an effective treatment, and the 400-mg dose was superior to the 200-mg dose.

Aspirin, ibuprofen and paracetamol have been the subjects of a Cochrane review for episodic tension-type headache in adults. Stephens et al. (2016) investigated 23 trials involving paracetamol ($N = 8079$ people). Overall, paracetamol, 1000 mg, was found to provide a small benefit in terms of being pain free at 2 hours (an IHS preferred outcome). For ibuprofen, 400 mg, Derry et al. (2015) included 12 studies ($N = 3094$ people) and found stronger evidence than paracetamol for being pain free at 2 hours. Finally, aspirin was also reviewed by Derry et al. (2017) who reviewed five studies ($N = 1812$ people). Unlike the two other reviews, there were no data reported about being pain free at 2 hours; the authors found that a single dose of aspirin between 500 mg and 1000 mg provided some benefit, but data was based on relatively poor studies.

Combinations of simple analgesics with codeine are available (see later discussion) and are promoted for strong pain relief. However, there is doubt whether the amount of codeine in these preparations is sufficient to provide any additional pain relief (Murnion, 2010). In addition, codeine requires conversion to morphine by cytochrome P450 2D6 to exert its analgesic effects. There is genetic variability in this metabolism, with up to 30% of the population being poor metabolizers and in whom codeine has little or no analgesic effect. Furthermore, there is growing evidence of problems with the overuse of these products, resulting from dependence on the codeine components (Frei et al., 2010).

In response to the ongoing concerns about codeine-containing products, the Medicines and Healthcare products Regulatory Agency (MHRA), in 2009, issued new guidance to restrict codeine-containing products for the short-term (3 days) treatment of acute moderate pain that is not relieved by paracetamol, ibuprofen or aspirin alone. In 2013, the MHRA issued further guidance that codeine should not be given to children under the age of 12.

In summary, simple analgesia should be tried as first-line options for the relief of pain in migraine and tension-type headache.

Complementary therapies

Feverfew (*Tanacetum parthenium*) is a medicinal herb used for the treatment of fever, headaches and digestive problems. It is available in a number of commercially produced herbal products to prevent migraine (e.g., MigraHerb–migraine relief capsules). A Cochrane review identified six randomized, double-blind trials ($N = 561$) comparing feverfew extract or powdered feverfew to placebo in the prevention of migraine (Wider et al., 2015). The latest study in this review was relatively large ($N = 218$) and well conducted. This study reported that feverfew reduced migraine frequency by 1.9 attacks from 4.8 to 2.9, and placebo reduced the frequency by 1.3 from 4.8 to 3.5, per month, resulting in a difference in effect between feverfew and placebo of 0.6 attacks per month. Overall, the authors concluded that there was low-quality evidence that feverfew is effective in migraine prevention.

Additionally, four UK products are specifically marketed to aid in the relief of pain and/or nausea associated with migraine: Migraleve, Midrid, Buccastem M and sumatriptan. The evidence for these products is reviewed.

Migraleve

Migraleve is available as Migraleve Pink tablets, which contain a paracetamol-codeine combination (500/8 mg) plus buclizine, 6.25 mg, or Migraleve Yellow tablets, which contain only the analgesic combination. A number of trials have investigated Migraleve Pink tablets against placebo, buclizine, and ergotamine products in an attempt to establish clinical effectiveness.

A review of two trials in which Migraleve was compared against buclizine (Jorgensen, 1974) and placebo (Scopet et al., 1974) showed that Migraleve was as effective as buclizine and superior to placebo in reducing the severity of migraine attacks. However, patient numbers were small ($N = 21$ and 20 , respectively), and statistical significance was not reported. Migraleve has also been compared with ergotamine-containing products, the standard drug at the time the trial was conducted. Results from a GP research group (Anonymous, 1973) concluded that Migraleve was equally as effective as Migril in treating migraine. However, results should be viewed with caution because the trial suffered from poor design and lacked randomization, placebo, and/or proper blinding. A further trial (Carasso & Yehuda, 1984) also reported beneficial effects of Migraleve. The most recent trial (Adam, 1987) was well designed, being double-blind, randomized and placebo-controlled. The author concluded that compared with placebo, Migraleve did significantly reduce the severity of attacks but not their total duration.

Midrid

Midrid capsules contain isometheptene mucate, 65 mg, and paracetamol, 325 mg. A number of trials have investigated the effect of Midrid on reducing the severity of migraine attacks. Trials date back to 1948, although it was not until the 1970s that soundly designed trials were performed. Two studies (Diamond, 1976; Diamond & Medina, 1975) using similar methodology investigated isometheptene versus placebo and paracetamol. Both were double-blind, placebo-controlled trials and had identical inclusion criteria. The 1975 trial concluded that isometheptene was superior in relieving headache severity compared with placebo, although the dose of isometheptene used was double that found in Midrid. The 1976 trial also concluded that isometheptene was significantly superior to placebo and appeared to be better than paracetamol alone, but this did not reach statistical significance. A further trial (Behan, 1978) compared Midrid against placebo and ergotamine. Fifty patients who suffered four or more migraine attacks per month were recruited to the study. Diary cards were completed for six attacks in which patients rated relief from headache on a four-point rating scale. The author concluded that Midrid was as effective as ergotamine and that both were more beneficial than placebo, although it is unclear whether this was statistically significant.

Summary

Limited trial data for both products suggest that they might be more effective than placebo. They could be recommended, but it is not known which product is most efficacious.

Prochlorperazine (Buccastem M)

Prochlorperazine has been found to be a potent antiemetic in a number of conditions, including migraine. It works by blocking dopamine receptors found in the chemoreceptor trigger zone. It is administered via the buccal mucosa, and therefore patients will need to be counselled on correct administration.

Sumatriptan

Sumatriptan was the first triptan to be marketed in the UK and, subsequently, deregulated to OTC status. Triptans are 5-HT₁ agonists and stimulate 5-HT_{1B} and 5-HT_{1D} receptors. Triptans cause constriction of the cranial blood vessels, stop the release of inflammatory neurotransmitters at the trigeminal nerve synapses, and reduce pain signal transmission. As a class of medicines, they have been extensively researched. Most trials with sumatriptan (and

other triptans) use endpoint data of a 2-hour pain-free response, headache relief and functional disability. In all endpoints, sumatriptan, 100 mg, was significantly superior to placebo. At the lower dose of 50 mg, OTC dose evidence of efficacy is weaker than 100 mg but is still effective (Derry et al., 2012).

Practical prescribing and product selection

Prescribing information relating to specific products used to treat migraine is discussed and summarized in [Table 5.5](#), and useful tips relating to patients presenting with migraine are given in [Box 5.1](#).



Table 5.5
Practical prescribing: Summary of medicines for migraine

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy & breastfeeding
Migravele	>12 years	Headache, somnolence, dizziness, flushing, nausea and vomiting, dry mouth, sedation, constipation	Increased sedation with alcohol, opioid analgesics, anxiolytics, hypnotics, antidepressants	Glaucoma, prostate enlargement	Pregnancy: avoid in third trimester Breastfeeding OK, but infant drowsiness reported
Midrid	>12 years	Dizziness, rash	Avoid concomitant use with MAOIs and moclobemide due to risk of hypertensive crisis Avoid in patients taking beta blockers and TCAs	Control of hypertension and diabetes may be affected, but a short treatment course is unlikely to be clinically important	Avoid
Buccastem M	>18 years	Drowsiness	Increased sedation with alcohol, opioid analgesics, anxiolytics, hypnotics, antidepressants	Patients with Parkinson disease, epilepsy, prostatic hypertrophy, glaucoma	Manufacturers advise avoidance, but it has been used safely in both pregnancy and breastfeeding
Sumatriptan	>18 years	Dizziness; drowsiness; tingling feeling; warm, flushed or weak and sensation of heaviness in any part of the body; pressure in the throat, neck, chest and arms or legs; shortness of breath	MAOIs, ergotamine	Avoid in people with a previous MI, IHD, TIA, peripheral vascular disease, cardiac arrhythmia, hypertension; history of seizures; hepatic and renal impairment; atypical migraines	Avoid, but evidence suggests it can be used safely Only use if absolutely necessary

IHD, Ischaemic heart disease; *MAOI*, monoamine oxidase inhibitor; *MI*, myocardial infarction; *TCA*, tricyclic antidepressant; *TIA*, transient ischaemic attack.

HINTS AND TIPS BOX 5.1: MIGRAINE

ID Migraine: This is a screening tool that has shown to be a valid and reliable screening test for migraine. Nearly all patients that answer yes to two of the questions opposite have migraine.

Analgesia

Administration of buccal tablets

During the last 3 months, did you have any of the following symptoms together with a headache?

Question 1: Did you feel nauseated or sick?

Question 2: Did light bother you (a lot more than when you didn't have a headache)?

Question 3: Did your headache limit your ability to work, study, play or do what you wanted to do for at least 1 day?

Recommend a soluble or orodispersible formulation to maximize absorption before it is inhibited by gastric stasis.

1. Place the tablet either between the upper lip and gum, above the front teeth or between the cheek and upper gum.
2. Allow the tablet to dissolve slowly. The tablet will soften and form a gel-like substance after 1–2 hours.
3. The tablet will take from 3 to 5 hours to dissolve completely. If food or drinks are to be consumed during this time, place the tablet between the upper lip and gum, above the front teeth.
4. The tablets should not be chewed, crushed or swallowed.
5. Touching the tablet with the tongue or drinking fluids can cause the tablet to dissolve faster.

Migraleve

The dose for adults and children older than 16 years is two Migraleve Pink tablets when the attack is imminent or has begun. If further treatment is required, one or two Migraleve Yellow tablets can be taken every 4 hours. The dose for children aged between 12 and 15 years is half that of the adult dose. The maximum adult dose is eight tablets (two Migraleve Pink and six Migraleve Yellow) in 24 hours and, for children aged between 12 and 15 years, the maximum dose is four tablets (one Migraleve Pink and three Migraleve Yellow) in 24 hours.

The buclizine component of Migraleve Pink tablets can cause drowsiness and antimuscarinic effects, whereas the codeine content might result in patients experiencing constipation. Other side effects are possible and listed in [Table 5.5](#). Buclizine and codeine can interact with prescription-only medicine (POM) and OTC medication, especially those that cause sedation. The combined effect is to potentiate sedation, and it is important to warn the patient of this. It appears that Migraleve is safe in pregnancy but, because of the codeine component, it is best avoided in the third trimester. It is also generally safe in breastfeeding, but drowsiness in the baby is

possible. However, MHRA advice (2013) stated that codeine should not be given during breastfeeding.

Midrid

Midrid is licensed for use only in adults. The dosage is two capsules at the start of an attack, followed by one capsule every hour until relief is obtained. A maximum of five capsules can be taken in a 12-hour period. It is a sympathomimetic agent and, like decongestants, it interacts with monoamine oxidase inhibitors (MAOIs), which might lead to fatal hypertensive crisis. It can also affect diabetes and hypertension control. Side effects reported with Midrid include transient rashes and other allergic reactions. Midrid is best avoided in pregnancy and breastfeeding due to lack of data.

Buccastem M

Buccastem M is indicated for previously diagnosed migraine sufferers aged 18 years and older who experience nausea and vomiting. The dosage is one or two tablets twice daily. Side effects reported include drowsiness, dizziness, dry mouth,

insomnia, agitation and mild skin reactions, but their incidence is not known from the available data. Because it crosses the blood-brain barrier, it will potentiate the effect of other CNS depressants and interact with alcohol. Prochlorperazine has been safely used in pregnancy, although the manufacturer advises avoidance unless absolutely necessary. Minimal prochlorperazine passes into the breast milk and could be used in breastfeeding mothers.

Sumatriptan

Patients over the age of 18, but younger than 65, should take a single tablet of sumatriptan (Migratan; 50 mg) as soon as possible after the onset of the headache. If the headache clears and then recurs, a second tablet can be taken, provided there was a response to the first tablet and more than 2 hours have elapsed between the first and second tablets. No more than 100 mg can be taken during any 24-hour period. If there is no response to the first tablet, a second tablet should not be taken for the same attack. Sumatriptan is associated with a well-recognized side effect profile, with the most common adverse events being dizziness, drowsiness, tingling, feeling warm, flushed or weak, sensation of heaviness in any part of the body, shortness of breath, and pressure in the throat, neck, chest and arms or legs. Triptans are associated with rare cases of cardiac disorders and therefore, to allow wider availability via OTC sales, the warnings associated with prescription use have become contraindications. Those patients ineligible for OTC use are as follows:

- A previous myocardial infarction, ischaemic heart disease, peripheral vascular disease, cardiac arrhythmias, and history of transient ischaemic attack and stroke
- Known hypertension
- History of seizures
- Hepatic and renal impairment
- Atypical migraines
- Concomitant administration of MAOIs and ergotamine or other 5-HT₁ receptor agonists

The manufacturer advocates avoidance in pregnancy and breastfeeding; however, data in the Summary of Products Characteristics, state it has been used safely in the first trimester of pregnancy, and breastfeeding can be continued providing that 12 hours have elapsed since taking the dose. Given that triptans are not given continuously, and that the drug has poor bioavailability (14%), the amount of sumatriptan that reaches the infant's circulation is expected to be very low (<1%).

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Further reading

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Websites

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- International Headache Society: <http://www.ihs-houreadache.org>
- National Headache Foundation: <http://www.headaches.org>
- Organisation for the understanding of cluster headaches (OUCH-UK): <https://ouchuk.org>

Insomnia

Background

Insomnia can be defined as difficulty initiating or maintaining sleep or early-morning awakening that leads to dissatisfaction with sleep quantity or quality. This leads to

impairment in, for example, social and behavioural functioning, as well as causing significant distress.

It is likely that everyone at some point will experience insomnia because it can arise from many different causes (Fig. 5.3); however, for most people the problem will be of nuisance value, affecting next-day alertness. The pharmacist can manage most patients with short-term insomnia; however, cases of chronic insomnia are best referred to the doctor, as there is usually an underlying cause. Insomnia is classified by its duration or likely duration: short term (between 1 and 4 weeks) and long term (>4 weeks).

Prevalence and epidemiology

Insomnia is a common condition with estimates of prevalence varying depending on the definitions of insomnia used. Approximately 20% to 40% of adults report occasional sleep difficulty (Cunnington et al., 2013; Morphy et al., 2007; Wilshire et al., 2013), and insomnia increases with advancing age. It has been reported that women report more subjective sleep abnormalities than men.

Aetiology

Sleep is essential to allow the body to repair and restore brain and body tissues. The mechanisms controlling sleep are complex and not yet fully understood but reflect disturbances of arousal and/or sleep-promoting systems in the brain. Their relative activities determine the degree of alertness during wakefulness and depth and quality of sleep. Insomnia may be caused by any factor that increases activity in arousal systems or decreases activity in sleep systems.

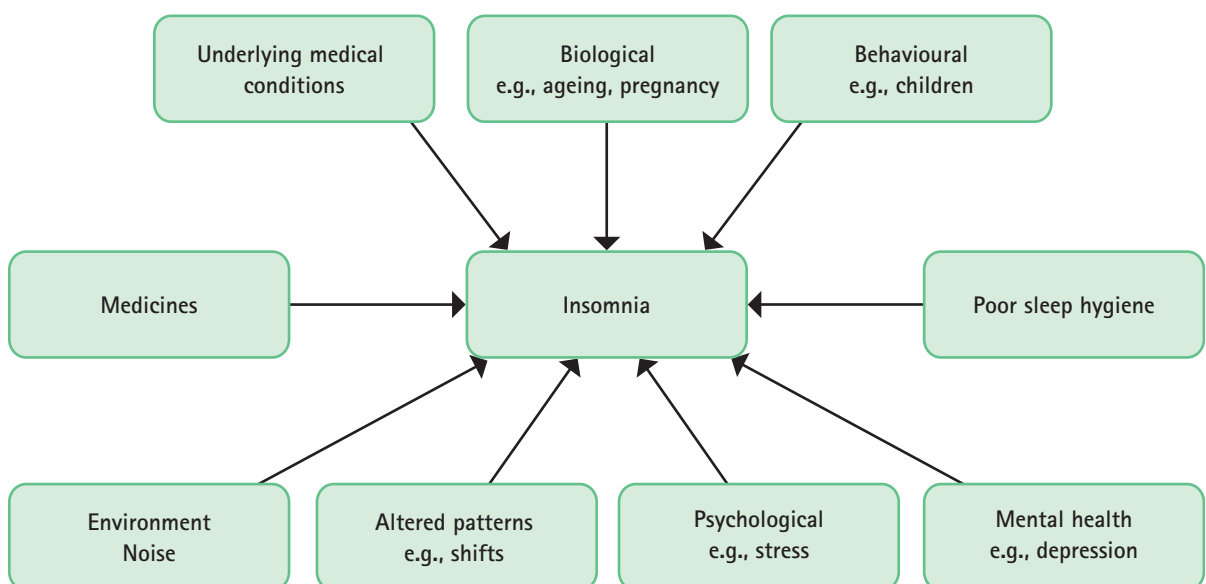


Fig. 5.3 Causes of insomnia.

Arriving at a differential diagnosis

The length of sleep people need varies but typically sleep requirements decrease with increasing age and people older than 80 years commonly have less than 6 hours of sleep per day (Ohayon et al., 2004). Therefore, the key to arriving at a differential diagnosis is to take a detailed sleep history. Asking symptom-specific questions will help the pharmacist determine the most likely cause of the person's insomnia (Table 5.6). Two key features of insomnia need to be determined: if there is an attributable cause and how it affects the person. Insomnia lasting only a few days is often caused by a change of routine including, for example, time zone changes or a change to shift patterns, excessive noise, sleeping in a new environment (e.g., hotel), and extremes of temperature. Short-term insomnia is usually related to acute stress such as sitting for exams, bereavement, loss of job, forthcoming marriage, or house move. Asking patients to tell you what they are thinking about before they fall asleep and when they awake; this will give you a clue to the cause of the insomnia. Often, it can be difficult to determine the cause of insomnia, and getting the patient to keep a sleep diary (e.g., including retiring and waking times, time taken to fall asleep) is sometimes beneficial because it allows an objective measure of the person's habits compared with their subjective perceptions.

Clinical features of insomnia

Insomnia is a subjective complaint of poor sleep in terms of its quality and duration. Patients will complain of difficulty in falling asleep, staying asleep, and/or lack of refreshment by sleep. Sometimes patients will experience daytime fatigue but not generally sleepiness. This tiredness can lead to poor performance at work.

Conditions to eliminate

Insomnia in children

Bedwetting is the most common sleep arousal disorder in children. If this is not the cause, then insomnia invariably stems from a behavioural problem, such as fear of the dark, insecurity or nightmares. Children should not be given sleep aids but referred to their doctor for further evaluation because the underlying cause needs to be addressed.

Medicine-induced insomnia

Medication can cause insomnia (Table 5.7). The stimulant effects of caffeine (in chocolate, tea, coffee and cola drinks) should not be underestimated. Drinking four or more cups of coffee can cause insomnia in the average healthy adult. It is therefore advisable to instruct patients to avoid caffeine-containing products 6 hours before bedtime.



Table 5.6
Specific questions to ask the patient: Insomnia

Question	Relevance
Pattern of sleep	An emotional disturbance (predominantly anxiety) is commonly associated in patients who find it difficult to fall asleep; patterns that include patients who fall asleep but wake early and cannot fall asleep again, or who are then restless, are sometimes associated with depression.
Daily routine	Has there been any change to the work routine, such as changes to shift patterns and additional workload, resulting in longer working hours and greater daytime fatigue? Too much exercise or intellectual arousal before going to bed can make sleep more difficult.
Underlying medical conditions	Medical conditions likely to cause insomnia are gastro-oesophageal reflux disease (GORD) pregnancy, pruritic skin conditions, asthma, Parkinson disease, painful conditions (osteoarthritis), hyperthyroidism (night sweats), menopausal symptoms (hot flushes) and depression.
Recent travel	Time zone changes will affect the person's normal sleep pattern, and it can take a number of days to re-establish normality.
Daytime sleeping	Older adults might nap throughout the day, which results in less sleep needed in the evening, making patients believe they have insomnia.



Table 5.7
Medications that may cause insomnia
(commonly/very commonly reported)

Medication	Comments
Stimulants	Caffeine, theophylline, sympathomimetics amines (e.g., pseudoephedrine), MAOIs, especially in early treatment
Antiepileptics	Carbamazepine, phenytoin
Alcohol	Low to moderate amounts can promote sleep but when taken in excess or over a long period, it can disturb sleep.
Beta blockers	Can cause nightmares, especially propranolol. Limit by swapping to a beta blocker that does not readily cross the blood-brain barrier.
SSRIs	Especially fluoxetine
Diuretics	Ensure that doses should not be taken after midday to stop the need to urinate at night.
Donepezil	Abnormal dreams and nightmares
<i>MAOIs</i> , Monoamine oxidase inhibitors; <i>SSRIs</i> , selective serotonin reuptake inhibitors.	

Abruptly stopping some medications can also lead to insomnia. This is particularly seen with the long-term use of sedative drugs, such as benzodiazepines and tricyclic antidepressants.

Underlying medical conditions

Many medical conditions may precipitate insomnia (see [Table 5.6](#)). It is therefore necessary to establish a medical history from the patient. A key role for the pharmacist in these situations is to ensure that the underlying condition is being treated optimally and to check that the medication regimen is appropriate. If improvements to prescribing could be made, the prescriber should be contacted to discuss possible changes to the patient's medication.

Depression

Between one-third and two-thirds of patients suffering from chronic insomnia will have a recognizable psychiatric illness, most commonly depression. Many of these patients do not seek medical help and will self-medicate. The patient will complain of having difficulty staying asleep and suffer from early morning waking. The pharmacist should look for other symptoms of depression, such as fatigue, loss of interest and appetite, feelings of guilt, low self-esteem, difficulty in concentrating and constipation.

[Fig. 5.4](#) will help in the differential diagnosis of the different types of insomnia.



TRIGGER POINTS indicative of referral: Insomnia

Symptoms/signs/ population	Possible danger/ reason for referral	Urgency of referral
Duration >4 weeks; children Insomnia for which no cause can be ascertained	Outside the remit of community pharmacists; likely to be associated with underlying causes and requires investigation	Soon as practicable
Symptoms suggestive of anxiety or depression	Insomnia is one of the cardinal symptoms of depression and anxiety and needs investigation	

Evidence base for over-the-counter medication

Many cases of short-term insomnia should be managed initially by nonpharmacological measures. If these fail to rectify the problem, short-term use of sedating antihistamines may be tried.

Sleep hygiene

Once a diagnosis of insomnia has been reached, underlying causes ruled out, and any misconceptions about normal sleep addressed, then educating patients about behaviour and practices which affect sleep should be tackled ([Table 5.8](#)).

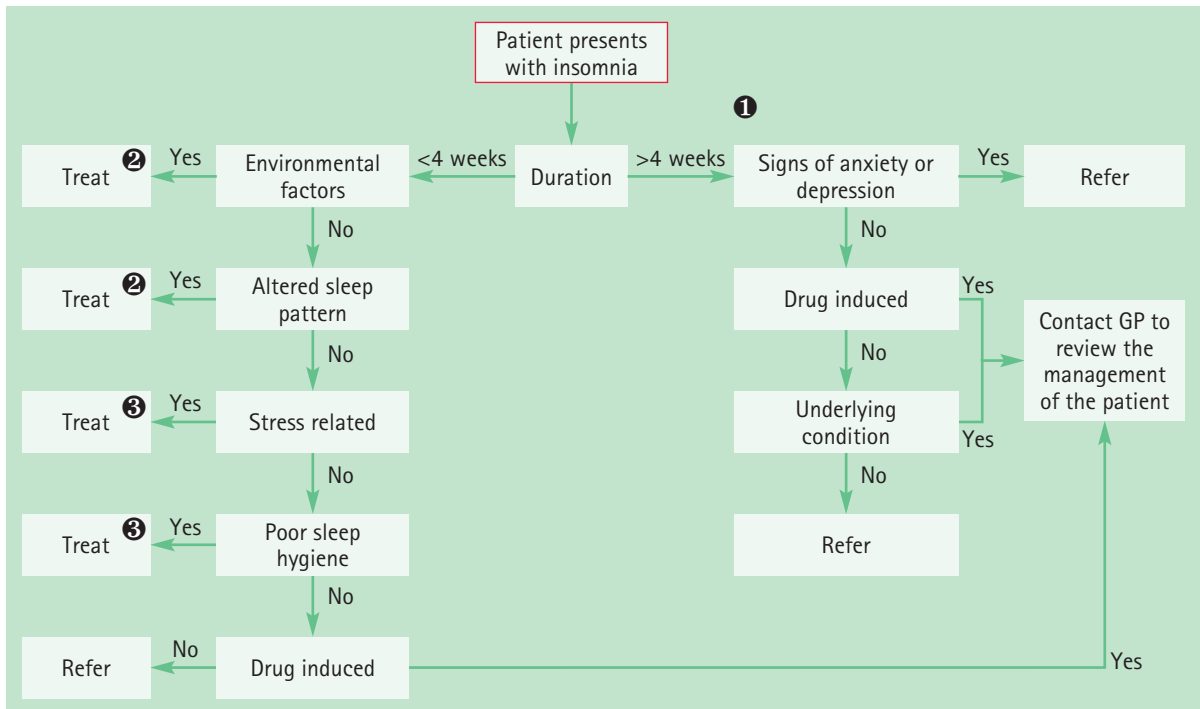


Fig. 5.4 Primer for differential diagnosis of insomnia.

❶ No cases of insomnia lasting longer than 4 weeks should be treated with OTC medication. If a previously undiagnosed medical condition is suspected, most often anxiety or depression, or if insomnia has possibly been caused by the patient's preexisting condition or medicines, the GP should be consulted, and treatment options discussed and suggested.

❷ Patients should not take antihistamines for more than 7 to 10 continuous days because tolerance to their effect can develop.

❸ In the first case, strategies to manage the patient's insomnia should be suggested rather than issuing medication.

Table 5.8

Key steps to good sleep hygiene

Maintain a routine, with a regular bedtime and awakening time. Food snacks, alcoholic- and caffeine-containing drinks should be avoided.

Avoid sleeping in very warm rooms.

Avoid stimulants and alcohol within 6 hours of going to bed.

Avoid exercise within 4 hours of bedtime.

No daytime naps.

No sleeping in to catch up on sleep.

No strenuous mental activity at bedtime (e.g., doing a crossword in bed).

Solve problems before retiring.

Associate bed with sleep; try not to watch TV or listen to music.

If unable to get to sleep, get up and do something and return to bed when sleepy.

Medication

The sedating antihistamines diphenhydramine (DPH) and promethazine are the mainstays of OTC pharmacological treatment.

Diphenhydramine

A number of studies support the clinical effectiveness of DPH as a sleep aid. At doses of 50 mg, DPH has been shown to be consistently superior to placebo in inducing sleep and as effective as 60 mg of sodium pentobarbital (Rickels et al., 1983; Teutsch et al., 1975) and 15 mg of temazepam (Meuleman et al., 1987). Doses higher than 50 mg of DPH do not produce statistically superior clinical effect, and nighttime doses should therefore not exceed this amount. It appears to be most effective at shortening sleep onset time.

Promethazine

Promethazine is widely accepted to cause sedation when used for its licensed indications; however, few trials have investigated its use as a hypnotic. A study by Adam and Oswald (1986) recruited 12 healthy volunteers who took placebo or promethazine, 20 or 40 mg, in a blinded trial. The authors concluded that both doses of promethazine increased the length of sleep, and sleep disturbances were reduced compared with placebo. However, it was not clear if this reached statistical significance. Another small study comparing diazepam, 5 mg, and promethazine, 25 mg, in older patients found both to be effective (Viukari & Miettinen, 1984).

Summary

Of the two sedating antihistamines, DPH has the stronger evidence base to substantiate its use as a hypnotic. It therefore seems prudent to use this as the treatment of choice. However, antihistamines are less effective than gamma-aminobutyric acid A (GABA_A) receptor hypnotics (e.g., the 'z' drugs available on prescription).

Complementary therapies

These products are used by a substantial number of patients as a self-care measure (Byrne, 2006; Pearson et al., 2006). Herbal remedies containing hops, German chamomile, skullcap, wild lettuce, lavender, passiflora and valerian are available. However, there is little evidence to support their use. Most information available in the literature relates to the hypothesised actions of chemical constituents or studies in animals. Valerian appears to be the only product in which more than one trial has been conducted on humans. One systematic review (Bent et al., 2006) identified 16 studies comparing valerian to placebo and found a statistically

significant improvement in the outcome of sleep quality (improved or not). However, most studies had significant methodological problems, and there was evidence of publication bias. Furthermore, there was a lack of standardization of the doses used, thus it is not possible to determine an effective dose.

A number of branded products, containing combinations of herbal ingredients, are available OTC (e.g., Kalms range, Nytol herbal tablets, NiteHerb).

Melatonin

Melatonin is advocated for sleep disturbance, particularly associated with jet lag. A Cochrane review (Herxheimer & Petrie, 2002) found melatonin to be effective in reducing jet lag. The timing of the dose is critical. It has to be taken at bedtime after darkness has fallen on the first day of travel, then again in the same way on the second, and any subsequent day of travel. Once at the final destination, it should be taken for the following few days at the same time.

Practical prescribing and product selection

Prescribing information relating to medicines for insomnia is discussed and summarized in [Table 5.9](#), and useful tips relating to patients presenting with insomnia are given in 'Hints and Tips' in [Box 5.2](#).

Antihistamines used for insomnia are first-generation antihistamines and interact with other sedating medication, resulting in potentiation of sedation. Additionally, they possess antimuscarinic side effects, which commonly lead to dry mouth and possibly to constipation. It is these antimuscarinic properties that mean that patients with glaucoma and prostate enlargement should ideally avoid their use because it could lead to increased intraocular pressure and precipitation of urinary retention.



Table 5.9
Practical prescribing: Summary of medicines for insomnia

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy & breastfeeding
Diphenhydramine	>16 years	Dry mouth, sedation, and grogginess next day	Increased sedation with alcohol, opioid analgesics, anxiolytics, hypnotics and antidepressants	Glaucoma, prostate enlargement	Some manufacturers advise avoidance In breastfeeding, occasional use OK, but discontinue if baby becomes drowsy
Promethazine					

HINTS AND TIPS BOX 5.2: INSOMNIA

Antihistamines

Patients who self-treat for depression

Tolerance can develop with continuous use

St John's wort (*hypericum*) is used by many patients to treat depression. There is a growing body of evidence that it is more effective than placebo for mild depression and is comparable in effect to tricyclic antidepressants. However, pharmacists should not recommend it routinely. If depression is suspected, the patient should be referred for further assessment. St John's wort also interacts with other medicines, including warfarin, SSRIs, antiepileptics, digoxin, ciclosporin, theophylline and contraceptives

SSRIs, Selective serotonin reuptake inhibitors.

Diphenhydramine

Diphenhydramine (e.g., Nytol, Nightcalm) is licensed only for adults and children older than 16 years. The dose is 50 mg taken 20 minutes before going to bed. Nytol is available as tablets (two tablets [Nytol] or one tablet [Nytol one-a-night]) or liquid (10 mg/5 mL) and Nightcalm as a once-daily capsule.

Promethazine

Proprietary brands of promethazine available to the public include Sominex (20 mg) and Phenergan (10 or 25 mg). Adults and children older than 16 years should take one tablet 1 hour before bedtime.

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- National Sleep Foundation: <http://www.sleepfoundation.org/>

Nausea and vomiting

Background

Nausea is an unpleasant sensation, which may be a precursor to the forceful expulsion of gastric contents (vomiting).

Prevalence and epidemiology

Nausea and vomiting are extremely common symptoms and caused by numerous conditions. As such, their prevalence and epidemiology are dictated by the underlying condition causing the symptoms.

Aetiology

Two main mechanisms are involved in inducing nausea and vomiting—neurological and peripheral. Nausea occurs because activity in the vomiting centre (located in the medulla oblongata) increases. Information received from the receptor cells in the walls of the gastrointestinal tract and parts of the nervous system reach a *threshold value* that induces the vomiting reflex. Additionally, further input is received at the vomiting centre from an area known as the *chemoreceptor trigger zone*. This is highly sensitive to certain circulating chemicals; for example, substances released by damaged tissues as a result of bacterial infection.

Arriving at a differential diagnosis

Nausea and/or vomiting are common symptoms of many disorders, including infection, acute alcohol ingestion, anxiety, severe pain and labyrinth and cardiovascular causes.

Symptoms rarely occur in isolation, and other symptoms are usually present to help aid in the differential diagnosis. Most cases will have a gastrointestinal origin, with viral gastroenteritis and food poisoning being the most common acute cause in all age groups. Questioning the patient about associated symptoms should be made to eliminate other conditions (Table 5.10).

Clinical features associated with gastroenteritis

Gastroenteritis is characterized by acute onset, vomiting, and/or diarrhoea and systemic illness (e.g., fever). Most cases, regardless of the infecting pathogen, resolve in a few days and rarely last more than 10 days. In children under 5 years old over 60% of cases are viral in origin, with rotavirus and small, round, structured viruses most commonly identified. Vomiting usually precedes diarrhoea by several hours. Bacterial gastroenteritis presents with similar symptoms, although fever is usually a more prominent feature. In food poisoning, violent vomiting and diarrhoea within 24 hours of eating contaminated food is usual.

Conditions to eliminate

Gastritis

Gastritis is often alcohol- or medicine-induced and can present as acute or chronic nausea and vomiting. Epigastric pain is usually present. For further information on gastritis, see the dyspepsia section in chapter 7.

Nausea and vomiting associated with headaches

Vomiting and especially nausea are common symptoms in patients who suffer from migraines. However, other causes



Table 5.10
Specific questions to ask the patient: Nausea and vomiting

Question	Relevance
Presence of abdominal pain	Certain abdominal conditions, such as appendicitis, cholecystitis and cholelithiasis, can also cause nausea and vomiting. However, for all three conditions, abdominal pain would be the presenting symptom, not nausea and vomiting. The severity of the pain alone would trigger referral.
Timing of nausea and vomiting	Early morning vomiting is often associated with pregnancy or excess alcohol intake. If vomiting occurs immediately after food, this suggests gastritis, and if vomiting begins 1 or more hours after eating, peptic ulcers are possible.
Signs of infection	Acute cases of gastroenteritis will normally have other associated symptoms, such as diarrhoea, fever and abdominal discomfort. If infection is due to food contamination, other people are often affected at the same time.

of headache, such as raised intracranial pressure, can also cause nausea and vomiting.

Nausea and vomiting in neonates (up to 1 month old)

Vomiting in neonates should always be referred because it suggests some form of congenital disorder; for example, Hirschsprung's disease.

Nausea and vomiting in infants (1 month to 1 year old)

In the first year of life, the most common causes of nausea and vomiting are feeding problems and gastrointestinal and urinary tract infections. Vomiting in infants needs to be differentiated from regurgitation. Regurgitation is an effortless backflow of small amounts of liquid and food between meals or at feeding times; vomiting is the forceful expulsion of gastric contents. The infant will usually have a fever and be generally unwell if vomiting is associated with infection. If projectile vomiting occurs in an infant younger than 3 months, pyloric stenosis should be considered. Due to the higher risk of dehydration in this age group, it is prudent to refer to a doctor if symptoms persist for more than 24 hours.

Nausea and vomiting in children (1 to 12 years old)

Children under 12 years old who experience nausea and vomiting will usually have gastroenteritis, fever, or otitis media. In most cases, the conditions are self-limiting, and medication designed to reduce pain and temperature (analgesia) and replace fluid (oral rehydration therapy) will help resolve symptoms.

Pregnancy

Pregnancy should always be considered in women of childbearing age if nausea and vomiting occur in the absence of other symptoms. Sickness affects more than 50% of women, tends to be worse in the early morning, and peaks at 9 weeks' gestation.



TRIGGER POINTS indicative of referral: Nausea and vomiting

Symptoms/signs/populations	Possible danger/reason for referral	Urgency of referral
Early-morning vomiting in women of childbearing age	Suspect pregnancy	Perform test as soon as practicable
Vomiting in children <1 year lasting >24 hours; children who fail to respond to OTC treatment	Risk of dehydration	Same-day referral
Unexplained nausea and vomiting in any age group	Identifiable causes account for the vast majority of presentations Unknown causes should be viewed with caution	Same-day referral to GP
Moderate to severe abdominal pain	Requires further and fuller investigation	

Excess alcohol consumption

The patient should always be asked about recent alcohol intake because excess quantities are associated with nausea and early morning vomiting.

Medicine-induced nausea and vomiting

Many medications can cause nausea and vomiting. Frequently implicated medicines are cytotoxics, opiates, iron,



Table 5.11

Practical prescribing: Summary of medicine for nausea and vomiting

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
Prochlorperazine	>18 years	Drowsiness	Increased sedation with alcohol, opioid analgesics, anxiolytics, hypnotics, antidepressants	Patients with Parkinson disease, epilepsy, glaucoma	Manufacturers advise avoidance, but it has been used safely in both pregnancy and breastfeeding

antibiotics, nonsteroidal antiinflammatory drugs (NSAIDs), potassium supplements, selective serotonin reuptake inhibitors (SSRIs), nicotine gum (ingestion of nicotine rather than buccal absorption), theophylline and digoxin toxicity. If medication is suspected then the pharmacist should contact the prescriber to discuss alternative treatment options.

Product selection

Deregulation of domperidone and prochlorperazine once meant that community pharmacists could more effectively manage nausea and vomiting. Unfortunately, in 2014, domperidone was reclassified back to prescription-only status over fears about its potential cardiac side effects.

This now means that UK pharmacists only have prochlorperazine to use to combat nausea and vomiting associated with migraine (Table 5.11). For dosing and counselling on prochlorperazine, refer to page 107. If dehydration is suspected, the patient should replace fluids. Oral rehydration solutions should be offered. For further information on these products, see chapter 7 under diarrhoea.

Further reading

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Self-assessment questions

The following questions are intended to supplement the text. Two levels of questions are provided, multiple-choice questions and case studies. The multiple-choice questions are designed to test knowledge and application of knowledge; the case studies allow this knowledge to be put in context in patient scenarios.

Multiple-choice questions

- 5.1** A 32-year-old woman presents to the pharmacy one Monday afternoon complaining of a headache. Based on epidemiology alone, what would be the most likely cause of the headache?
- Migraine
 - Eye strain
 - Tension-type headache
 - Sinusitis
 - Cluster headache
- 5.2** A 41-year-old man wants some advice about his headache. He reveals that the pain is towards the back of his head. Knowing this information, what headache conditions cannot be ruled out based on location?
- Migraine
 - Temporal arteritis
 - Subarachnoid haemorrhage
 - Sinusitis
 - Cluster headache
- 5.3** When differentiating headaches from one another, it is useful to consider other symptoms to aid diagnosis, with some symptoms warranting referral. From the list of symptoms below, which would indicate referral for a patient suffering with headache?
- Flashing or flickering lights
 - Pins and needles in the arms
 - Scalp tenderness
 - Symptoms that improve as the day progresses
 - Symptoms that last longer than 1 week
- 5.4** From the following descriptions, which one best describes the headache symptoms of migraine?
- Pain that is unilateral and lancinating
 - Pain that is unilateral, orbital and boring
 - Pain that is unilateral, frontal and dull
 - Pain that is unilateral and temporal
 - Pain that is unilateral and throbbing
- 5.5** A 41-year-old man wants some advice about his headache. He tells you that he has had the symptoms for a couple of days. The headache is at the front of his head, and it feels like a dull throb. Which of the questions listed below would be most discriminatory in assessing if it were a migraine or tension-type headache?
- How severe is the pain?
 - What medicines does the patient take?
 - What medicines has the patient tried to ease the pain?
 - Where is the pain?
 - Does the patient feel sick?
- 5.6** Which sign or symptom warrants referral?
- Headache lasting 7 to 10 days
 - Headache described as vice-like
 - Headache associated with the workplace environment
 - Headache in children younger than 12 years, with no sign of infection
 - Headache associated with cough and cold symptoms
- 5.7** Chronic insomnia is associated with which of the following?
- Change in work shift patterns
 - Acute stressful situations
 - Foreign travel
 - Excessive caffeine intake
 - None of the above
- 5.8** Which complementary therapy/medicine has the most evidence to support its use in treating insomnia?
- Acupuncture
 - Lavender
 - Chamomile
 - Valerian
 - Reflexology

- 5.9** Many medicines can induce nausea and/or vomiting. From the list below, which medicine is most likely to have this effect?
- Paracetamol
 - Diphenhydramine
 - Omeprazole
 - Sumatriptan
 - Thyroxine
- 5.10** A patient has nausea and vomiting. Which statement would potentially alert you to refer the patient:
- Symptoms more than 48 hours in an adult
 - Symptoms more than 24 hours in an 18-month-old
 - Symptoms more than 24 hours in a 9-month-old
 - Symptoms less than 24 hours in an adult
 - Symptoms less than 48 hours in an adult
- 5.11** An elderly woman presents with headache. Which one of the following symptoms require you to make an urgent referral to the doctor?
- Unilateral headache with associated nausea
 - Bilateral headache with symptoms that worsen as the day progresses
 - Unilateral frontal headache, which worsens on bending down
 - Bilateral generalized headache
 - Unilateral headache with malaise
- 5.12** From the list of conditions known to cause nausea and/or vomiting, which is most associated with additional symptoms of diarrhoea?
- Cholecystitis
 - Migraine
 - Gastritis
 - Gastroenteritis
 - Otitis media
- 5.13** A 51-year-old woman wants some advice about her headache. She reveals that the pain is toward the front and affects both sides of her head. Knowing this information, what headache condition is most likely?
- Migraine
 - Temporal arteritis
 - Subarachnoid haemorrhage
 - Sinusitis
 - Cluster headache
- 5.14** Mrs Jones presents to the pharmacy complaining of headaches. She tells you that the pain has been present for the last 24 hours and is at the front of her head, and she has felt a little sick. Based on this information, what would be the most likely diagnosis?
- Tension-type headache
 - Temporal arteritis
 - Migraine
 - Sinusitis
 - Haematoma
- 5.15** Nausea and vomiting in children under 1 year of age is common. In which condition listed below is nausea and vomiting most commonly seen in this age group?
- Otitis media
 - Ménière's disease
 - Urinary tract infection
 - Upper respiratory tract infection
 - Feeding difficulties
- Questions 5.16 to 5.25 concern the following conditions:
- Sinusitis
 - Cluster headache
 - Migraine
 - Temporal arteritis
 - Meningitis
 - Tension-type headache
 - Subarachnoid haemorrhage
 - Medication overuse headache
 - Glaucoma
- Select, from A to I, which statement is most closely associated with the above conditions:
- 5.16** Is more common in men?
- 5.17** Is seen with advancing age but shows no gender bias?
- 5.18** Onset tends to be in early adulthood
- 5.19** Is more common in women?
- 5.20** Is frequently seen in older women?
- 5.21** Is secondary to infection?
- 5.22** Is most frequently seen in young children?
- 5.23** Is the most prevalent headache condition?
- 5.24** Is associated with nasal congestion and severe headache?
- 5.25** Pain is occipital.

Answers

5.1 Answer: c

Rationale: Tension-type headaches (c) are most prevalent in all age groups. Migraine (a) is more common in women and needs to be considered more carefully. Eye strain (b) and sinusitis (d), although common causes of headache, are far less prevalent than tension headache. Cluster headache (e) is unusual and much more common in men than in women.

5.2 Answer: c

Rationale: Answers a (migraine), b (temporal arteritis), d (sinusitis), and e (cluster headache) are frontal-occurring headaches.

5.3 Answer: c

Rationale: a and b are symptoms associated with migraine, d suggests tension-type headache, and headaches often last longer than 1 week (e). Symptoms of scalp tenderness (c) are suggestive of temporal arteritis, a condition that warrants referral.

5.4 Answer: e

Rationale: Migraine is usually unilateral but this is stated for all options and so is mostly unhelpful. Therefore, the nature of the pain helps differentiate causes. Lancing (a) could be trigeminal neuralgia, orbital and boring (b) indicates cluster headache, frontal and dull suggests sinusitis (c), and a temporal location suggests temporal arteritis (d). This leaves unilateral and throbbing as the best descriptor for migraine (e).

5.5 Answer: e

Rationale: Nausea is experienced by about 90% of migraine sufferers and is rarely associated with tension headache; it is therefore the most discriminatory in this case. Location (d) is also a good question to ask because approximately 70% of patients with migraine have one-sided pain, whereas tension-type headache is usually bilateral. Severity (a) is subjective and, although useful, needs to be quantified by using some form of scale. Asking about medicines (b and c) taken or tried will not be of particular help.

5.6 Answer: d

Rationale: Duration of 7 to 10 days (a) is not unusual, especially tension-type headache; a vice-like description (b) suggests tension headache also. If workplace implicated (c), the cause needs exploring but does not warrant referral; headache associated with upper respiratory tract infections (e) are commonly seen.

5.7 Answer: e

Rationale: Options a to d all suggest short-term causes.

5.8 Answer: d

Rationale: Based on evidence from sources such as Cochrane reviews, only valerian (d) has evidence of efficacy.

5.9 Answer: c

Rationale: Omeprazole is a common cause, as is sumatriptan, but the relationship between medicine and symptoms is difficult to differentiate.

5.10 Answer: c

Rationale: Nausea and vomiting can have many causes, and most cases result in acute and short-lived episodes. Age is an important consideration, and younger patients should be viewed with greater caution in management, especially the very young. In this case, c would be the most appropriate answer.

5.11 Answer: e

Rationale: Option a suggests migraine, options b and d could be tension-type headache, option c suggests sinusitis and option e could be temporal arteritis.

5.12 Answer: d

Rationale: Cholecystitis (a), migraine (b), and otitis media (e) are associated with pain, and gastritis (c) with abdominal discomfort. None routinely has diarrhoea as a symptom.

5.13 Answer: d

Rationale: A and b (migraine and temporal arteritis) are normally one-sided, c (subarachnoid haemorrhage) presents at the back of the head, and e (cluster headache) is one-sided.

5.14 Answer: c

Rationale: Unilateral headache associated with sickness in women is highly suggestive of migraine (c). Haematoma (e) can cause sickness but the duration of symptoms is too short for this to be considered. Other conditions listed do not have sickness as a symptom, although temporal arteritis (b) can cause malaise.

5.15 Answer: c

Rationale: Ménière's disease (b) is not associated with this age group, and nausea and vomiting are unusual in upper respiratory tract infection (d). Feeding difficulties (e) are

commonly associated with food regurgitation rather than with nausea and vomiting. Otitis media (a) does occur in this age group but nausea and vomiting are not common.

5.16 Answer: B

Rationale: Epidemiological data clearly shows that cluster headache (B) is much more common in men compared to the conditions listed.

5.17 Answer: I

Rationale: Temporal arteritis (D) and glaucoma (I) are the only two conditions listed that are strongly associated with advancing age. However, temporal arteritis is more common in women.

5.18 Answer: C

Rationale: Options D and I can be eliminated (see answer to 5.17), cluster headache (B) and tension-type headache (F) are associated with onset in adulthood, sinusitis (A) is a complication of colds and shows no real pattern with regard to age of onset, as is the case with medication-overuse headache (H) and meningitis (E) is seen in young children. Migraine (C), however, does often start in adolescence.

5.19 Answer: C

Rationale: Epidemiological data shows migraine (C) to be more common in women compared to men. Temporal arteritis is more common in older women.

5.20 Answer: D

Rationale: See answer to 5.17.

5.21 Answer: A

Rationale: Infective causes on the list only relate to sinusitis and meningitis. Sinusitis occurs as a result of a previous infection, whereas headache associated with meningitis is one of the symptoms of the infection itself.

5.22 Answer: E

Rationale: See answer to 5.18.

5.23 Answer: F

Rationale: Most listed conditions are uncommon or rarely seen in primary care. Only migraine (A) and tension-type headache (F) are regularly encountered. Of the two, tension-type headache is the most prevalent.

5.24 Answer: B

Rationale: Accompanying symptoms with headache are useful in helping with a differential diagnosis. Nasal congestion associated with headache is not common, and the only conditions listed where this would be seen are sinusitis (A) and cluster headache (B). The pain is described as severe, so this indicates cluster headache as being the most likely diagnosis.

5.25 Answer: G

Rationale: Sinusitis (A), cluster headache (B), migraine (C), temporal arteritis (D), and glaucoma (I) are associated with frontal headache. Meningitis (E), tension-type headache (F) and medication overuse headache (H) are more generalized in nature.

Self-assessment questions

The following questions are intended to supplement the text. Two levels of questions are provided: multiple choice questions and case studies. The multiple choice questions are designed to test knowledge and application of knowledge, and the case studies allow this knowledge to be put in context in patient scenarios.

Multiple choice questions

- 5.1** The most common cause of nausea and vomiting is:
- Excess alcohol consumption
 - Gastritis
 - Gastroenteritis
 - Medicine induced
 - Migraine
- 5.2** Unilateral, throbbing headache in a women is most suggestive of:
- Migraine
 - Sinusitis
 - Space occupying lesion
 - Temporal arteritis
 - Tension-type headache
- 5.3** Cluster headache could be best described as:
- Bilateral orbital piercing pain only
 - Bilateral piercing pain that lasts for a matter of only minutes
 - Bilateral orbital piercing pain with associated nasal congestion
 - Unilateral piercing pain that lasts for a matter of only minutes
 - Unilateral orbital piercing pain with associated unilateral nasal congestion
- 5.4** Nausea and vomiting is associated with:
- Cluster headache
 - Sinusitis
 - Subarachnoid haemorrhage
 - Tension headache
 - Trigeminal neuralgia
- 5.5** What herbal remedy is used to help treat insomnia?
- Burdock
 - Golden Rod
 - Mugwort
 - Passion Flower
 - Tolu Balsam
- 5.6** Which trigger sign or symptom warrants referral?
- Headache associated with fever
 - Headache associated with the workplace environment
 - Headache described as vice-like
 - Headache in children under 12 with no sign of infection
 - Headache lasting 7 to 10 days
- 5.7** The amount of sleep needed with increasing age:
- Decreases
 - Increases
 - Stays the same
- 5.8** Which of these statements is true when giving advice on sleep hygiene?
- Drinking coffee and tea is OK before bedtime
 - Sleep in a warm room
 - Take light exercise before going to bed
 - Try not to nap through the day
 - Try to vary the time when you go to bed
- Questions 5.9 to 5.11 concern the following anatomical locations of the head:**
- Generalized
 - Occipital
 - Orbital
 - Temporal
 - Frontal
- Select, from A to E, which of the above locations:
- 5.9** Is associated with cluster headache?
- 5.10** Is associated with subarachnoid haemorrhage?
- 5.11** Is associated with tension-type headache?

Questions 5.12 to 5.14 concern the following medicines:

- A. Buccastem
- B. Midrid
- C. Migraitan
- D. Migralve Yellow
- E. Migril

Select, from A to E, which of the above medicines:

- 5.12 Should be avoided by patients taking paracetamol?
 5.13 Should be avoided in patients taking MAOIs?
 5.14 Requires buccal absorption

Questions 5.15 to 5.17: for each of these questions *one or more* of the responses is (are) correct. Decide which of the responses is (are) correct. Then choose:

- A. If a, b and c are correct
- B. If a and b only are correct
- C. If b and c only are correct
- D. If a only is correct
- E. If c only is correct

Directions summarized

A	B	C	D	E
a, b and c	a and b only	b and c only	a only	c only

5.15 Tension-type headache can be described as:

- a. Dull ache, not normally throbbing
- b. Worsens as day progresses
- c. Unilateral

5.16 Symptoms of the aura associated with migraine include:

- a. Scotomas
- b. Flashing lights
- c. Pins and needles

5.17 Which statements relating to headache are true:

- a. Common migraine is more common in women than men
- b. Cluster headache is more common in women than men
- c. Temporal arteritis affects mainly middle-aged men

Questions 5.18 to 5.20: these questions consist of a statement in the left-hand column followed by a statement in the right-hand column. You need to:

- Decide whether the first statement is true or false
- Decide whether the second statement is true or false

Then choose:

- A. If both statements are true and the second statement is a correct explanation of the first statement
- B. If both statements are true but the second statement is NOT a correct explanation of the first statement
- C. If the first statement is true but the second statement is false
- D. If the first statement is false but the second statement is true
- E. If both statements are false

Directions summarized

	1st statement	2nd statement	
A	True	True	2nd explanation is a correct explanation of the 1st
B	True	True	2nd statement is not a correct explanation of the 1st
C	True	False	
D	False	True	
E	False	False	
	First statement	Second statement	
5.18	Migraine without aura is more common in women than men	Trigger factors may precipitate attacks	
5.19	Insomnia can be caused by depression	Patients should be advised to try St John's Wort	
5.20	Headache in VDU operators is common	Throbbing headache is caused by flickering of VDU screens	

Answers

5.1 Answer: c

Rationale: All options can cause nausea and vomiting; gastritis (b) from the list is least likely; migraine (e) usually causes nausea but not necessarily vomiting. Medicines (d) can cause this but is specific to certain classes, and this question is very generic. Options a and c do tend to cause nausea and vomiting if experienced, but gastroenteritis is more prevalent.

5.2 Answer: a

Rationale: Space occupying lesions (c) and tension-type headache (e) are not restricted to being unilateral in location. Sinusitis (b) pain tends to be dull. Temporal arteritis (d) has severe headache rather than throbbing.

5.3 Answer: e

Rationale: Cluster headache is unilateral thus options a to c can be discounted. Associated nasal congestion is common with cluster headache, so d can be excluded.

5.4 Answer: c

Rationale: Options b, d and e are not associated with nausea and vomiting. Symptoms of cluster headache are generalized and severity of pain could produce nausea and vomiting but this is not common.

5.5 Answer: d

Rationale: Burdock (a) has been used for GI disorders; Golden rod (b) for musculoskeletal problems; Mugwort (c) for GI disorders too; Tolu Balsam is advocated for cough and skin problems.

5.6 Answer: d

Rationale: Headache and fever (a) are often seen in infection; headaches in the work environment (b) are common and often associated with computer use and may require the patient to have a sight test; vice-like headaches (c) are associated with tension-type headaches; and headaches often last more than a week depending on the cause, although it would be something that might start to be of concern. Headache in young children with no identifiable cause (d) would be unusual and requires further evaluation.

5.7 Answer: a

Rationale: It is well known that sleep requirements decrease with increasing age.

5.8 Answer: d

Rationale: Increasing caffeine intake (a) will stimulate and hinder sleep; likewise exercise (c) will promote production of endorphins and hinder sleep; varying sleep times (e) is not advocated as getting in to a regular routine will help with sleep patterns; an overly warm room (b) will also hinder sleep.

5.9 Answer: c

Rationale: Cluster headache is associated with the front of the head, meaning C to E are most likely. However, cluster headache has piercing orbital pain.

5.10 Answer: b

Rationale: Sub-arachnoid haemorrhage is experienced at the back of the head and therefore is occipital in nature.

5.11 Answer: a

Rationale: Tension-type headache does not show an obvious pattern of location and is classed as generalized.

5.12 Answer: d

Rationale: Only one of the options listed is a combination product, Migralve Yellow (D) which contains paracetamol and codeine.

5.13 Answer: B

Rationale: Any medicine that has ephedrine-like qualities has the ability to have a serious interaction with MAOIs. MAOIs increase the amount of noradrenaline stored in the noradrenergic nerve terminals and so medicines like ephedrine that release stored noradrenaline will have serious detrimental effects; in this case this is isometheptene found in Midrid.

5.14 Answer: A

Rationale: Only Buccastem is not a standard oral dose form and formulated for buccal absorption to negate the risk of expulsion through vomiting.

5.15 Answer: B (a and b)

Rationale: Tension-like headache tends to be diffuse and bilateral.

5.16 Answer: A (a, b and c)

Rationale: All three options are associated with aura, as they can be visual or neurological.

5.17 Answer: D (a only)

Rationale: An understanding of epidemiology and prevalence within populations is useful as it can indicate what the condition is. Cluster headache is much more common in men and temporal arteritis is more associated with elderly women.

5.18 Answer: B (True/True: statement 2 not correct explanation of statement 1)

Rationale: Triggers can be identified that precipitate migraine but does not account for why they are more common in women.

5.19 Answer: C (True/False)

Rationale: Underlying conditions can cause insomnia especially if the insomnia is classed as chronic as most short-term causes are due to external environmental stimuli. St John's Wort is advocated for depression but should not be routinely used as other medicines with greater evidence exist.

5.20 Answer: C (True/False)

Rationale: Prolonged use of monitors can cause headache but the nature of the headache is more tension-type in symptom presentation.

Case studies

CASE STUDY 5.1

Mr AM, a male in his early 30s, presents in the pharmacy at lunchtime complaining of headaches. The following questions are asked, and responses are received.

Below summarizes the expected findings for questions when related to the different conditions that can be seen by community pharmacists.

Information gathering	Data generated
<i>Presenting complaint</i>	
What symptoms? Describe the symptoms.	General aching feeling all over the head
How long has he or she had the symptoms?	Had headaches for the last week
Other symptoms	No problems with lights, other issues; no sickness; no recent trauma
Where exactly	As above
Any time worse or better?	Seems to get worse as day goes on
Severity of pain (1–10)	4
Frequency of pain	Most of the time
Eye test, recent trauma	Eyes OK, no need for glasses
Drugs (OTC, prescription medicine)	None
Previous history of presenting complaint	None
Past medical history	None
Social history – may include questions relating to smoking, alcohol intake, employment, personal relationships	Nonsmoker, drinks red wine (a couple of glasses each night); works in marketing; married with two young children; job OK, but busy with new promotion
Family history	Not known

CASE STUDY 5.1 (Continued)

Type of headache	Duration	Timing & nature	Location	Severity (pain score, 0–10)	Precipitating factors	Who is affected?
Tension-type headache	Can last days	Symptoms worsen as day progresses; nonthrobbing pain	Bilateral; most often at back of the head	2–5	Stress due to changes in work or home environment	All age groups; both genders equally affected
Migraine	Average attack lasts 24 hours	Associated with menstrual cycle and weekends; throbbing pain and nausea. Dislike of bright lights and loud noise	Usually unilateral	4–7	Food (in 10% of sufferers) & family history	Three times more common in women; rare in children.
Cluster headache	1–3 hours	Attacks occur at same time of day; intense boring pain	Unilateral	>7	Alcohol	Three to five times more common in men
Sinusitis	Days	Dull ache that starts off being unilateral	Frontal	2–6	Valsalva movements	Adults
Eye strain	Days	Aching	Frontal	2–5	Close vision work	All ages
Temporal arteritis	Hours to days	Variable	Unilateral around temples	3–6	None	Older adults
Trigeminal neuralgia	Minutes	Lancing pain at any time	Face	>7	None	Adults
Depression	Days to months	Nonthrobbing pain	Generalized	2–5	Social factors	Adults
Glaucoma	Hours	Often in the evening and of sudden onset	Unilateral and orbital	>7	Darkness	Older adults
Meningitis	Hours to days	Associated with systemic infection	Generalized	>7	None	Children
Subarachnoid haemorrhage	Minutes to hours	Variable	Occipital	>7	None	Adults
Raised intracranial pressure	Days to months	Worse in the mornings	Variable	>4/5	None	Older adults

CASE STUDY 5.1 (Continued)

When this information is applied to that gained from our patient, and linking this with known epidemiology on

headache (see Table 5.1), it should be possible to make a differential diagnosis.

Type of headache	Duration	Timing and nature	Location	Severity (pain score from 0 to 10)	Precipitating factors	Who is affected?
Tension	✓	✓	✓	✓	✓	✓
Migraine	✗	✗	✗	✓	✗	✓?
Cluster	✗	✗	✗	✗	?	✓
Sinusitis	✓	✓?	✗	✓	✗	✓
Eye strain	✓	✓	✗	✓	✗	✓
Temporal arteritis	✓	✓?	✗	✓	N/A	✗
Trigeminal neuralgia	✗	✗	✗	✗	N/A	✓
Depression	✓	✓?	✓	✓	✓?	✓
Glaucoma	✗	✗	✗	✗	✗	✗
Meningitis	✗	✗	✓	✗	N/A	✗
Subarachnoid haemorrhage	✗	✗	✗	✗	N/A	✓
Raised intracranial pressure	✓	✗	✓	✓	N/A	✗

We see that his symptoms most closely match tension-type headache, which may (or may not) be triggered by extra pressure at work (✓ represents symptom match). Given that epidemiology states that this is the most common cause of headache, this strongly points to this being the diagnosis.

To 'safety net': it is worth making sure that the person has none of the referral signs or symptoms. (See Trigger points for referral.)

Case studies

CASE STUDY 5.1

Mr RC, a 33-year-old man, asks you for Solpadeine tablets for his headache. After talking with him, you find out the following:

- The headache is located in the frontal area and is unilateral (left side).
- He describes the pain as throbbing.
- He feels very sensitive to light.
- He has had these headaches since he was an adolescent and it occurs two or three times in a 6-month period.
- Solpadeine eases the pain.
- He feels a little sick.
- He takes no other medications.
- He has a computer-based job with periods of stress.

- a. Using epidemiological information on headache alongside his signs and symptoms, what is the likely differential diagnosis?

Epidemiology: Most common headaches seen by community pharmacists will be tension-type headache, migraine, sinusitis (or headache associated with an upper respiratory tract infection [URTI]) and eye strain.

Patient symptoms: All point to migraine: unilateral, throbbing, light sensitive, previous personal history.

He has no symptoms suggestive of infection, and although he has a computer-based job that can cause eye strain, the pattern of symptoms does not fit. Migraine is therefore most probable and supported by stress experienced at work because migraine can be triggered by stress.

- b. What extra questions could you still ask to help confirm your differential diagnosis?

- *Family history: Migraine can show a family history, although it is not obvious in this case*
- *Any symptoms before the headache? Sometimes patients suffer from an 'aura' that comes on before the migraine symptoms; however, the most common type of migraine is not associated with any aura.*

- c. Is the request for Solpadeine to treat his symptoms appropriate?

A combination product of paracetamol and codeine may relieve headache symptoms, although doses of codeine of 30 mg or higher are generally needed to provide any additional analgesic effect above that from simple analgesics alone. Given that Mr RC experiences nausea, it may be appropriate to try simple analgesia plus prochlorperazine. However, because he has recurrent episodes, the use of a triptan for acute and long-term management may offer a longer term solution.

CASE STUDY 5.2

Mrs PC, a 36-year-old woman, asks you for something to treat her headache.

On questioning, you find out the following:

- The pain is located mainly behind the left eye and at the front and back of the head.
- Mrs PC is experiencing aching, but no sickness or visual disturbances.
- She has had the headache for about 5 days.
- There is no recent history of head trauma.
- The pain worsens as the day progresses.
- She has not had this type of headache before.
- Her work at the moment is busy because of a conference she is organizing.
- She has tried paracetamol, which helps for a while but the pain comes back after a few hours.
- She takes nothing from her GP, except the minipill.

a. Using the tabulated information on symptom presentation about conditions causing headache from [Case Study 5.1](#), what is the likely differential diagnosis?

Tension-type headache, probably as a result of additional stress at work while organizing the conference.

b. From the above responses, why did you come to this conclusion?

- *Age (36): Most likely causes are tension-type and migraine headaches based solely on age.*
- *Gender (female): Women experience more migraines than men and less cluster headache; therefore, migraine is a possibility.*
- *Duration (5 days): Most migraines do not last longer than 72 hours. Cluster headache duration is even less.*
- *Location (behind eye and back of the head): The pain seems fairly generalized, which is indicative of tension-type headache.*

- *Nature of pain (ache): Again, tension-type headaches are often described as nonthrobbing. Pain does not appear to be severe, which means that a sinister pathology is less likely.*

- *Associated symptoms (none): No nausea or vomiting. This tends to exclude migraine and conditions causing raised intracranial pressure.*

- *Medication (paracetamol): This appears to work but does not really help in establishing the cause of the headache.*

- *New headache (yes): The patient has not suffered from this type of headache before, a fact that might be suggestive of a more serious cause of headache. Further questioning is needed to make a judgement on whether referral would be appropriate.*

- *Lifestyle (work is busy): Stress is a contributing factor of tension-type headache. It appears that the patient is suffering from more stress than normal, which could be a cause of the headache.*

- *Medication from GP (minipill): This is unlikely to cause the headache, but further questions should be asked about how long she has been taking the medication. Most adverse drug reactions (ADRs) normally coincide with new medication or an alteration to the dosage regimen.*

- *Recent trauma (none): This tends to exclude headache caused by space-occupying lesions. It is worth remembering that symptoms manifest themselves once pressure is exerted on adjacent structures to a haematoma, tumour or abscess. It might therefore take longer than several weeks for the patient to notice symptoms. As a result, always ask about any trauma experienced over the last 6 to 12 weeks.*

- *Periodicity (worse as day goes on): This is suggestive of tension-type headache. It therefore appears that most questions point to tension-type headache as the most likely cause of headache.*

CASE STUDY 5.2

Ms JB, a 23-year-old woman, asks for St John's wort to help her relax so she can get to sleep at night.

a. What questions would you ask?

- *What is the problem you have with sleeping (e.g., getting to sleep, staying asleep, waking early)?*
- *How do you feel the next day?*
- *When do you usually go to sleep?*
- *When do you get up in the morning?*
- *Have any of your daily habits changed (e.g., exercise routine, consumption of alcohol or caffeine products)?*
- *Has anything changed about your bedroom (e.g. different mattress, heating, cooling)?*

Questions relating to her social, medical and family history:

- *Do you have any medical conditions?*
- *Do you take any medications?*
- *Has there been any major change in your life recently (i.e., any stressful event)?*

Ms JB tells you that she has had problems sleeping and was recently diagnosed with anxiety and depression. She has been under some financial stress lately and finds that it takes her a long time to fall asleep. She normally goes to bed about 10 PM but can't get to sleep until 2 or 3 in the morning and has to get up by 5 AM for work. To stay alert, she has started drinking six to eight cups of coffee a day. She has seen her physician about her depression and has just started taking escitalopram, 20 mg daily. She took her first dose 2 days ago.

b. What do you think is causing JB's inability to fall asleep?

JB appears to be suffering from insomnia due to depression and/or anxiety related to financial stress. She is also consuming large amounts of caffeine, which is likely to be contributing to her inability to fall asleep.

c. What would you recommend for Ms JB?

Ms JB should reduce the amount of coffee and any other sources of caffeine she might be drinking throughout the day. She should be having no more than four cups of coffee a day, and her last coffee should be no later than 6 hours before she intends to go to bed. If she is going to reduce her caffeine intake, she needs to do it gradually to avoid any issues such as rebound headaches.

Selective serotonin reuptake inhibitors (SSRIs) such as escitalopram can take from 1 to 2 weeks to start having a noticeable effect and up to 6 weeks for maximum benefit. Ms JB should be advised that she may not see the effects immediately and that it is normal to experience good and bad days, but an overall improvement in her mood will be likely. If she sees no improvement in 6 weeks, she should consult with her doctor again.

Ms JB needs to be careful when considering any complementary medications and should always check with her doctor or pharmacist beforehand. There is a known interaction between St John's Wort with SSRIs such as escitalopram (known as serotonin syndrome), and the combination should be avoided.

CASE STUDY 5.3

Mr FD, a 67-year-old man, asks you for a strong painkiller for his headache. He has had the headache for a few days, but it does not seem to be going away. After talking with the man, you find out the following:

- *The headache is located in the frontal area and is unilateral.*
- *He describes the pain as throbbing.*
- *He has never had a headache like this before.*
- *He has not suffered from migraines in the past.*
- *There are no symptoms of nausea or vomiting.*
- *There are no associated symptoms of upper respiratory tract infection.*
- *He is retired and has a nonstressful lifestyle.*
- *He has tried paracetamol but without much success.*
- *He takes atenolol for hypertension.*

- a. Using the tabulated information on symptom presentation about conditions causing headache from [Case Study 5.1](#), what is the likely differential diagnosis?

It appears that tension-type headache and migraine can be ruled out based on location and lack of nausea. Cluster headache is a possibility, but the type of pain and location is not right. This suggests that the headache might be a secondary type of headache, requiring referral. Sinusitis is a secondary cause of headache, but the patient shows no recent symptoms of an upper respiratory tract infection (URTI). From the remaining secondary causes of headache, the symptoms may suggest temporal arteritis.

- b. What extra questions could you have asked to support this conclusion?

Enquire about tenderness in the temple region or if the scalp was tender to touch.

CASE STUDY 5.4

The wife of a 54-year-old man enters the pharmacy and asks for sumatriptan; she has seen it advertised in the paper and her husband seems to have all the symptoms.

Information gathering	Data generated
<i>Presenting complaint</i>	
Describe symptoms	Very painful headache; worst towards the back of the head; feels nauseous and vomited twice, but vomiting seems to have subsided
How long has he had the symptoms?	12 hours
Severity of pain	Very painful (7–8 out of 10)
Nature of the pain	Just said it is very painful
Other symptoms, provoking factors	Cannot do anything; painful even to do normal tasks, such as showering, dressing
Eye test, recent trauma	Not had eye test for a year, but eyes OK; no recent trauma
Any symptoms before headache?	No
Previous history of presenting complaint	None
On examination	His wife states that he generally looks tired, and pain is aggravated by light.

Information gathering	Data generated
Drugs (OTC, prescriptions)	Simvastatin, 40 mg, 1 on Ezetrol, 10 mg, 1 od Uses antihistamines OTC during spring and summer
Past medical history	Hypercholesterolaemia
Social history, which may include questions relating to smoking, alcohol intake, employment, personal relationships	Executive for a marketing firm—busy job
Family history	None for presenting complaint

- a. Considering the information the woman has given you, is her husband a suitable candidate for sumatriptan?

Sumatriptan is not indicated in this case because it is the first presentation of symptoms and he has heart disease.

- b. If the patient was suitable for sumatriptan, given his symptoms, would you sell them to his wife?

No. The symptoms are not fully consistent with migraine. The severity, location, and lack of previous history suggest that it may not be migraine, and other more sinister pathologies need to be excluded.

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Women's health

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Background

Women have unique health care needs. Many of these conditions are outside the remit of the community pharmacist, and specialist care is needed, but a small number of conditions can be adequately treated with over-the-counter (OTC) remedies. This chapter explores these conditions and attempts to outline when referral should be made.

General overview of the female reproductive and urological anatomy

The female reproductive anatomy is comprised of internal and external genital organs. The external genital organs include the mons pubis, labia majora and minora, Bartholin glands, and clitoris. Their role is to allow sperm to enter the vagina, protect the internal genital organs, and provide sexual pleasure. The internal genital organs are comprised of the vagina, uterus, fallopian tubes and ovaries. The vagina is approximately 4 to 5 cm long and is a muscular tubelike organ. It is lined by a mucous membrane and is kept moist by fluids produced by the lining and the cervix, which is found at the opening of the uterus. The main function of the uterus is to sustain a developing foetus. It is a muscular, pear-shaped organ, lined with two layers of cells called the *endometrium*. The outer layer of the endometrium, called the *functional layer*, changes in response to oestrogen and progesterone as part of the menstrual cycle. Oestrogen secretion in the follicular phase (first half) of the menstrual cycle causes the

endometrium to proliferate and thicken. The increase in progesterone during the luteal phase (second half) causes the endometrium to move into a secretory phase, which is designed to make the endometrium more receptive to implanting an embryo. If fertilization and implantation of the embryo do not occur, the lining of the endometrium is shed during menses. Ovulation, when the release of an oocyte ready for potential fertilization takes place, involves the ovaries and fallopian tubes. The oocyte is released from the graafian follicles in the ovary after a surge in levels of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) secreted from the pituitary. The released oocyte travels down the fallopian tubes towards the uterus, where, if fertilized, it will implant.

The female urological anatomy is the same as in men in that it is comprised of the kidneys, ureters, a bladder and a urethra. However, the proximity of these to the female reproductive organs means that a woman often suffers more urological problems, particularly caused by pressure during pregnancy and damage during childbirth. In addition, the female urethra is much shorter (~5 cm) compared with males (~20 cm). This makes it much easier for bacteria to travel to the bladder, leading to cystitis.

History taking

It is essential to take an accurate history from the patient; however, the patient might feel uncomfortable or embarrassed about discussing such symptoms, especially in a busy pharmacy. It is important that the patient is made to feel at ease, and using a consultation room can help provide adequate privacy.

Cystitis

Background

Cystitis literally means inflammation of the bladder, although, in practice, cystitis refers to inflammation of the urethra and bladder. In men, cystitis is uncommon because of the longer urethra, which provides a greater barrier to bacteria entering the bladder, and fluid from the prostate gland also confers some antibacterial property.

Prevalence and epidemiology

Urinary tract infections (UTIs) are one of most common infections treated in general medical practice and will affect up to 15% of women each year. Patients aged between 15 and 34 years account for most cases seen within a primary care setting; it is estimated that up to 50% of all women will experience at least one episode of cystitis in their lifetime, half of whom will have further attacks. Certain factors increase the risk of a UTI. For example, in young women, frequent or recent sexual activity, previous episodes of cystitis, the use of diaphragms or spermicidal agents, advancing age (e.g., postmenopausal), pregnancy, and diabetes can be risk factors. Recurrent cystitis (usually defined as three or more episodes in the past 12 months or two episodes in the past 6 months) is relatively common, even though no identifiable risk factors are present.

Aetiology

Infection is caused, in most cases, by the patient's own bowel flora that ascend the urethra from the perineal and perianal areas. Bacteria are thus transferred to the bladder, where they proliferate. The most common bacterial organisms implicated in cystitis are *Escherichia coli* (>80% of cases),

Table 6.1
Causes of dysuria and their relative incidence in community pharmacy

Incidence	Cause
Most likely	Acute uncomplicated cystitis
Likely	Pyelonephritis
Unlikely	Sexually transmitted disease, oestrogen deficiency
Very unlikely	Medicine-induced cystitis, vaginitis

Staphylococcus (up to 10% of cases), and *Proteus*. However, several studies have shown that up to 50% of women do not have positive urine cultures according to traditional criteria (>10⁵ bacteria/mL of urine), although they do have signs and symptoms of infection. These patients with *low-count bacteriuria* are classed as having a urinary tract infection.

Arriving at a differential diagnosis

Most patients who present in the community pharmacy will have acute uncomplicated cystitis (Table 6.1) and will have made a self-diagnosis. Therefore, the aims of the pharmacist are to confirm a patient's self-diagnosis, rule out upper urinary tract infection (pyelonephritis), and identify patients who are at risk of complications as a result of cystitis. Asking symptom-specific questions will help the pharmacist establish a differential diagnosis (Table 6.2).

Clinical features of acute uncomplicated cystitis

Cystitis is characterized by pain when passing urine and is associated with frequency, urgency, nocturia, and changes to urine's appearance. The diagnostic probability of cystitis is over



Table 6.2
Specific questions to ask the patient: Cystitis

Question	Relevance
Duration	Symptoms that have lasted longer than 5–7 days should be referred because of the risk that the woman might develop pyelonephritis.
Age of the patient	Cystitis is unusual in children and should be viewed with caution. This might be a sign of a structural urinary tract abnormality. Referral is needed. Older female patients (>70 years) have a higher rate of complications associated with cystitis and are therefore best referred.
Presence of fever	Referral is needed if the woman presents with fever associated with dysuria, frequency and urgency because fever is a sensitive indicator of an upper urinary tract infection.
Vaginal discharge	If a patient reports vaginal discharge, the likely diagnosis is not cystitis but a vaginal infection.
Location of pain	Pain experienced in the loin area suggests an upper urinary tract infection.

90% of patients exhibit dysuria and frequency without vaginal discharge or irritation. In addition, the patient might report only passing small amounts of urine, with pain worsening at the end of voiding urine. Symptoms usually start suddenly. Suprapubic discomfort not associated with passing urine might also be present but is not common. Haematuria, although common, should be viewed with caution because it might indicate stones or a tumour. Such cases are best referred.

Conditions to eliminate

Likely condition

Pyelonephritis

The most frequent complication of cystitis is when the invading pathogen involves the ureter or kidney by ascending from the bladder to these higher anatomical structures. The triad of flank pain, fever, and nausea and vomiting are typically associated with pyelonephritis. Onset is typically sudden. Pain relief can be offered, but a medical referral is needed to confirm the diagnosis, exclude pelvic inflammatory disease, and initiate appropriate treatment (7- to 10-day course of antibiotics).

Unlikely causes

Sexually transmitted diseases

Sexually transmitted diseases (STDs) can be caused by a number of pathogens; for example, *Chlamydia trachomatis* (most common but generally asymptomatic) and *Neisseria gonorrhoea*.

Symptoms are similar to those of acute uncomplicated cystitis in that pain and dysuria are experienced, but symptoms tend to be more gradual in onset and last for a longer period of time. In addition, up to 50% of people experience increased or altered vaginal discharge, and pyuria (pus in the urine) is usually present. Although STDs are an unlikely cause in older adults, they should be considered more likely in young adults (18–25 years) in whom the prevalence of conditions such as gonorrhoea and chlamydia has been increasing.

Oestrogen deficiency (atrophic vaginitis)

Postmenopausal women experience thinning of the endometrial lining as a result of a reduction in the levels of circulating oestrogen in the blood. This increases the likelihood of irritation or trauma, leading to cystitis-like symptoms. If the symptoms are caused by intercourse, symptomatic relief can be gained with a lubricating product. Referral for possible topical oestrogen therapy would be appropriate if the symptoms recur.

Very unlikely causes

Medicine-induced cystitis

Nonsteroidal antiinflammatory drugs (NSAIDs, especially tiaprofenic acid), allopurinol, danazol and cyclophosphamide have been shown to cause cystitis.

Vaginitis

Vaginitis exhibits similar symptoms to cystitis in that dysuria, nocturia and frequency are common. Bleeding or spotting may also be present. It can be caused by direct irritation (e.g., use of vaginal sprays and toiletries). All patients should be questioned about an associated vaginal discharge. The presence of vaginal discharge is highly suggestive of vaginitis.

Fig. 6.1 will aid in the differentiation of cystitis from other conditions.



TRIGGER POINTS indicative of referral: Cystitis

Symptoms/signs	Possible danger/reason for referral	Urgency of referral
Children <16 years	Cystitis unusual in this age group	As soon as practicable
Patients with diabetes	More likely to develop complications from a UTI	
Duration >7 days	Does not suggest an uncomplicated UTI	
Vaginal discharge	May indicate vaginitis	
Women >70 years	More susceptible to complicated UTIs and pyelonephritis; also, symptoms may be indicative of atrophic vaginitis	
Pregnancy	Pressure on the urinary tract caused by an infant makes management of UTIs more difficult and can increase the risk of pyelonephritis	
Haematuria	Blood may indicate a stone or a tumour	Immediate to GP
Immuno compromised	More likely to develop complications from a UTI	
Patients with associated fever and flank pain	Suggestive of a complicated UTI and/or pyelonephritis	

UTI, Urinary tract infection.

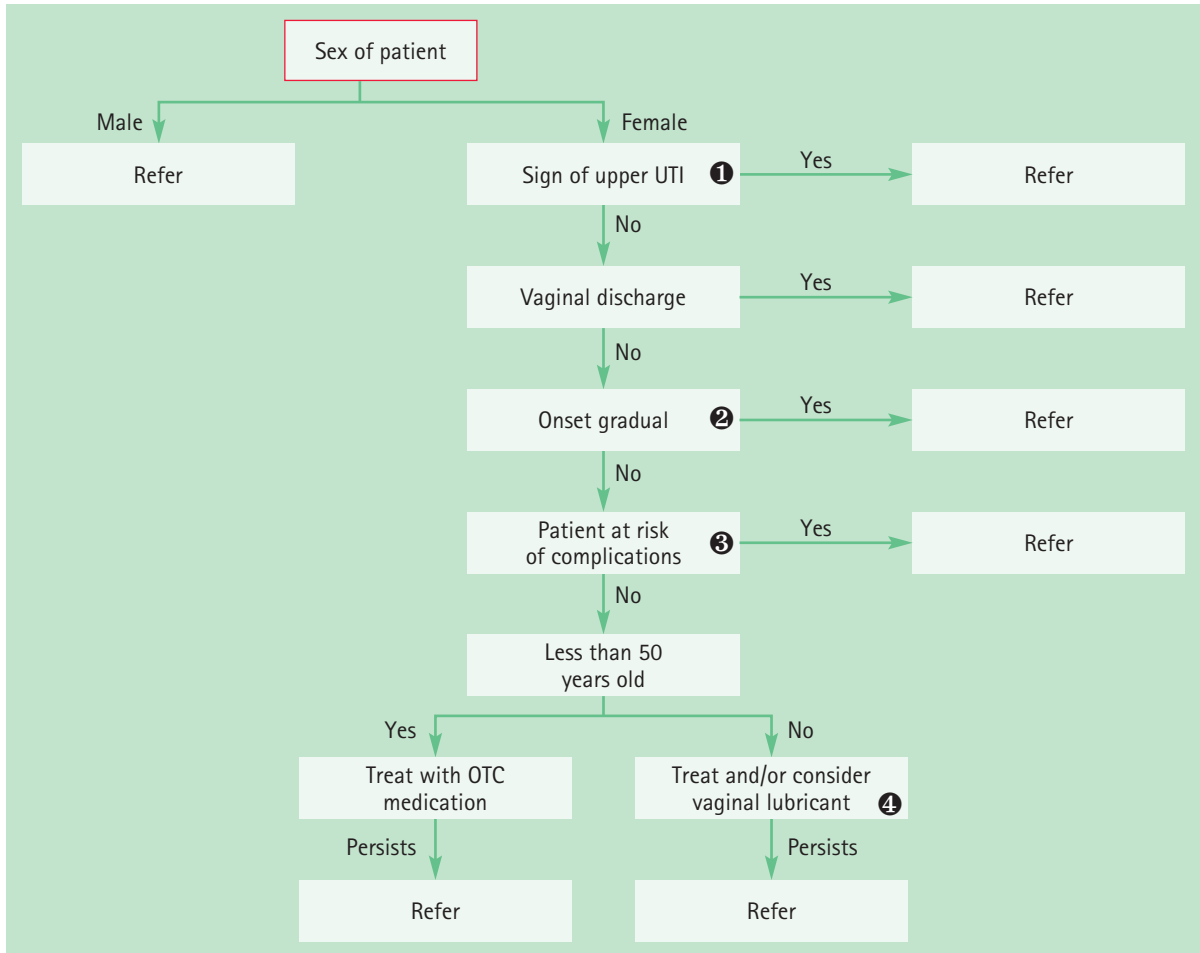


Fig. 6.1 Primer for the differential diagnosis of cystitis.

1 Involvement of the higher urinary tract structures.

Symptoms such as fever, flank pain, nausea and vomiting suggest conditions such as pyelonephritis.

2 Gradual onset. Sexually transmitted disease (STDs) should be considered in patients whose symptoms are not sudden.

3 At-risk patients. Patients at risk of developing an upper urinary tract infection (UTI) include those with diabetes,

pregnant women, the immunocompromised, older adults and those patients in whom symptoms have been present for more than 5 to 7 days.

4 Patients older than 50 years. Oestrogen deficiency might account for the patient's symptoms, resulting in local atrophy of the vagina. *OTC*, Over-the-counter.

Evidence base for over-the-counter medication

Alkalinizing agents

Current OTC treatment is limited to products that contain *alkalinizing* agents, such as sodium citrate, sodium bicarbonate,

and potassium citrate. (Previous applications to reclassify trimethoprim and nitrofurantoin in the UK have been made but were withdrawn. Trimethoprim is, however, available OTC in some countries such as New Zealand.) *Alkalinizing* agents are used to return the urine pH back to normal, thus

theoretically relieving symptoms of dysuria. However, they have little trial data to support their use. Only one trial by Spooner (1984) could be found to support their efficacy. Spooner concluded that when treated with a 2-day course of sodium citrate (Cymalon), 80% of patients with cystitis for whom there was no clear clinical evidence of bacterial infection did obtain symptomatic relief.

Cranberry juice and extract

Cranberry is a popular alternative remedy to treat and prevent urinary tract infections, although few clinical trials have been performed to substantiate or refute its clinical effectiveness. A Cochrane review (Jepson et al., 2012) identified 24 studies comparing cranberry juice or cranberry tablets to alternatives (e.g., placebo, hexamine hippurate, antibiotics, *Lactobacillus*) to prevent UTIs. The review found that cranberry products did not significantly reduce the incidence of UTIs compared with placebo, water, or no treatment. They noted high dropout rates in the trials, suggesting that many patients may not be able to tolerate cranberry juice long term. The authors concluded that cranberry juice did not offer protection against recurrence of UTIs and may be unacceptable to consume over the long term. A later systematic review examining the effect of cranberry in patients with a history of UTIs, but who were otherwise healthy, found seven studies that met their inclusion criteria (Fu et al., 2017). The results suggested that cranberry reduced the risk of UTIs by 26% relative to placebo or control (relative risk [RR] = 0.74; 95% confidence index [CI], 0.55–0.98). However, the authors noted that most studies were small, and two studies had a high loss to follow-up. They recommended that larger high-quality studies are needed to confirm these findings.

The authors of the 2012 Cochrane review also reviewed the use of cranberry juice in the treatment of existing UTIs (Jepson et al., 1998, updated in 2010). However, they were unable to find any randomized controlled trials (RCTs) that met their criteria. The authors concluded that there was no good evidence yet to support the use of cranberry juice for the treatment of UTIs.

Studies involving cranberry juice were not associated with any serious adverse events, but widespread use of cranberry juice has resulted in the identification of a possible interaction with warfarin, although evidence is currently conflicting (Jepson et al., 2012). Until evidence is conclusive, it would seem prudent that patients on warfarin be advised not to take products containing cranberry.

Practical prescribing and product selection

Prescribing information relating to cystitis medicines is discussed and summarized in [Table 6.3](#), and useful tips relating to patients presenting with cystitis are given in [Box 6.1](#).

Alkalinizing agents

All marketed products are presented as a 2-day treatment course and taken three times a day, although potassium citrate can be bought as a ready-made solution (the dosage is 10 mL three times a day, diluted well with water). They have very few side effects and can be given safely with other prescribed medication, although, in theory, products containing potassium should be avoided in patients taking angiotensin-converting enzyme (ACE) inhibitors, potassium-sparing diuretics and spironolactone. However, in practice, it is highly unlikely that a 2-day course of an *alkalinizing* agent will be of any clinical consequence. They can also be prescribed to most patient



Table 6.3
Practical prescribing: Summary of medicines for cystitis

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
Potassium citrate	Not recommended	None	None	Patients taking ACE inhibitors, potassium-sparing diuretics, spironolactone	OK
Sodium citrate (Cymalon, CanesOasis, Cystitis Relief, Care Cystitis Relief)	Not recommended	None	None	Patients with heart disease, hypertension, or renal impairment	OK

ACE, Angiotensin-converting enzyme.

HINTS AND TIPS BOX 6.1: CYSTITIS

Fluid intake	Patients should be advised to drink about 5 L of fluid during every 24-hour period. This will help promote bladder voiding, which is thought to help flush bacteria out of the bladder.
Product taste	The taste of potassium citrate mixture is unpleasant. Patients should be advised to dilute the mixture with water to make the taste more palatable

groups and can be given to pregnant women, although most manufacturers advise against prescribing in pregnancy, presumably because pregnant women have a higher incidence of complications resulting from cystitis.

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Website

Cystitis and overactive bladder foundation: <http://www.cobfoundation.org>

Table 6.4
Causes of vaginal discharge and their relative incidence in community pharmacy

Incidence	Cause
Most likely	Bacterial vaginosis
Likely	Thrush
Unlikely	Trichomoniasis, atrophic vaginitis, cystitis, chlamydia

Prevalence and epidemiology

It has been reported that sexually active women have a 75% chance of experiencing at least one episode of thrush during their childbearing years, and half of these will have more than one episode. Most cases are acute attacks, but some women can develop recurrent thrush, defined as four or more attacks each year. The condition is uncommon in prepubertal girls unless they have been receiving antibiotics.

Aetiology of thrush

The vagina naturally produces a watery discharge (physiological discharge), the amount and character of which varies depending on many factors, such as ovulation, pregnancy and concurrent medication. At the time of ovulation, the discharge is greater in quantity and of higher viscosity. Normal secretions have no odour. The epithelium of the vagina contains glycogen, which is broken down by enzymes and bacteria (most notably lactobacilli) into acids. This maintains the low vaginal pH, creating an environment inhospitable to pathogens. The glycogen concentration is controlled by oestrogen production; therefore, any changes in oestrogen levels will result in increased or decreased glycogen concentrations. If oestrogen levels decrease, glycogen concentration also decreases, giving rise to an increased vaginal pH and making the vagina more susceptible to opportunistic infection, such as *Candida albicans*; 95% of thrush cases are caused by *C. albicans*. The remaining cases are caused by *Candida glabrata*, although symptoms are indistinguishable.

Vaginal discharge**Background**

Patients of any age can experience vaginal discharge. The three most common causes of vaginal discharge are bacterial vaginosis (most common), vulvovaginal candidiasis (thrush), and trichomoniasis (Table 6.4). Because thrush is the only condition that can be treated OTC (although products are on the market for bacterial vaginosis) the text concentrates on differentiating this from other conditions.



Table 6.5
Specific questions to ask the patient: Vaginal discharge

Question	Relevance
Discharge	Any discharge with a strong odour should be referred. Bacterial vaginosis and trichomoniasis are associated with a fishy odour. Discharge in bacterial vaginosis tends to be grey-white and trichomoniasis greenish-yellow. By contrast, discharge associated with thrush is often described as curdlike or cottage cheese-like, with little or no odour. Note that the physiological discharge is clear and odourless but can cause slight staining of underwear.
Age	Thrush can occur in any age group, unlike bacterial vaginosis and trichomoniasis, which are rare in premenarchal girls. In addition, trichomoniasis is also rare in women >60 years.
Pruritus	Vaginal itching tends to be most prominent in thrush compared with bacterial vaginosis and trichomoniasis, where itch is slight or absent.
Onset	In thrush, the onset of symptoms is sudden, whereas in bacterial vaginosis and trichomoniasis onset tends to be less sudden.

Arriving at a differential diagnosis

Many patients will present with a self-diagnosis, and the pharmacist's role will often be to confirm a self-diagnosis of thrush. This is very important because studies have shown that misdiagnosis by patients is common (Ferris et al., 2002) and can have important consequences because other conditions can lead to greater health concerns. For example, bacterial vaginosis has been linked with pelvic inflammatory disease (PID) and the preterm delivery of low-birth-weight infants, and *Chlamydia trachomatis* can cause infertility. Symptoms of pruritus, burning and discharge are possible in all three common causes of vaginal discharge; therefore, no one symptom can be relied on with 100% certainty to differentiate among thrush, bacterial vaginosis and trichomoniasis. However, certain symptom clusters are strongly suggestive of a particular diagnosis. Asking symptom-specific questions will help the pharmacist establish a differential diagnosis (Table 6.5).

Clinical features of thrush

The defining feature of thrush is vulval itching. Vulval soreness and irritation are also common. Discharge occurs only in about 20% of patients and, if present, has little or no odour and is described as resembling cottage cheese or is curd-like. Symptoms are generally acute in onset.

Conditions to eliminate

Bacterial vaginosis

Many patients are asymptomatic but, when symptoms occur, the condition is characterized by a thin white discharge with a strong fishy odour. Odour is worse after sexual intercourse and may worsen during menses. Itching and soreness are not

usually present. The exact cause of bacterial vaginosis is unknown but results from an overgrowth of anaerobic bacteria and reduction in lactobacilli concentration. *Gardnerella vaginalis* is often implicated.

Certain risk factors include change in sexual partner, multiple sexual partners, low social class and race (more common in African and African American women). It may remit and relapse for several months. OTC products are marketed, such as a product to differentiate between thrush and bacterial vaginosis (Canestest), and works on changes in pH levels (>4.5 can suggest bacterial vaginosis); Canesbalance is marketed for its treatment because it alters pH back to normal physiological levels. However, this should not be recommended because treatment requires antibiotics (oral metronidazole, 400 mg, twice daily for 5–7 days or local application of metronidazole or clindamycin).

Unlikely causes

Trichomoniasis

Trichomoniasis, a protozoan infection (*Trichomonas vaginalis*), is primarily transmitted through sexual intercourse. Up to 50% of patients are asymptomatic. If symptoms are experienced, approximately 30% experience a profuse, frothy, greenish-yellow and fishy-smelling discharge. Other symptoms include vulvar itching and soreness, vaginal spotting, dysuria, and lower abdominal pain. Referral for metronidazole (400 mg bd for 5–7 days) is required.

Chlamydia

Most people with chlamydial infection are asymptomatic but, when symptoms are experienced, the patient may complain of purulent or mucopurulent discharge, dysuria, urinary frequency, and intermenstrual or postcoital bleeding.

Cystitis

Dysuria can affect up to one in three women with a vaginal infection. Other symptoms such as nocturia and urgency will be more prominent in cystitis, and discharge is uncommon.

Atrophic vaginitis

Symptoms consistent with thrush in postmenopausal women, especially vaginal itching and burning, may be due to atrophic vaginitis. However, clinically significant atrophic vaginitis is uncommon in postmenopausal women and should be referred to rule out malignancy.

There are also several factors that predispose women to thrush and require consideration before initiating treatment.

Medicine-induced thrush

Corticosteroids, immunosuppressants and medications affecting the oestrogen status of the patient (e.g., oral contraceptives, hormone replacement therapy, tamoxifen, raloxifene), can predispose women to thrush. This is also true with the use of broad-spectrum antibiotics, and it is not unusual to see a patient prescribed an antibiotic and treatment for thrush at the same time.

Diabetes

Patients with poorly controlled diabetes (type 1 or 2) are more likely to suffer from thrush because hyperglycaemia can enhance production of protein surface receptors on *C. albicans* organisms. This hinders phagocytosis by neutrophils, thus making thrush more difficult to eliminate.

Pregnancy

Hormonal changes during pregnancy will alter the vaginal environment and have been reported to make eradication of *Candida* more difficult. Topical agents are safe and effective in pregnancy, but OTC-licensed indications state that patients should be treated by a doctor or midwife; therefore, these patients should be referred to the doctor.

Chemical and mechanical irritants

Ingredients in feminine hygiene products; for example, bubble baths, vaginal sprays, and douches, are said to precipitate attacks of thrush by altering the vaginal pH, although evidence for this is limited. Condoms have also been reported to irritate and alter the vaginal pH.

Recurrent thrush

After treatment, a minority of patients will present with recurrent symptoms (four or more episodes per year). This may be due to poor adherence, misdiagnosis, resistant strains of

Candida, undiagnosed diabetes, or the presence of a mixed infection. Such cases are outside the remit of community pharmacy and have been shown to be difficult to treat. Often, specialist care is needed through a genitourinary medicine clinic.

Fig. 6.2 will help in the differentiation of vaginal thrush from other conditions in which vaginal discharge is a major presenting complaint.



TRIGGER POINTS indicative of referral: Thrush

Symptoms/signs	Possible danger/ reason for referral	Urgency of referral
Discharge that has a strong smell	Thrush has no or little odour and therefore this suggests other causes, such as bacterial vaginosis or trichomoniasis	As soon as possible
Women <16 and >60 years	Thrush is unusual in these age groups	
Patients with diabetes	Might suggest poor diabetic control	As soon as practicable
OTC medication failure	Suggests underlying problem or misdiagnosis	
Patients predisposed to thrush		
Recurrent attacks		

Evidence base for over-the-counter medication

Topical imidazoles and one systemic triazole (fluconazole) are available OTC to treat vaginal thrush. They are potent and selective inhibitors of fungal enzymes necessary for the synthesis of ergosterol, which is needed to maintain the integrity of cell membranes.

Imidazoles and triazoles have proven and comparable efficacy, with clinical cure rates between 85% and 90%. Additionally, cure rates between single- or multiple-dose therapy and multiple-day therapy show no differences (Nurbhai et al., 2007). Treatment choice will, therefore, be driven by patient acceptability and cost.

Practical prescribing and product selection

Prescribing information relating to medicines for thrush is discussed in the next section and summarized in Table 6.6; useful tips relating to patients presenting with thrush are given in 'Hints and Tips' in Box 6.2.

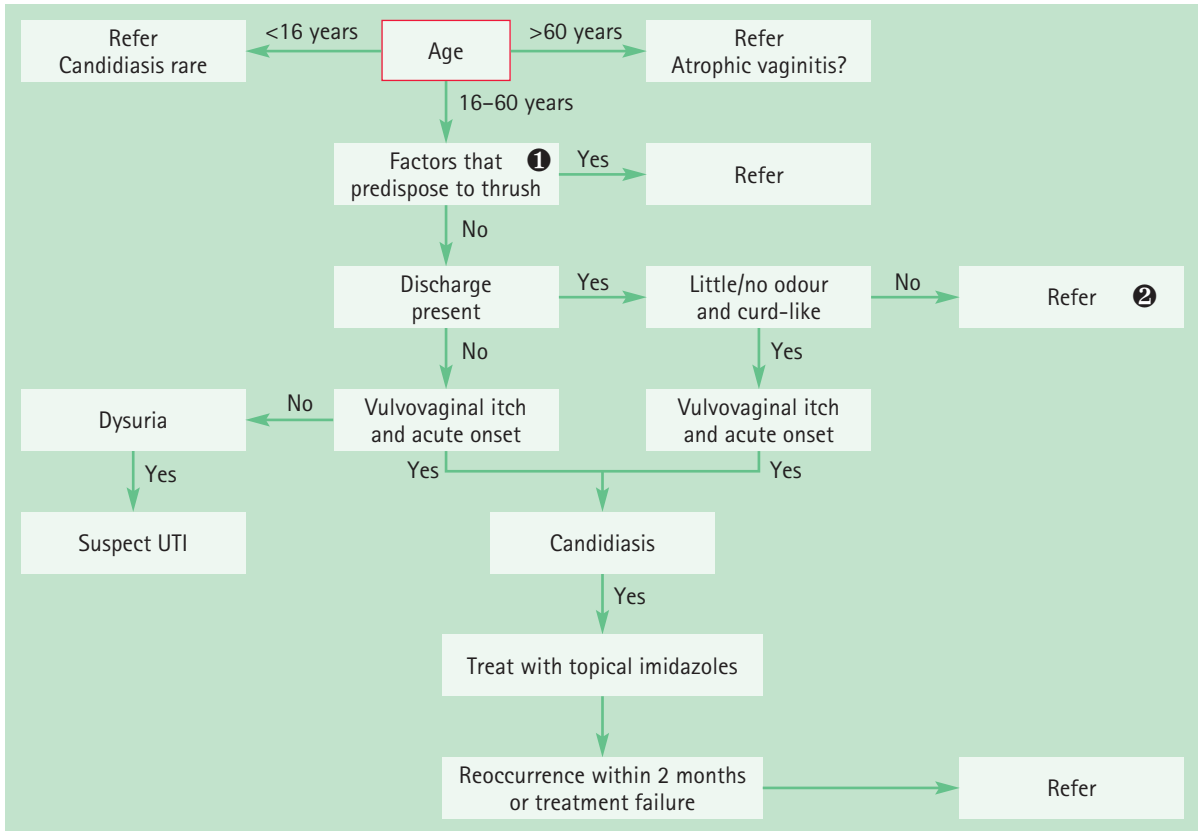


Fig. 6.2 Primer for the differential diagnosis of vaginal thrush.

❶ If the woman is pregnant or has diabetes, referral is the most appropriate option. If the person is suffering from medicine-induced candidiasis, the prescriber should be contacted to discuss suitable treatment options and, if appropriate, alternative therapy.

❷ Discharge that has a strong odour and is not white and curdlike should be referred because trichomoniasis or bacterial vaginosis are more likely causes. *OTC*, Over-the-counter; *UTI*, urinary tract infection.



Table 6.6 Practical prescribing: Summary of medicines for thrush

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
Imidazoles	Not applicable	Vaginal irritation	None	None	OK, but pregnant women should be referred; OK in breastfeeding
Fluconazole		GI disturbances, headache, rash	Anticoagulants, ciclosporin, rifampicin, phenytoin, tacrolimus		Avoid

GI, Gastrointestinal.

HINTS AND TIPS BOX 6.2: THRUSH

Applying a pessary	<p>Because the dosage is at night, patients should be advised to use the pessary when in bed.</p> <ol style="list-style-type: none"> 1. Wash your hands. 2. Pull out the plunger from the applicator. 3. Remove the pessary from the packaging and place firmly into the applicator (the end of the applicator needs to be gently squeezed to allow the pessary to fit). 4. Lying on your back, with knees drawn towards the chest, insert the applicator as deeply as is comfortable into the vagina. 5. Slowly press the plunger of the applicator until it stops. 6. Remove and dispose of the applicator. 7. Remain on your back for as long as possible.
Administration of vaginal creams	<ol style="list-style-type: none"> 1. Wash your hands. 2. Pull out the plunger from the applicator. 3. Remove the tube of cream and one applicator from the box (if the applicator is prefilled, skip to point 6). 4. Squeeze the cream from the tube until it reaches the dose level on the applicator. 5. Remove the tube from the end of the applicator. 6. Lying on your back, with knees drawn towards the chest, insert the applicator as deeply as is comfortable into the vagina. 7. Slowly press the plunger of the applicator until it stops. 8. Remove and dispose of the applicator. 9. Remain on your back for as long as possible.
Use of yoghurt	<p>Some people recommended live yoghurt as a natural treatment. This is based on sound rationale because lactobacilli in the yoghurt produce lactic acid, which inhibits the growth of <i>Candida</i>. However, to date, there is a lack of evidence to prove or disprove this theory.</p>
General advice to help prevent infection	<p>Avoid tight clothing, such as underwear, jeans. Use simple nonperfumed soaps when washing.</p>
Symptom resolution	<p>The symptoms of thrush (burning, soreness or itching of the vagina) should disappear within 3 days of treatment. If no improvement is seen after 7 days the patient should see their GP.</p>
Vaginal douching	<p>This should not be encouraged, has no evidence of efficacy, and is associated with serious complications such as pelvic inflammatory disease.</p>

Topical imidazoles (*clotrimazole, econazole, miconazole*)

A number of formulations are available for local application including creams, vaginal tablets, and pessaries. Pharmacists and the public are probably most familiar with the clotrimazole range of products. All internal preparations should be administered at night. This gives the medicine time to be absorbed and eliminates the possibility of accidental loss, which is more likely to occur if the person is mobile. Slight irritation on application is infrequently reported (~5% of users) and has been linked to the vehicle and not the active

ingredient. Systemic absorption is minimal and, therefore, there are no interactions of note, although they may damage latex condoms and diaphragms. Consequently, the effectiveness of such contraceptives may be reduced. Topical imidazoles have a number of product license restrictions, which should be observed when recommending these products, and are listed in [Table 6.7](#).

Fluconazole (e.g., Canesten thrush oral capsule)

Fluconazole is a single oral dose treatment that can be taken at any time of the day. Fluconazole is generally well tolerated

Table 6.7
Product license restrictions: Imidazoles

Product license restriction	Suspected rationale
<16 or >60 years of age	Thrush less common in these age groups
Has systemic symptoms	Suggests infection from a cause other than thrush
Has symptoms that are not entirely consistent with a previous episode (e.g., discharge is coloured or malodorous; ulcers or blisters present)	Suspect bacterial vaginosis or trichomoniasis
Has had two episodes in 6 months, and has not consulted her GP about the condition for more than 1 year	Good practice because repeat infection may be due to misdiagnosis or predisposing risk factors
May be pregnant or is breastfeeding	Safe in both pregnancy and breastfeeding, although thrush is more common during pregnancy; it is also important to rule out gestational diabetes
Has had a previous STD (or her partner has)	Rule out STD
Has had abnormal menstrual bleeding or lower abdominal pain	Symptoms not suggestive of thrush
Does not experience complete resolution of symptoms after 7 days of treatment	Imidazoles are highly effective; continuing symptoms point to a misdiagnosis

STD, Sexually transmitted disease.

but side effects of nausea, abdominal discomfort, diarrhoea, headache and rash are most commonly experienced. There are a number of established clinically important drug interactions with fluconazole, including anticoagulants, ciclosporin, rifampicin, phenytoin and tacrolimus. However, these drug interactions relate to the use of multiple-dose fluconazole, and the relevance to single-dose fluconazole has not yet been established. It would be prudent to avoid these combinations until further evidence is available with single-dose fluconazole.

Combination products

A number of marketed products are available that combine clotrimazole as pessaries and cream or cream and oral fluconazole.

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Websites

Embarrassing problems: <http://www.embarrassingproblems.com/problem/vaginal-vulva-problems>

NHS choices: Sex and young people: <https://www.nhs.uk/live-well/sexual-health/15-things-young-people-should-know-about-sex/>

Primary dysmenorrhoea (period pain)

Background

Menstruation spans the years between menarche to menopause. Typically, this will last 30 to 40 years, starting around the age of 12 and ceasing around the age of 50. The menstrual cycle usually lasts 28 days, but this can vary and last any time between 21 and 45 days. Menstruation itself lasts between 3 and 7 days. Individuals can also exhibit differences in menstrual cycle length and blood flow. Dysmenorrhoea is usually categorized as primary or secondary; primary dysmenorrhoea (PD) is defined as menstrual pain without organic pathology, whereas in secondary dysmenorrhoea an identifiable pathological condition can be identified.

Prevalence and epidemiology

PD is very common but establishing prevalence rates is difficult due to varying definitions of dysmenorrhoea used in studies, with one systematic review reporting rates between 47% and 97%. Upward of 15% of patients experience severe symptoms that are debilitating and cause regular school and work absence.

Aetiology

Overproduction of uterine prostaglandins E_2 and $F_2\alpha$ are major contributory factors in causing painful cramps. Prostaglandin production is controlled by progesterone and, before menstruation starts, progesterone levels decrease, allowing prostaglandin production to increase; if overproduced, cramps occur. Ovulation inhibition can also improve symptoms (by using the oral contraceptive pill) because it lessens the endometrial lining of the uterus, reducing menstrual fluid volume and prostaglandin production.

Table 6.8
Causes of period pain and their relative incidence in community pharmacy

Incidence	Cause
Most likely	Primary dysmenorrhoea
Likely	Endometriosis
Unlikely	Pelvic inflammatory disease, fibroids
Very unlikely	Cervical and ovarian cancer

Arriving at a differential diagnosis

The main consideration of the community pharmacist is to exclude conditions that have a pathological cause (secondary dysmenorrhoea). Fortunately, the most likely problem seen in primary care is PD (Table 6.8).

It is essential to take a detailed history of the patient's menstrual history because PD is a diagnosis based on exclusion. The frequency, severity, and relationship of symptoms to the menstrual cycle need to be established. Asking symptom-specific questions will help the pharmacist establish a differential diagnosis (Table 6.9).



Table 6.9
Specific questions to ask the patient: Primary dysmenorrhoea

Question	Relevance
Age	PD is most common in adolescents and women in their early 20s. Secondary dysmenorrhoea usually affects women many years after the menarche, typically after the age of 30 years.
Nature of pain	A great deal of overlap exists between PD and secondary dysmenorrhoea, but generally PD results in cramping, whereas secondary causes are usually described as dull, continuous, diffuse pain.
Severity of pain	Pain is rarely severe in PD; the severity decreases with the onset of menses. Any patient presenting with moderate to severe lower abdominal pain should be referred.
Onset of pain	PD starts very shortly before or within 24 hours of the onset of menses and rarely lasts for more than 3 days. Pain associated with secondary dysmenorrhoea typically starts a few days before the onset of menses.

PD, Primary dysmenorrhoea.

Clinical features of primary dysmenorrhoea

A typical presentation of PD is of lower abdominal cramping pains shortly before (6 hours) and for 2 or possibly 3 days after the onset of bleeding. Commonly associated symptoms include fatigue, back pain, nausea and/or vomiting and diarrhoea. Pain may radiate to the back and inner thigh. It is typically associated with young women who have recently (6–12 months) started having regular periods. However, there may be a gap of months or years between menarche and the onset of symptoms. This is due to as many as 50% of women being anovulatory in the first year (and still 10% of women 8 years after the menarche). This is important to know because anovulatory cycles are usually pain free.

Conditions to eliminate

Likely causes

Secondary dysmenorrhoea

Endometriosis is the most common cause of secondary dysmenorrhoea and simply means the presence of endometrial tissue outside of the uterus. The exact incidence of endometriosis is unclear, although reports suggest it may occur in up to 50% of menstruating women, but many are asymptomatic. Symptoms usually occur many years after the start of menstruation, so secondary dysmenorrhoea should be considered in any person older than 30 years, either presenting for the first time with dysmenorrhoea or who has noticed worsening symptoms. Patients experience lower abdominal pain (aching, rather than cramping) that usually starts 5 to 7 days before menstruation begins and can be constant and severe. The pain may worsen through menstruation.

Unlikely causes

Pelvic inflammatory disease

It most commonly develops in sexually active women under 24 years who have a history of an STD. It is associated with lower abdominal pain, which is generally bilateral, abnormal vaginal discharge, irregular menses and dyspareunia. Other symptoms include fever, malaise and dysmenorrhoea. It is often asymptomatic and usually only diagnosed during infertility investigation.

Fibroids

The peak incidence of fibroids is in women in their 40s, although they are often asymptomatic. When symptoms are experienced, they are characterized by lower abdominal pain, and are frequently accompanied by menorrhagia and abdominal distension.

Very unlikely causes

Ovarian and cervical cancers

Pelvic and abdominal pain is common in both cancers. Additionally, ovarian cancer is associated with increased urinary urgency, loss of appetite, and nausea, especially in women older than 50 years, when symptoms are persistent or frequent. Cervical cancer involves intermenstrual bleeding and vaginal discharge. Postmenopausal bleeding can also be seen in both types of cancer. Bleeding starts as slight and intermittent but, over time, becomes heavy and continuous. Irregular bleeding between periods, especially if associated with postcoital bleeding, is extremely significant and suggests a precancerous state or cancer of the cervix.



TRIGGER POINTS indicative of referral: Primary dysmenorrhoea

Symptoms/signs	Possible danger/ reason for referral	Urgency of referral
Heavy or unexplained bleeding	Possibly dysfunctional uterine bleeding	As soon as practicable
Pain experienced days before menses	Possibly secondary dysmenorrhoea	
Pain that increases at the onset of menses		
Women >30 years with new or worsening symptoms		
Accompanying systemic symptoms, such as fever and malaise	Suggests possible infection or pelvic inflammatory disease	
Vaginal bleeding in postmenopausal women	Suggests potentially more sinister cause, such as carcinoma	Urgent same-day

Evidence base for over-the-counter medication

Nonsteroidal antiinflammatory drugs

The use of NSAIDs would be a logical choice because raised prostaglandin levels cause PD. In multiple clinical trials, they have been shown to be effective in 80% to 85% of women.

A Cochrane review (Marjoribanks et al., 2015) concluded that NSAIDs were significantly more effective in relieving pain associated with PD compared. However, there was little evidence of superiority of any individual NSAID.

Hyoscine butylbromide (Buscopan)

In one study, Buscopan was given to 17 patients in a double-blind, placebo, crossover trial. The study failed to demonstrate a significant effect compared with placebo, or the comparator drug, aspirin, although in the authors' opinion Buscopan was a good alternative to NSAIDs.

Alverine

Alverine is licensed for the treatment of PD. It is an anticholinergic antispasmodic that relaxes the uterine smooth muscle; however, there is a lack of published evidence regarding its efficacy.

Low-dose combined oral contraceptives

Although not available OTC, oral contraceptives have been reported to be beneficial in treating PD. A Cochrane review (Wong et al., 2009) identified 10 trials and found improvements in pain compared with placebo (odds ratio [OR], 2.01; 95% CI, 1.32–3.08); therefore, if standard OTC treatment is not controlling symptoms adequately the patient should be referred, because contraceptives provide an alternative treatment option.

Other treatment options

A number of alternative treatments have been tested in PD, most notably transcutaneous electrical nerve stimulation (TENS), acupuncture, exercise and dietary supplements. Of these, high-frequency TENS appears to have the strongest body of evidence to support its use (Proctor et al., 2002). Exercise may be effective, although this is based on low-to moderate-quality evidence (Matthewman et al., 2018), and acupuncture may also reduce PD but is based on small studies of low quality (Smith et al., 2016). A wide range of dietary and herbal intervention is frequently recommended. Most trials were conducted with low patient numbers and have reported inconsistent results or no benefit (Pattanittum et al., 2016). Limited evidence was found for fenugreek, fish oil, ginger, valerian and vitamin B₁. The authors concluded there was currently no high-quality evidence to support any dietary supplements for dysmenorrhoea.

Summary

NSAIDs (ibuprofen or naproxen) should be used as first-line therapy unless the patient is contraindicated from using an NSAID. A trial of two to three cycles should be long enough to determine whether NSAID therapy is successful. If NSAIDs are ineffective or poorly tolerated, paracetamol should be offered.

Practical prescribing and product selection

Prescribing information relating to the medicines is discussed and summarized in [Table 6.10](#); useful tips relating to patients presenting with PD are in [Box 6.3](#).

Ibuprofen

There is a plethora of marketed ibuprofen products, all of which have a standard dose for the relief of PD. Adults should take 200 to 400 mg (one or two tablets) three times a day, although most patients will need the higher dose of 400 mg three times a day. Because ibuprofen is only used for a few days during each cycle, it is generally well tolerated. However, gastric irritation is possible, and bronchospasm can be triggered in asthmatics who have a history of hypersensitivity to aspirin or NSAIDs. Ibuprofen can interact with many medicines, although most are not clinically significant (see [Table 6.19](#)).

Naproxen (Feminax Ultra)

Naproxen is indicated for PD for women between 15 and 50 years old. The dose is two tablets (500 mg) initially, followed 6 to 8 hours later by a second tablet (250 mg), if needed. No more than three tablets should be taken in a 24-hour period. The same side effects, cautions and contraindications with ibuprofen apply to naproxen.

Hyoscine hydrobromide (Buscopan Cramps)

The dosage frequency is two tablets four times a day. It is contraindicated in patients with narrow-angle glaucoma and myasthenia gravis, and care should be exercised in patients whose conditions are characterized by tachycardia (e.g., hyperthyroidism, cardiac problems). Anticholinergic side effects can occur but are uncommon; these include dry mouth, visual disturbances and constipation. Side effects are potentiated if it is given with tricyclic antidepressants, antihistamines, butyrophenones, phenothiazines and disopyramide.



Table 6.10
Practical prescribing: Summary of medicines for primary dysmenorrhoea

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
Ibuprofen	Unlikely to be having a period; not recommended	Gastrointestinal discomfort, nausea, diarrhoea	Lithium, anticoagulants, methotrexate	Older adults (increased risk of side effects)	Not applicable in pregnancy, because patients do not menstruate during pregnancy;
Naproxen					
Hyoscine		None	Other anticholinergics, (e.g., tricyclic antidepressants)	Glaucoma	NSAIDs OK in breastfeeding, but avoid hyoscine, if possible, due to lack of data

NSAID, Nonsteroidal antiinflammatory drug.

HINTS AND TIPS BOX 6.3: PRIMARY DYSMENORRHOEA

Hot water bottles The application of warmth to the lower abdomen may confer some relief of the pain.

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Websites

- Endometriosis UK: <https://www.endometriosis-uk.org/>
- British Association for sexual health and HIV: <https://www.bashh.org/>
- Royal College of Obstetricians and Gynaecologists: <http://www.rcog.org.uk>

Premenstrual syndrome

Background

Premenstrual syndrome (PMS) is a broad term that encompasses a wide range of symptoms; physical, behavioural and psychological. Symptoms range from mild to very severe; severe symptoms, especially mood symptoms, affect approximately 5% of patients and can interfere with daily functioning and relationships (Freeman, 2003). In these women, a diagnosis of premenstrual dysphoric disorder is given.

Prevalence and epidemiology

The exact prevalence of PMS is hard to determine because of varying definitions attributed to PMS and the number of people that do not seek medical help. Surveys have shown that over 90% of women have experienced PMS symptoms, but only 20% seek medical help, and 13% to 25% have taken time off from work. There appears to be no marked racial or ethnic differences in the prevalence, but age appears to be a risk factor; most women affected tend to be older than 30 years.

Causes

The precise pathophysiology of PMS is still unclear. A number of theories have been advanced; for example, excess oestrogen and a lack of progesterone or ovarian function. Most researchers now believe that PMS is a complex interaction between ovarian steroids and the neurotransmitters serotonin and gamma-aminobutyric acid (GABA).

Arriving at a differential diagnosis

Owing to the varying and wide-ranging symptoms associated with PMS, the pharmacist must endeavour to differentiate PMS from other gynaecological and mental health disorders.

Careful questioning of when the symptoms occur (symptoms are seen in the second half of the menstrual cycle and significantly improve or resolve by the end of menstruation) and which symptoms are experienced will hopefully give rise to a differential diagnosis of PMS. It is important not to focus on one cycle's symptoms, but ask the patient to describe her symptoms over previous cycles. A diary over three cycles should be maintained to allow a fuller picture of symptoms to be elucidated (symptom diaries are available; e.g., the Daily Record of Severity of Problems; see www.rcog.org.uk). Asking symptom-specific questions will help the pharmacist establish a differential diagnosis (Table 6.11).

Clinical features of premenstrual syndrome

Many symptoms have been attributed to PMS; the most common symptoms are listed in Table 6.12.

Conditions to eliminate

Primary dysmenorrhoea

Abdominal cramps and suprapubic pain might be experienced by PMS sufferers, although these symptoms are

Table 6.12
Common symptoms of premenstrual syndrome

Physical	Behavioural	Psychological
Swelling	Sleep disturbances	Irritability
Breast tenderness	Appetite changes	Mood swings
Aches	Poor concentration	Anxiety, tension
Headache	Decreased interest	Depression
Bloating/weight	Social withdrawal	Feeling out of control



Table 6.11
Specific questions to ask the patient: Premenstrual syndrome

Question	Relevance
Onset of symptoms	Symptoms experienced 7–14 days before, and that disappear a few hours after the onset of menses, are suggestive of PMS.
Age of patient	PMS is most common in women in their 30s and 40s.
Presenting symptoms	Patients with PMS will normally have symptoms suggestive of mental health disorders, such as a depressed mood, insomnia and irritability. This can make excluding mental health disorders, such as depression, difficult. However, the cyclic nature of the symptoms in conjunction with symptoms such as breast tenderness, bloating and fluid retention point to PMS.

PMS, Premenstrual syndrome.

uncommon. Key distinguishing features between PMS and primary dysmenorrhoea are the lack of behavioural and mood symptoms in primary dysmenorrhoea and the difference in the timing of symptoms in relation to the menstrual cycle.

Mental health disorders

Depression and anxiety are common mental health disorders, which often go undiagnosed and can be encountered by community pharmacists. Patients with PMS might experience symptoms similar to such conditions; namely, depressed or sad mood, loss of interest or pleasure, and prominent anxiety or worry. Other symptoms may include disturbed sleep and appetite, dry mouth and poor concentration. However, the symptoms are not cyclic and are not associated with other symptoms of PMS, such as breast tenderness and bloating.

! TRIGGER POINTS indicative of referral: Premenstrual syndrome

Symptoms and signs	Possible danger and reason for referral	Urgency of referral
Psychological symptoms alone	If not occurring in sync with usual menstrual cycle, these could indicate potential anxiety or depressive disorders	As soon as practicable
Severe or disabling symptoms	May indicate a more severe form, such as premenstrual dysphoric disorder	
Symptoms that worsen or stay the same after the onset of menses	Does not suggest PMS symptoms should decrease once menstruation starts	

Evidence base for over-the-counter medication

There are many drug and nondrug treatments advocated for the treatment of PMS, yet most lack evidence from well-conducted RCTs. A lack of evidence or no evidence exists to support the use of reflexology, exercise, chiropractic manipulation, bright light therapy and relaxation.

Acupressure has shown some limited effect on the psychological and physical symptoms of PMS; however, this is based on low or very low levels of evidence, and there are no comparisons with active treatments (Armour et al., 2018).

Regarding vitamin or mineral supplementation, calcium supplements have shown good evidence of effectiveness (Whelan et al., 2009). A recent RCT comparing calcium 400 mg plus vitamin D 400 IU with both placebo and an oral contraceptive in patients with mild to moderate PMS found that both active treatments were significantly more effective than placebo (Shehata, 2016). However, the oral contraceptive was found to be better than the calcium supplement.

Trials involving vitamin B₆ have shown that overall symptoms of PMS improve over a period of 1 to 3 months and help with behavioural and mood symptoms, such as depression (Wyatt et al., 1999). A more recent review also found similar results (Kiani et al., 2016). Caution is needed in interpreting these review findings because most of the included trials were small, of poor quality and had significant heterogeneity.

Vitex agnus-castus (VAC), from the fruit of the chaste tree, is also promoted for the relief of various menstrual problems, including PMS. A recent, well-conducted, systematic review found four studies using VAC at doses of 20 to 40 mg daily; in all studies, it was found to reduce physical and psychological symptoms by more than 50% compared with the control (Jang et al., 2014). The same review located one study that compared VAC with fluoxetine, 20 to 40 mg daily, and found no significant difference in efficacy between the two. However, it must be noted that although the quality of the studies was assessed in the systematic review, most studies involving VAC lacked information on randomization and concealment of allocation.

Summary

The evidence is limited for dietary and herbal supplements for the treatment of PMS. However, calcium supplements, vitamin B₆ and VAC have the best evidence of effectiveness and could be considered for use in mild to moderate PMS.

Practical prescribing and product selection

Prescribing information relating to medicines for PMS is discussed and summarized in [Table 6.13](#).

Calcium

Calcium supplementation should provide at least 1200 mg of elemental calcium per day. It is important to ensure that a product taken by the patient provides the required amount of elemental calcium. For example, a calcium lactate 300-mg tablet provides only 39 mg of elemental calcium; calcium carbonate 1.25-g tablets (e.g., Calci Chew) provide 500 mg of



Table 6.13
Practical prescribing: Summary of medicines used in premenstrual syndrome

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
Pyridoxine	Not applicable	Very high doses can cause toxicity (>500 mg daily)	Levodopa when administered alone	None	Not applicable in pregnancy – patients do not menstruate during pregnancy; OK in breastfeeding
Calcium		Nausea, flatulence, constipation	None	Renally impaired patients	
VAC		Skin reactions	None known	None	

VAC, *Vitex agnus-castus*.

elemental calcium per tablet. Calcium supplements can cause mild gastrointestinal disturbances, such as nausea and flatulence, but taking high doses could cause constipation. If the patient is taking tetracycline antibiotics or iron, a 2-hour gap should elapse between doses to avoid the decreased absorption of the antibiotic or iron.

Vitamin B₆ (pyridoxine)

There is no definitive dose of vitamin B₆ required to alleviate symptoms of PMS. However, doses of up to 100 mg daily have been shown to help reduce symptoms. Side effects are extremely rare with doses at this level, although, at higher doses, this can cause numbness and peripheral neuropathy. A number of drug interactions have been observed in patients taking vitamin B₆, most notably phenytoin, phenobarbital and levodopa. Only the vitamin B₆–levodopa interaction is significant and should be avoided. Although doses as low as 5 mg of vitamin B₆ will reduce the effects of levodopa, the problem of this interaction in clinical practice is almost always negated because combinations of levodopa-carbidopa (Sinemet) or levodopa plus benserazide (Madopar) are unaffected by vitamin B₆.

Vitex agnus-castus

The key clinical trials using VAC used a dose of 20 to 40 mg of VAC extract, equating to approximately 180 to 360 mg of crude dried fruit per day. There are a number of preparations available in the UK; however, there is little standardization of dosing. VAC is generally well tolerated, with no known

interactions, but limited adverse effects, mainly skin reactions, can occur.

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Website

National Association for Premenstrual Syndrome: <http://www.pms.org.uk/>

Heavy menstrual bleeding (menorrhagia)

Background

Heavy menstrual bleeding (HMB) has been quantified (in research settings) as from 60 to 80 mL of blood loss per cycle, but this is impractical to use in a clinical setting. A more useful and practical definition is excessive menstrual blood loss over several consecutive cycles, which interferes with a woman's physical, social, emotional and/or material quality of life.

Prevalence and epidemiology

The prevalence of HMB is difficult to establish due to varying definitions. However, 5% of women aged between 30 and 49 years consult their GP each year (Vessey et al., 1992), and one-third of women describe their periods as being heavy. In the UK, 20% of women have had a hysterectomy by the age of 60 years, usually because of heavy bleeding.

Causes

In approximately half of cases, no identifiable cause can be found. Identifiable causes can result from uterine and pelvic

pathology (e.g., fibroids, polyps, carcinoma), systemic disorders (e.g., hypothyroidism) and iatrogenic factors (e.g., medication, intrauterine devices).

Arriving at a differential diagnosis

The main consideration of the community pharmacist is to exclude sinister pathology. A detailed history of the patient's menstrual cycle is essential. Asking symptom-specific questions will help the pharmacist establish a differential diagnosis (Table 6.14).

Clinical features of heavy menstrual bleeding

The key symptom will be blood loss that is perceived to be more than normal. The patient's bleeding pattern is usually the same as during normal menses, although it can be longer, but heavier.

Conditions to eliminate

Medicine-induced menstrual bleeding

Occasionally, medicines can change menstrual bleeding patterns (Table 6.15). If an adverse drug reaction is suspected, the pharmacist should contact the prescriber and discuss



Table 6.15
Medications that can alter menstrual bleeding

Anticoagulants
Monoamine oxidase inhibitors
Phenothiazines
Steroids
Tamoxifen
Thyroid hormones



Table 6.14
Specific questions to ask the patient: Heavy menstrual bleeding

Question	Relevance
Timing of bleeding	Symptoms that might suggest structural or pathological abnormality include bleeding at times other than at menses.
Effect on quality of life	An assessment should be made to determine what effect menstrual bleeding is having on the patient.
Symptoms in relation to normal cycles	Patients will show cycle to cycle variation in the amount of blood loss. It is important to discuss this normal variation with the patient and to determine from the patient whether the patient thinks that blood loss is within the normal range.

other treatment options. Additionally, the incidence of menstrual pain is higher in patients who have had an intrauterine device fitted.

Endometrial and cervical carcinoma

Although rare causes of menorrhagia, these need to be considered. A description of symptoms of these cancers is given under primary dysmenorrhoea.

! TRIGGER POINTS indicative of referral: Menorrhagia

Symptoms and signs	Possible danger and reason for referral	Urgency of referral
Intermenstrual bleeding, postcoital bleeding, pelvic pain	Possibly a sign of cervical or endometrial cancer	Urgent same-day referral
Treatment failure	May indicate alternative diagnosis or more serious pathology	As soon as practicable

Evidence base for over-the-counter medication

Tranexamic acid has been in clinical use in the UK for approximately 30 years and has established itself as a clinically effective medicine in decreasing menstrual blood loss. It reduces blood loss by up to 50%. It provides symptomatic relief but does not resolve underlying causes.

Practical prescribing and product selection

If the patient history suggests no abnormalities, drug treatment can be given (Box 6.4). This is hormonal (currently still prescription-only medication [POM]) or nonhormonal

[NSAIDs or tranexamic acid]). Tranexamic acid is an antifibrinolytic that stops the conversion of plasminogen to plasmin, an enzyme that digests fibrin and thus brings about clot dissolution. As an OTC product, it is restricted to women with a history of heavy bleeding who have regular (21- to 35-day) cycles that show no more than 3 days of individual variability in cycle duration.

Tranexamic acid

Tranexamic acid (Cyklo-f) should be taken once bleeding starts. The dosage is two tablets three times a day for a maximum of 4 days. The dosage can be increased to two tablets, four times a day, with very heavy menstrual bleeding. The maximum dose is eight tablets (4 g) daily. Common side effects experienced are mild nausea, vomiting and diarrhoea.

Visual disturbances and thromboembolic events have been reported but are very rare. The causal relationship of thromboembolic events and tranexamic acid is unclear, and National Institute for Health and Care Excellence (NICE) guidelines (2018) state that no increase in the overall rate of thrombosis has been identified with women taking tranexamic acid. Nevertheless, women at high risk of thrombosis have been excluded from pharmacy supply. Tranexamic acid should not be taken by patients on anticoagulants or who are taking the combined oral contraceptive, unopposed oestrogen or tamoxifen. In breastfeeding women, one small unpublished study suggests that only low levels of tranexamic acid pass into breast milk, and that waiting 3 to 4 hours before breastfeeding will minimize any risk.

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HINTS AND TIPS BOX 6.4: HEAVY MENSTRUAL BLEEDING

Which treatment?	If menorrhagia and HMB coexist with dysmenorrhoea, the use of NSAIDs should be preferred to tranexamic acid.
Treatment failure (National Institute for Health and Care Excellence guidance)	If there is no improvement in symptoms within three menstrual cycles, the use of NSAIDs and/or tranexamic acid should be stopped.

HMB, Heavy menstrual bleeding; NSAID, nonsteroidal antiinflammatory drug.

Self-assessment questions

The following questions are intended to supplement the text. Two levels of questions are provided, multiple-choice questions and case studies. The multiple-choice questions are designed to test factual recall, and the case studies allow knowledge to be applied to a practice setting.

Multiple-choice questions

- 6.1** Which of the following is not a product license restriction on the OTC sale of tranexamic acid?
- A woman with polycystic ovary syndrome
 - A woman older than 45 years
 - A woman with a 2-day variation in a menstrual cycle lasting 30 days
 - A woman taking unopposed tamoxifen
 - A woman taking an oral contraceptive
- 6.2** Which of the following would you not recommend as suitable OTC treatment for vulvovaginal candidiasis?
- Clotrimazole, 10% vaginal cream
 - Fluconazole, 150-mg oral capsule
 - Clotrimazole, 500 mg pessary
 - Ketoconazole, 2% cream
 - Clotrimazole, 1% topical cream
- 6.3** A 39-year-old woman presents with what she describes as 'period pain'. On further questioning, you ascertain that the aching pain, which can be quite severe, seems to be worse about 1 week before her period and is also worse during intercourse. Which condition is she most likely to be suffering from?
- Pelvic inflammatory disease
 - Primary dysmenorrhoea
 - Endometrial carcinoma
 - Endometriosis
 - Cervical carcinoma
- 6.4** Which of the following symptoms are not commonly associated with premenstrual syndrome?
- Sleep disturbances
 - Breast tenderness
 - Vaginal discharge
 - Headache
 - Fluid retention
- 6.5** Which set of symptoms most closely matches that of vaginal thrush?
- Itch and discharge described as having an offensive odour
 - Itch, burning sensation, and curdlike discharge
 - Little itching but frothy yellow discharge
 - Little or no itch but increased urgency and pain on passing urine
 - Little itching but associated with blood-stained discharge
- 6.6** Which of the following symptoms is commonly associated with trichomoniasis?
- Frothy, green-yellow, vaginal discharge
 - Clear, watery, vaginal discharge
 - Cottage cheese-like vaginal discharge
 - White, fishy-smelling, vaginal discharge
 - Small ulcers on the external genitalia
- 6.7** A woman presents with what she thinks is cystitis. Which of the following symptoms would cause you to refer her to a doctor?
- Pain when passing urine
 - Increased frequency of urination
 - Increased urgency of urination
 - Pain in the loin area
 - Voiding small amounts of urine
- 6.8** Which patient group is not considered at risk of developing an upper UTI?
- Patients with gout
 - Diabetic patients
 - Those who have an indwelling catheter
 - Immunocompromised patients
 - Patients with history of kidney stone

- 6.9** Dysuria accompanied by fever and flank pain is indicative of which of the following?
- Cystitis
 - Trichomoniasis
 - Pyelonephritis
 - Vaginitis
 - Salpingitis
- 6.10** Jane Williams, a 53-year-old woman, asks for fluconazole. You remember her from about 1 month ago when she also had thrush. On questioning, you discover that this is her fourth attack of thrush in the last 12 months. Jane uses a beclometasone inhaler (200 µg twice a day) for her asthma and takes the minipill. You inform Jane that she should see her GP. Jane asks why she cannot just buy it because she knows it will relieve her symptoms. Please select the most appropriate response to Jane's question.
- Due to her age, she will have less oestrogen, which will make her more prone to fungal infection. Her GP needs to review her.
 - Due to her inhaler, she is more prone to thrush, and her GP needs to be aware of these symptoms.
 - Fluconazole can interfere with the minipill, and she would be better off using a clotrimazole pessary.
 - Repeated thrush may indicate diabetes, so her GP will need to check her blood glucose level.
 - Tell her that the guidelines suggest referral to a doctor but, on this occasion, you will sell her the pessary as long as she books an appointment with her GP within 3 days.
- 6.11** Sarah Hart has just purchased some clotrimazole 1% cream, and clotrimazole 500-mg pessary, to treat her thrush. Sarah asks how long should she wait following treatment before visiting her GP if she sees no improvement in her symptoms. Which would be the most appropriate answer to Sarah's question?
- 3 days
 - 5 days
 - 7 days
 - 10 days
 - 14 days
- 6.12** When should you refer a patient with cystitis?
- If the urine is cloudy.
 - If the patient is suffering from dysuria.
 - If pain is felt in the loin area.
 - The onset of the attack is sudden.
 - Micturition is frequent.
- 6.13** Which symptom is least likely experienced in vulvovaginal candidiasis?
- Superficial dyspareunia
 - Vaginal itching and soreness
 - Dysuria
 - A thin white discharge
 - Discharge associated with a strong odour
- 6.14** In which circumstances involving PMS would you consider that referral is required?
- Symptoms in a 21-year-old woman
 - Cyclic episodes of anxiety and tension
 - Breast tenderness
 - Fluid retention
 - Sleep disturbances
- 6.15** Which of the following statements is false with regard to primary dysmenorrhoea?
- It is most common in adolescents and women in their early 20s.
 - Pain typically starts just before the period starts.
 - Pain is described as dull and continuous.
 - Pain tends to decrease once the period has begun.
 - Back pain is often experienced.
- Questions 6.16 to 6.21 concern the following conditions:**
- Primary dysmenorrhoea
 - Pelvic inflammatory disease
 - Endometriosis
 - Menorrhagia
 - Endometrial carcinoma
 - Bacterial vaginosis
 - Thrush
- Select, from A to G, which is:
- 6.16** Most common in sexually active women 15 and 24 years old
- 6.17** Caused by the overproduction of uterine prostaglandins
- 6.18** Key symptom is blood loss perceived to be more than normal
- 6.19** Pain that typically presents shortly before, and for, 2 to 3 days after commencement of menses
- 6.20** Usually seen in postmenopausal women
- 6.21** Associated with strong odour

Questions 6.22 to 6.25 concern the following conditions:

- A. Cystitis
- B. Vulvovaginal candidiasis
- C. Trichomoniasis
- D. Bacterial vaginosis
- E. Atrophic vaginitis
- F. Endometriosis

Select, from A to E, which of the above conditions:

- 6.22 Has a frothy greenish-yellow discharge?
- 6.23 Can be treated with topical imidazoles?
- 6.24 Is commonly caused by *Escherichia coli*?
- 6.25 Usually seen in postmenopausal women

Answers

6.1 Answer: c

Rationale: Details listed in the Summary of Product Characteristics detail all options other than c as 'special warnings and precautions in use' that a patient should consult a doctor prior to taking.

6.2 Answer: d

Rationale: Azole preparations are the mainstay of treatment for candidiasis but the licence for ketoconazole (d) states it is for tinea pedis, tinea cruris and candidal intertrigo.

6.3 Answer: d

Rationale: Endometrial (c) and cervical (e) cancers are not commonly associated with period pain as the predominant symptom; pelvic inflammatory disease (a), primary dysmenorrhoea (b), and endometriosis (d) can cause pain. Typically, however, endometriosis (d) presents with pain several days before menses.

6.4 Answer: c

Rationale: Premenstrual syndrome exhibits a wide range of physical and psychological symptoms. Of those listed, however, vaginal discharge is not associated with this condition.

6.5 Answer: b

Rationale: Odour of thrush is unoffensive (a); itch is prominent, so this excludes options c, d and e. This leaves option b as the correct answer.

6.6 Answer: a

Rationale: Discharge is observed, so e can be excluded; discharge is also coloured, so b can also be excluded. The colour of discharge with trichomoniasis tends to be greenish-yellow, and thus the answer is a.

6.7 Answer: d

Rationale: Pain in the loin area suggests that the infection might have risen to a higher anatomical structure and could be a sign of pyelonephritis.

6.8 Answer: a

Rationale: A suppressed immune systems mean that a UTI is more likely (i.e., options b, diabetics and d,

immunocompromised individuals); kidney stones (e) and catheters (c) could interfere with urine flow.

6.9 Answer: c

Rationale: Fever suggests infection; from this list, cystitis (a), vaginitis (d), and salpingitis e are not infections and are not associated with fever as a symptom. This leaves trichomoniasis (b) and pyelonephritis (c). Pyelonephritis is associated with fever and flank pain compared to trichomoniasis, whose predominant feature is discharge.

6.10 Answer: d

Rationale: Glycogen concentrations can be altered in diabetic patients, and these individuals are therefore predisposed to thrush.

6.11 Answer: c

Rationale: Product licences state a 7-day conditional referral if symptoms have not resolved. This and seems appropriate because the trials included in the Cochrane review had varying follow-up periods to establish a cure rate, but most were between 5 and 7 days.

6.12 Answer: c

Rationale: Cystitis often presents with sudden symptoms (d), frequency (e), dysuria (b) and, less commonly, cloudy urine (a). Loin pain (c) might suggest that the infection has ascended to a higher anatomical structure and needs further evaluation.

6.13 Answer: e

Rationale: Itching (b) is the hallmark symptom; a white discharge (d) does occur in a proportion of patients; dyspareunia (a) and dysuria (c) are possible but uncommon. However, discharge with odour is very unlikely.

6.14 Answer: a

Rationale: Symptoms are wide-ranging but experienced normally by older women; thus, a is the most appropriate to refer.

6.15 Answer: c

Rationale: Period pain usually begins around the onset of menstruation (a), pain is seen prior (b) to the period

starting and lessens once it has started (c), and not all but a substantial number of women experience back pain (e).

6.16 Answer: F

Rationale: STDs are most commonly seen in young women. From this list, the only STD is bacterial vaginosis (F).

6.17 Answer: A

Rationale: Options B, F and G are infections; menorrhagia (D) is excessive blood loss; carcinoma can obviously be ruled out. This leaves endometriosis (C) and primary dysmenorrhoea (A). The exact cause of endometriosis is unknown but a genetic link has been observed.

6.18 Answer: D

Rationale: Blood loss not associated with menstruation is not a common symptom. It can be observed in cancer (E). When blood loss is greater than normal and associated with menstruation, the term menorrhagia is used.

6.19 Answer: A

Rationale: See answer 6.15.

6.20 Answer: E

Rationale: As is the case with most cancers, they are associated with advancing age.

6.21 Answer: F

Rationale: Only one condition listed would be associated with strong odour, and that is bacterial vaginosis.

6.22 Answer: C

Rationale: Discharge is observed in thrush (B), trichomoniasis (C), and bacterial vaginosis (D). Thrush and bacterial vaginosis tend to have a white discharge.

6.23 Answer: B

Rationale: Trichomoniasis (C), bacterial vaginosis (D) and atrophic vaginitis (e) and Endometriosis (F) should be referred for suitable treatment; cystitis (A) can be initially managed with a 2-day course of OTC treatment of sodium or potassium citrate. Imidazoles (B) are the mainstay of treatment for thrush.

6.24 Answer: A

Rationale: This suggests a bacterial cause of the problem, so only cystitis (A), trichomoniasis (C) and bacterial vaginosis (D) need to be considered. Trichomoniasis is a protozoan infection, and bacterial vaginosis is most commonly associated with Gardnerella.

6.25 Answer: E

Rationale: STDs are associated with younger women, so trichomoniasis (C) and bacterial vaginosis (D) can be ruled out. Endometriosis (E) is associated with menstruating women. Although cystitis (A) and thrush (B) can be experienced by all women, atrophic vaginitis (E) is closely associated with postmenopausal women.

Self-assessment questions

The following questions are intended to supplement the text. Two levels of questions are provided: multiple choice questions and case studies. The multiple choice questions are designed to test knowledge and application of knowledge, and the case studies allow this knowledge to be put in context in patient scenarios.

Multiple choice questions

- 6.1** Primary dysmenorrhoea affects?
- 10% to 20% of women
 - 20% to 30% of women
 - 30% to 40% of women
 - 40% to 50% of women
 - Over 50% of women
- 6.2** When do PMS symptoms usually begin?
- At the start of menstruation
 - At the start of ovulation
 - Before ovulation
 - During menstruation
 - Following menstruation
- 6.3** What percentage of women of childbearing age will experience an episode of thrush?
- 50%
 - 55%
 - 60%
 - 70%
 - 75%
- 6.4** What medication can precipitate thrush?
- Ampicillin
 - Aspirin
 - Levothyroxine
 - Propranolol
 - Ramipril
- 6.5** Which condition is known to be a risk factor for developing complications in acute pyelonephritis?
- Asthma
 - Diabetes mellitus
 - Hyperlipidaemia
 - Hypertension
 - Rheumatoid arthritis
- 6.6** Lower quadrant pain is a primary symptom associated with which condition?
- Cystitis
 - Endometriosis
 - Pyelonephritis
 - Trichomoniasis
 - Vaginitis
- 6.7** What symptoms are commonly associated with primary dysmenorrhoea [PD]?
- Lower abdominal cramping pain that starts 7 to 10 days before onset of the period
 - Lower abdominal cramping pain that starts 2 to 3 days before onset of period
 - Lower abdominal cramping pain that starts 6 to 12 hours before onset of period
 - Lower abdominal gripping pain that starts 2 to 3 days before onset of period
 - Lower abdominal gripping pain that starts 6 to 12 hours before onset of period
- 6.8** Fluconazole can interact with a number of medicines. From the list below which medicine does it interact with?
- Amoxicillin
 - Cimetidine
 - Clarithromycin
 - Hyoscine
 - Phenytoin
- Questions 6.9 to 6.11 concern the following patient groups:**
- Children under 12 years old
 - Women aged over 60 years old
 - Women between the ages of 12 and 50
 - Women between the ages of 40 and 60
 - Women over 30 years old

Select, from A to E, which of the patient groups:

6.9 Are most likely to suffer from endometriosis?

6.10 Are least likely to suffer from cystitis?

6.11 Should be referred if they have vaginal discharge?

Questions 6.12 to 6.14 concern the following conditions:

- A. Atrophic vaginitis
- B. Bacterial vaginosis
- C. Cystitis
- D. Trichomoniasis
- E. Vaginal thrush

Select from A to E, which of the conditions:

6.12 Has a fishy-smelling green/yellow discharge?

6.13 Is more common in patients aged over 60 years old?

6.14 Has a cottage-cheese-like discharge?

Questions 6.15 to 6.17: for each of these questions *one or more* of the responses is (are) correct. Decide which of the responses is (are) correct. Then choose:

- A. If a, b and c are correct
- B. If a and b only are correct
- C. If b and c only are correct
- D. If a only is correct
- E. If c only is correct

Directions summarized

A	B	C	D	E
a, b and c	a and b only	b and c only	a only	c only

6.15 A pharmacist should refer patients with vaginal candidiasis when:

- a. They have had more than two attacks in the last 6 months
- b. Women are under 16 years old
- c. Women are taking antibiotics

6.16 Which of the following symptoms are associated with premenstrual syndrome?

- a. Fatigue
- b. Irritability
- c. Breast tenderness

6.17 Which of the following medicines can cause irregular menstrual bleeding?

- a. Levothyroxine
- b. Sertraline
- c. Amoxicillin

Questions 6.18 to 6.20: these questions consist of a statement in the left-hand column followed by a statement in the right-hand column. You need to:

- Decide whether the first statement is true or false
- Decide whether the second statement is true or false

Then choose:

- A. If both statements are true and the second statement is a correct explanation of the first statement
- B. If both statements are true but the second statement is NOT a correct explanation of the first statement
- C. If the first statement is true but the second statement is false
- D. If the first statement is false but the second statement is true
- E. If both statements are false

Directions summarized

	1st statement	2nd statement	
A	True	True	2nd explanation is a correct explanation of the 1st
B	True	True	2nd statement is not a correct explanation of the 1st
C	True	False	
D	False	True	
E	False	False	

First statement

- 6.18 Cystitis is uncommon in men
- 6.19 Vaginal discharge is uncommon in children under 12
- 6.20 Imidazoles have similar cure rates

Second statement

- They have a shorter urethra than women
- Antibiotic therapy may precipitate attacks in this age group
- Symptoms tend to improve in about 3 days

Answers

6.1 Answer: e

Rationale: Period pain is very common and multiple studies have shown prevalence rates consistently higher than 50%.

6.2 Answer: b

Rationale: PMS symptoms tend to start 5 to 11 days before menstruation but typically go away once menstruation begins.

6.3 Answer: e

Rationale: Like primary dysmenorrhoea, thrush is common and most people will experience an episode over their child-bearing years.

6.4 Answer: a

Rationale: Medicines can be implicated in causing thrush, especially those that alter the gut flora and allow opportunistic growth of candida, and is commonly seen with antibiotics.

6.5 Answer: b

Rationale: A number of conditions or disease states are known to be risk factors including renal tract abnormalities, pregnancy, immunocompromised patients and diabetes mellitus.

6.6 Answer: b

Rationale: Pain is not a prominent feature in trichomoniasis (d) or vaginitis (e). Pyelonephritis (c) pain is flank pain and cystitis (a) does cause lower quadrant pain but other symptoms will be more obvious such as dysuria.

6.7 Answer: c

Rationale: PD tends to start very close to the onset of menstruation, thus a, b and d can be discounted. The nature of the pain tends to be cramping and not griping so c would be the answer.

6.8 Answer: e

Rationale: Interactions with fluconazole are multiple and varied. However, there is no information in the SmPC that hyoscine nor amoxicillin interact. Macrolides do interact

but the SmPC lists erythromycin and not clarithromycin. Cimetidine is known to also have a wide range of drug interactions through inhibition of certain cytochrome P450 enzymes but does not effect fluconazole.

6.9 Answer: E

Rationale: Endometriosis is associated with women of child bearing age who have had regular periods for some time. Given menstruation starts in the middle teens (although younger women can have regular periods) and the menopause starts at a round the age of 50, then the answer that best fits this is E.

6.10 Answer: A

Rationale: Cystitis is a commonly experienced condition in women but is relatively unusual in young adults, and so A is the best option.

6.11 Answer: B

Rationale: Like 6.10 (cystitis) vaginal discharge is common but in older women should be viewed with caution. Atrophic vaginitis is likely, but the possibility of malignancy needs to be considered.

6.12 Answer: D

Rationale: Atrophic vaginitis (A), cystitis (C) and thrush (E) are not associated with discharge with odour. This leaves bacterial vaginosis (B) and trichomoniasis (D) as conditions that are associated with discharge with odour, both of which can be described as fishy smelling. However, in trichomoniasis the discharge is green/yellow compared to a thin white discharge in bacterial vaginosis.

6.13 Answer: A

Rationale: STDs and infections tend to be less common in older women but postmenopausal women can experience vaginal discomfort due to falling oestrogen levels that causes thinning of the vaginal wall (A).

6.14 Answer: E

Rationale: Discharge is associated with all but cystitis (C). As from 6.12, bacterial vaginosis and trichomoniasis can be excluded. Atrophic vaginitis (A) is not associated with any discernible coloured discharge.

6.15 Answer: B

Rationale: Product licence restrictions mean that patients should be referred if they are young and have regular bouts of thrush (options A and B), thus the answer is B.

6.16 Answer: C

Rationale: PMS symptoms are wide ranging and include both behavioural, psychological and physical symptoms. Of the three symptoms listed, irritability (psychological) and breast tenderness (physical) are often seen. Fatigue is less associated with PMS, so the answer is C.

6.17 Answer: B

Rationale: Data from the SmPc for each medicine show menstrual irregularities with thyroxine (incidence not stated) and sertraline (common). Therefore A and B are both correct and therefore B is the correct answer.

6.18 Answer: C (True/False)

Rationale: Cystitis is more uncommon in men than women but it is because men have a longer urethra, which means pathogens need to travel further to invade the anatomical structures.

6.19 Answer: B (True/True – statement 2 not correct explanation of statement 1)

Rationale: Generally young women do not experience pathological discharge but all patient groups can cause alteration in vaginal flora and this can lead to vaginal candidiasis manifested as vaginal discharge.

6.20 Answer: B (True/True – statement 2 not correct explanation of statement 1)

Rationale: Imidazoles have high cure rates and in head to head trials show similar efficacy and patients will see improvement in symptoms generally in 3 days, although eradication and full resolution of symptoms can take up to a week.

Case studies

CASE STUDY 6.1

A woman aged about 30 years comes into your pharmacy and asks to speak to you. She tells you that she thinks she has thrush again. When she had similar symptoms before, she saw the doctor, who prescribed her a cream to use. Although it was effective, it was messy, so she asks whether there is anything else she could use instead.

a. What questions do you need to ask?

It is best to confirm her self-diagnosis. Although she has had similar symptoms, it is always best to double check; therefore, ask questions about the nature of the symptoms, such as itch and discharge. It is also worth finding out how long ago she saw her physician to check for frequency of recurrence.

b. What other factors should be considered?

Questions should be aimed at deciding whether the patient is suitable for an OTC product, internal or oral. Questions of this nature are generally linked to ensuring that the patient does not fall outside the product license restrictions of an imidazole vaginal pessary or oral fluconazole.

c. In addition to supplying a product, is there anything else you could recommend?

- *Avoid local irritants: perfumed products such as vaginal deodorants, soaps, and bubble bath.*
- *Avoid wearing tight-fitting trousers or tights. Loose-fitting cotton underwear allows the skin to breathe more.*
- *Spermicides such as nonoxynol-9 may disturb the vaginal flora and precipitate infection.*
- *Probiotics (e.g., live yoghurt) may be used orally or topically. Although there is no evidence that they are effective, they will not cause any harm and can be cooling to the affected area when used topically. However, these are messy to use, which is something the patient wants to avoid.*

To 'safety net': It is worth making sure the person has none of the referral signs or symptoms. (See Trigger points for referral.)

Case studies

CASE STUDY 6.1

Mrs JB, a woman in her late 20s, has come into the pharmacy requesting to speak to the pharmacist. Mrs JB asks if there is somewhere private to talk. She agrees to talk in the consultation room. She is concerned about vaginal itching that she is experiencing.

a. What conditions are uppermost in your thinking that you need to consider for Mrs JB?

- *Bacterial vaginosis, thrush, trichomoniasis, cystitis, sexually transmitted disease.*

b. What questions do you need to ask to differentiate the conditions listed above?

- *Is itching the only symptom?*
 - o A key piece of information to determine is if itch is the only symptom. Itch only is suggestive of thrush.
- *Do you have any discharge?*
 - o Discharge is more common in bacterial vaginosis and trichomoniasis.
- *If discharge present, is there any odour?*
 - o Thrush has an inoffensive smell, whereas bacterial vaginosis and trichomoniasis are associated with a strong odour.
- *Do you have any pain or discomfort when going to the toilet?*
 - o If yes, this points more to cystitis.

Mrs JB says she hasn't noticed any discharge, and the itching only started a couple of days ago. She would like something that will work quickly because the itch makes her very uncomfortable. This is the first time she has had this problem.

c. What do you think is the problem?

Mrs JB is not having any discharge; therefore, it is unlikely that she has bacterial vaginosis or trichomoniasis. She isn't experiencing pain or urgency, so she is also unlikely to have cystitis.

Mrs JB most likely has vaginal thrush.

d. What would you recommend?

Topical imidazoles (miconazole and clotrimazole) and an oral triazole (fluconazole), are available without a prescription to treat vaginal thrush. Most commonly used products are the ranges of clotrimazole pessaries and creams. However, oral fluconazole can be used when topical therapy is poorly tolerated or oral therapy is preferred.

There are different dosing regimens available for the clotrimazole range: 1-, 3- and 6-day lengths of treatment. The 6-day product is usually recommended in recurring cases of thrush, making sure that the patient has seen their GP, and refer her if she has not consulted her physician. Either the 1- or 3-day clotrimazole cream, pessary option, should be recommended to Mrs JB with appropriate advice on how to administer it.

General advice: The symptoms of thrush should disappear within 3 days of treatment (regardless of treatment option). If no improvement is seen after 7 days, the patient should see the physician.

CASE STUDY 6.2

Mrs PR, a 26-year-old woman, presents to the pharmacy on Saturday afternoon asking for something for cystitis. The counter assistant finds out that the patient has had the symptoms for about 3 days and has tried no medication to relieve the symptoms. At this point, the patient is referred to the pharmacist.

- a. What are your initial thoughts about possible diagnoses?

Based on her age and presenting symptoms, a self-diagnosis of cystitis is likely. Kidney infections are common and is the major other condition to consider; her age also means that STDs are possible.

- b. What questions do you need to ask?

Obviously, finding out more about the presenting symptoms is important because this allows you to see a picture of the problem. However, once a general symptom profile has been established, you should use targeted questions to aid the diagnosis. These questions should be discriminatory among the likely causes of her symptoms to allow you to arrive at a diagnosis. Three questions that would help are as follows:

- *Location of the pain*
- *Kidney infections have loin pain; cystitis does not.*
- *Associated symptoms*
- *Kidney infections often have systemic symptoms such as fever.*
- *Any factors that might have precipitated the attack*
- *Sexual activity can predispose to a greater risk of STDs, although this could be a difficult question to ask in a pharmacy setting.*

You find out that Mrs PR is suffering from pain on urination, and discomfort, and she is going to the toilet frequently but has no other symptoms. She had these symptoms previously, about 2 years ago, but they went away on their own after 1 or 2 days. She has no medicine from her physician.

- c. What course of action are you going to take?

Symptoms suggest an uncomplicated, acute, UTI, and empirical treatment could be initiated, but the patient should be told that if treatment fails she should visit her physician. Advice about adequate fluid intake should also be given.

Mrs PR returns to the pharmacy on Monday evening with a prescription for erythromycin, 250 mg qd × 20.

- d. Is this an appropriate antibiotic for a urinary tract infection?

Trimethoprim (or nitrofurantoin) is first-line treatment unless local health policies advocate against its use due to resistance. Enquiry should be made with the patient about previous treatments because she may not be able to tolerate trimethoprim. Additionally, the course is for 5 days, and normally a 3-day course is sufficient (good evidence exists for 3-day treatment courses).

CASE STUDY 6.2

Ms AB comes into the pharmacy and asks to see the pharmacist. She had been in a week ago and purchased a 3-day course of clotrimazole cream to treat vaginal thrush. She has now just found out that she is 6 weeks pregnant. The thrush has resolved but she is concerned as to whether the treatment she used may have caused any harm.

- a. What is your advice to Ms AB?

Clotrimazole is safe to use in pregnancy. Pessary formulations are preferred in pregnancy as they can be inserted without the aid of an applicator though applicators may be used with care. However, it is unlikely that there would be any harm as a result of Mrs AB using the clotrimazole cream with the applicators.

- b. If you knew that Ms AB was planning a pregnancy or was pregnant during her first visit, what would your recommendation have been?

*Hormonal changes during pregnancy will alter the vaginal environment and can make eradicating *Candida* more difficult. Topical agents are safe and effective but all pregnant women are best referred, given the risk of misdiagnosis. It would still be safe recommending clotrimazole pessaries as a treatment option but without the aid of an applicator.*

- c. Would your recommendation change if Ms AB preferred an oral therapy?

Fluconazole is contraindicated in pregnancy. AB's options are limited to topical therapies. The pessary may be a less messy option compared to the cream.

CASE STUDY 6.3

A girl in her late teens or early 20s asks for some painkillers for period pain. The following questions are asked, and responses received.

Information gathering	Data generated
Presenting complaint	
Symptoms experienced	General aching pain in tummy
How long the symptoms have been manifest	2 days
Severity of pain	4/10 (using a scale of 1–10, where 1 is no or little pain and 10 is excruciating pain)
Any other symptoms	Felt a little sick
When is your period due?	Any time now
Additional questions asked	No systemic symptoms No discharge or unusual bleeding
Previous history of presenting complaint	Had period pain before but this seems worse than previous times

Information gathering	Data generated
Drugs (OTC, prescriptions)	Paracetamol for pain; helps a little but wants something a bit stronger
Past medical history	None
Social history, which may include questions relating to smoking, alcohol intake, employment, personal relationships	Not asked (not applicable)
Family history	Not asked (not applicable)

Below summarizes the expected findings for questions when related to the different conditions that can be seen by community pharmacists.

CASE STUDY 6.3 (Continued)

Condition	Age	Pain timing to period	Nature and severity of pain	Bleeding pattern	Discharge
Primary dysmenorrhoea	<30 years	Just prior	Aching, mild to moderate	Normal	Unusual
Secondary dysmenorrhoea	>30 years	Days before	Cramping, moderate to severe	Possible	Unusual
Pelvic inflammatory disease	Young, sexually active	Not associated with menstruation	Dull, can vary in severity	Irregular	Yes
Medicines	Any	N/A	None	Irregular	N/A
Dysfunctional uterine bleeding	Any	N/A	None	Irregular	No
Carcinoma	Postmenopausal	N/A	No (only in late stage of disease)	Irregular	Rare

When this information is compared to that gained from our patient, and linking this with known

epidemiology on period pain (See Table 6.8), it should be possible to make a differential diagnosis.

Condition	Age	Pain timing to period	Nature and severity of pain	Bleeding pattern	Discharge
Primary dysmenorrhoea	✓	✓	✓	✓	✓
Secondary dysmenorrhoea	✗	✗	✗?	✓?	✓
Pelvic inflammatory disease	✓	✗	✗	✗	✗
Medicines	Not applicable (no medicines taken)				
Dysfunctional uterine bleeding	✓	N/A	✗	✗	✗
Carcinoma	✗	N/A	✗	✗	✗

We see that her symptoms most closely match primary dysmenorrhoea (✓ represents symptom match). Given that epidemiology states this is the most common cause of period pain in this age group, this strongly points

to this being the diagnosis. A degree of caution needs to be exercised because her symptoms seem worse than previous episodes, and simple analgesia seems to be ineffective.

To 'safety net': It is best to treat her symptoms this time, but review over the next few cycles and, if symptoms are not improving, refer to the GP.

CASE STUDY 6.4

A female patient in her early 40s presents complaining of thrush. The following questions are asked, and responses received.

Information gathering	Data generated
Presenting complaint	
Symptoms experienced	Moderate itching
How long the symptoms have been manifest	Last 1–2 days
Any other symptoms	None
Additional questions asked	Slight nonodorous discharge No changes in feminine hygiene products used
Previous history of presenting complaint	Similar to last symptoms, which cleared with Canesten
Medicines (OTC, prescriptions)	Insulin
Past medical history	Diabetic

Information gathering	Data generated
Social history, which may include questions relating to smoking, alcohol intake, employment, personal relationships	Not asked
Family history	Mother diabetic; father died about 5 years ago from a fatal myocardial infarction.

Below summarizes the expected findings for questions when related to the different conditions that can be seen by community pharmacists.

CASE STUDY 6.4 (Continued)

Condition	Timing	Discharge	Odour	Itch
Thrush	Acute and onset quick	White curdlike or cottage cheese-like (one in five patients)	Little or none	Prominent
Bacterial vaginosis	Acute but onset slower	White and thin (one in two patients)	Strong and fishy, which might be worse during menses and after sex	Slight
Trichomoniasis	Acute but onset slower	Greenish-yellow, can be frothy	Malodorous	Slight

When this information is compared to that obtained from our patient and linking this with known epidemiology on vaginal discharge (see Table 6.4), it should be possible to make a differential diagnosis.

Condition	Timing	Discharge	Odour	Itch
Thrush	✓	?	✓	✓
Bacterial vaginosis	?	✓	✗	✗
Trichomoniasis	✗?	✓	✗	✗

We see that her symptoms most closely match thrush (✓ represents symptom match, even though epidemiology dictates that bacterial vaginosis is most prevalent in primary care).

To 'safety net': It is worth remembering that certain disease states and actions can precipitate thrush and should be excluded. Symptoms do not appear to be

brought on by any changes in toiletries, but the patient is diabetic. The patient has had symptoms previously (although questioning did not reveal when the last episode occurred), and it is possible that the symptoms are as a consequence of her diabetes. Enquiry about how well controlled is her diabetes should be made before supplying treatment.

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Gastroenterology

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Background

The main function of the gastrointestinal (GI) tract is to break down food into a suitable energy source to allow normal physiological function of cells. The process is complex and involves many different organs. Consequently, there are many conditions that affect the GI tract, some of which are acute and self-limiting and respond well to over-the-counter (OTC) medication and others that are serious and require referral.

General overview of the anatomy of the gastrointestinal tract

It is vital that pharmacists have a sound understanding of GI tract anatomy. Many conditions will present with similar symptoms and from similar locations; for example, abdominal pain, and the pharmacist will need a basic knowledge of GI tract anatomy, and in particular of where each organ of the GI tract is located, to facilitate a correct differential diagnosis (see [Fig. 7.15](#)).

Oral cavity

The oral cavity is comprised of the cheeks, hard and soft palates and tongue.

Stomach

The stomach is roughly J-shaped and receives food and fluid from the oesophagus. It empties into the duodenum. It is located slightly left of midline and anterior (below) to the rib cage. The lesser curvature of the stomach sits adjacent to the liver.

Liver

The liver is located below the diaphragm and mostly right of midline in the upper right quadrant of the abdomen. The liver performs many functions, including carbohydrate, lipid and protein metabolism and the processing of many medicines.

Gallbladder

The gallbladder is a pear-shaped sac that lies deep to the liver and hangs from the lower front margin of the liver. Its function is to store and concentrate bile made by the liver.

Pancreas

The pancreas lies behind the stomach. It is essential for producing digestive enzymes transported to the duodenum via the pancreatic duct and secretion of hormones such as insulin.

Small intestine

The small intestine is where most of the absorption of nutrients and medicines occur. It is comprised of three sections: the duodenum, the jejunum and the ileum. The duodenum starts at the exit of the stomach and its main roles are to neutralize stomach acid and initiate the chemical digestion of chyme (the partly digested food from the stomach). The jejunum is a small section that joins the duodenum and ileum. In the ileum, the mucosa becomes highly folded to form villi that increase the surface area and facilitate the absorption of soluble molecules.

Large intestine

The large intestine starts with the caecum, which is where the appendix connects to the gut. This is followed by the colon and ends with the rectum. The role of the large intestine is largely to absorb water and expel waste.

History taking and physical examination

A thorough patient history is essential because physical examination of the GI tract in a community pharmacy is generally limited to inspection of the mouth. This should allow confirmation of the diagnoses for conditions such as mouth ulcers and oral thrush. A description of how to examine the oral cavity appears in the following section.

Conditions affecting the oral cavity

Background

The process of digestion starts in the oral cavity. The tongue and cheeks position large pieces of food so that the teeth can tear and crush food into smaller particles. Saliva moistens, lubricates and begins the process of digesting carbohydrates (by secreting amylase enzymes) before swallowing.

The physical examination

The oral cavity (Fig. 7.1) can be easily observed in the pharmacy, provided the mouth can be viewed with a good light source, preferably a pen torch. Before performing the examination, it is important to explain to the patient fully what you are about to do and gain their consent. Steps involved in performing an oral examination are detailed as follows:

1. Examine the area where the lesion(s) and/or pain originates from. Look at the size, shape and colour of the lesion(s). Note any redness or swelling local to the area.

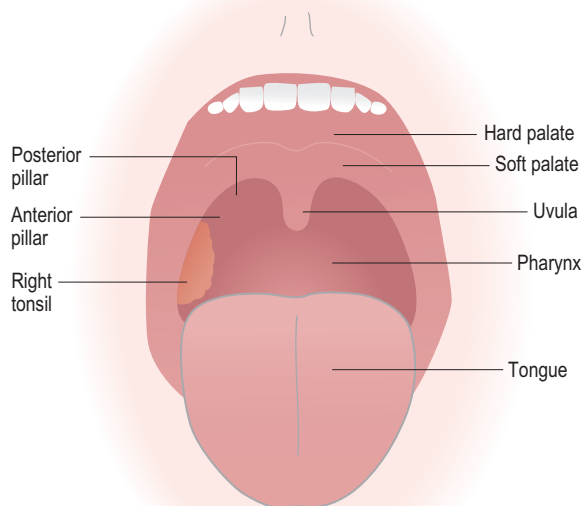


Fig. 7.1 The oral cavity.

2. Once the presenting problem has been inspected, check the rest of the oral cavity for any further signs or symptoms. It is possible that other parts of the mouth are affected but have not been noticed by the patient.
3. While inspecting the mouth also check for signs of a healthy mouth; that is, no signs of tooth decay or periodontal disease (bleeding gums).

Mouth ulcers

Background

Aphthous ulcers, more commonly known as *mouth ulcers*, is a collective term used to describe various different clinical presentations of superficial, painful oral lesions that occur in recurrent bouts at intervals from a few days to a few months. Most patients (80%) who present in a community pharmacy will have minor aphthous ulcers (MAUs). It is the community pharmacist's role to exclude more serious pathology; for example, systemic causes and carcinoma.

Prevalence and epidemiology

The prevalence and epidemiology of MAUs is poorly understood but probably affects 20% of the UK population. They occur in all ages, but it has been reported that they are more common in women and those under the age of 40.

Aetiology

The cause of MAUs is unknown, although about 40% of people have a family history of oral ulceration. A number of theories have been put forward to explain why people develop MAUs, including a genetic link, stress, trauma, food sensitivities, nutritional deficiencies (iron, zinc, and vitamin B₁₂) and infection, but none have so far been proven.

Arriving at a differential diagnosis

There are three main clinical presentations of ulcers: minor, major, and herpetic (Table 7.1). Although it is most likely

Table 7.1
Causes of ulcers and their relative incidence in community pharmacy

Incidence	Cause
Most likely	Minor aphthous ulcers (MAUs)
Likely	Major aphthous ulcers, trauma
Unlikely	Herpetiform ulcers, herpes simplex, oral thrush, medicine-induced, hand, foot, and mouth disease
Very unlikely	Oral carcinoma, erythema multiforme, Behçet syndrome, Crohn's disease and ulcerative colitis

that the patient will be suffering from MAUs, it is essential that these be differentiated from other causes and referred to the GP for further evaluation. A number of ulcer-specific questions should always be asked of the patient (Table 7.2), and an inspection of the oral cavity should be performed to help aid in the diagnosis.

Clinical features of minor aphthous ulcers

MAUs are roundish, grey-white in colour, and painful. They are small, usually less than 1 cm in diameter, and shallow, with a raised red rim. Pain is the key presenting symptom and can make eating and drinking difficult, although pain subsides after 3 or 4 days. They rarely occur on the gingival mucosa and occur singly or in small crops of up to five ulcers. It normally takes 7 to 14 days for the ulcers to heal, but recurrence typically occurs after an interval of 1 to 4 months (Fig. 7.2).

Conditions to eliminate

Likely causes

Major aphthous ulcers

These account for 10% to 15% of cases and are characterized by large (>1 cm in diameter) numerous ulcers, occurring in crops of 10 or more. The ulcers often coalesce to form one large ulcer. These ulcers are slower to heal than MAUs, typically taking 3 to 4 weeks and may cause scarring (Fig. 7.3).



Table 7.2
Specific questions to ask the patient: Mouth ulcers

Question	Relevance
Number of ulcers	Minor aphthous ulcers (MAUs) occur singly or in small crops. A single large ulcerated area is more indicative of pathology outside the remit of the community pharmacist. Patients with numerous ulcers are more likely to be suffering from major or herpetic ulcers rather than MAUs.
Location of ulcers	Ulcers on the side of the cheeks, tongue and inside of the lips are likely to be MAUs. Ulcers located towards the back of the mouth are more consistent with major or herpetic ulcers.
Size and shape	Irregular-shaped ulcers tend to be caused by trauma. If trauma is not the cause, referral is necessary to exclude sinister pathology. If ulcers are large or very small, they are unlikely to be caused by MAUs.
Painless ulcers	Any patient presenting with a painless ulcer in the oral cavity must be referred. This can indicate sinister pathology such as leukoplakia or carcinoma.
Age	MAUs in young children (<10 years) are not common, and other causes such as primary infection with herpes simplex should be considered.



Fig. 7.2 Minor aphthous ulcer. From Cawson, R. et al. (2002). *Essentials of oral pathology and oral medicine*. (7th ed.). London: Churchill Livingstone.

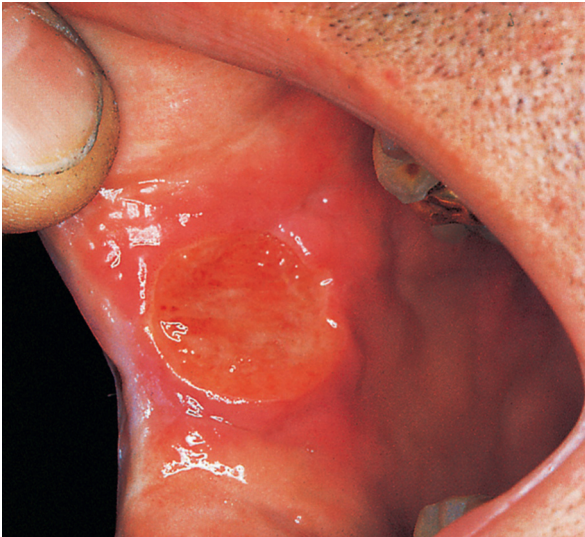


Fig. 7.3 Major aphthous ulcer. From Cawson, R. et al. (2002). *Essentials of oral pathology and oral medicine* (7th ed.). London: Churchill Livingstone.

Trauma

Trauma to the oral mucosa will result in damage and ulceration. Trauma may be mechanical (e.g., tongue biting) or thermal, resulting in ulcers with an irregular border. Patients should be able to recall the traumatic event and have no history of similar ulceration or signs of systemic infection (Fig. 7.4).

Unlikely causes

Herpetiform ulcers

Herpetiform ulcers are pinpoint, often occur in large crops of up to 100 at a time, and can be extremely painful.



Fig 7.4 Ulcer caused by trauma. From Wray, D., Lowe, G. D. O., Dagg, G. H. et al. (1999). *Textbook of general and oral medicine*. London: Churchill Livingstone.



Fig. 7.5 Herpetiform ulcer. From Cawson, R. et al. (2002). *Essentials of oral pathology and oral medicine* (7th ed.). London: Churchill Livingstone.

They are located in the posterior part of the mouth, an unusual location for MAUs (Fig. 7.5). They usually heal within 14 days.

Oral thrush

Oral thrush usually presents as creamy-white, soft elevated patches. It is covered in more detail in the next section.

Herpes simplex

Herpes simplex virus is a common cause of oral ulceration in young children. Primary infection results in ulceration of any part of the oral mucosa, especially the gums, tongue, and cheeks. The ulcers tend to be small and discrete and many in number. Before the eruption of ulcers, the person might show signs of systemic infection, such as fever, general malaise, and pharyngitis.

Medicine-induced ulcers

A number of case reports have been received of medication causing ulcers. These include cytotoxic agents, nicorandil, alendronate, nonsteroidal antiinflammatory drugs (NSAIDs), and beta blockers. Ulcers are often seen at the start of therapy or when the dose is increased.

Hand, foot and mouth disease

Hand, foot and mouth disease (HFMD) is generally a mild disease that is usually caused by the coxsackievirus A16. Although mainly seen in children under 10 years, it can appear in older children and adults. It presents with malaise and low-grade fever before the development of oral lesions that appear as shallow grey ulcers. Rash soon follows ulcer formation, affecting the sides of the fingers, top of the hands, and heel area of the foot. It is contagious, and good hygiene is required to prevent it from spreading to others.

Very unlikely causes

Oral carcinoma

Globally, and in the UK, the incidence of oral cancers has been increasing. In 2016, over 8000 cases of oral cancer in the UK were confirmed, with more than 3000 deaths. The 10-year survival rate is between 19% and 58% and is dependent on its location and how early it is diagnosed.

More than two thirds (67%) of all mouth cancer patients are male, and its incidence is strongly related to age. Incidence rates increase sharply beyond 45 years, and 75% of cases are diagnosed in those older than 55 years. Smoking and excessive alcohol consumption are known risk factors in developing oral cancer.

Almost 60% of cases affect the tongue (32%) or tonsils (26%), although it can occur in any part of the mouth (e.g., floor of mouth [7%], gums [5%], palate [5%]). Initial presentation ranges from painless spots, lumps, or ulcers in the mouth or lip area that fail to resolve. Over time, these become painful, change colour, crust over, or bleed. The painless nature of early symptoms leads people to seek help only when other symptoms become apparent. Symptoms therefore can be present for a number of weeks before the patient sees a health care practitioner. Any solitary ulcer

of longer than 3 weeks in duration should be viewed with caution. Urgent referral is needed because survival rates increase dramatically if the disease is diagnosed in its early stages.

Erythema multiforme

Infection or drug therapy can cause erythema multiforme, although in about 50% of cases no cause can be found. Symptoms are sudden in onset, causing widespread ulceration of the oral cavity. In addition, the patient can have annular and symmetric erythematous skin lesions located towards the extremities. Conjunctivitis and eye pain are also common.

Behçet's syndrome

Most patients will suffer from recurrent, painful major aphthous ulcers that are slow to heal. Lesions are also observed in the genital region, and eye involvement (iridocyclitis) is common.

Crohn's disease and ulcerative colitis

Both may exhibit mouth ulcers but will not be the major presenting complaint. For more details on these conditions, see page 185.

Fig. 7.6 will aid in the differentiation between serious and nonserious conditions that cause mouth ulcers.

! TRIGGER POINTS indicative of referral: Mouth ulcers

Symptoms/ signs	Possible danger/ reason for referral	Urgency of referral
Children <10 years	MAUs rare; hand, foot, and mouth disease possible in this age group	As soon as practicable
Ulcers >1 cm in diameter Ulcers in crops of 5–10 or more Associated eye involvement Duration longer than 14 days	Suggests other causes of ulceration outside scope of community pharmacist	
Painless ulcer	Possible sinister pathology	As soon as possible

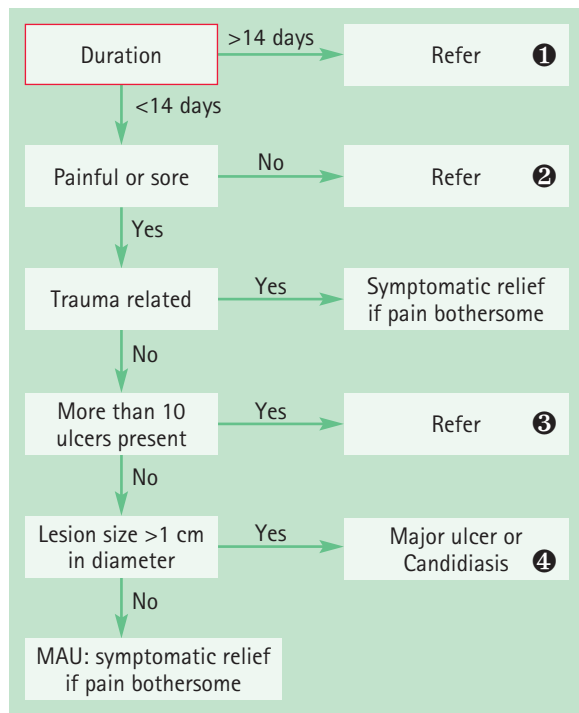


Fig. 7.6 Primer for differential diagnosis of mouth ulcers.

- ① Minor aphthous ulcers. (MAUs) normally resolve in 7 to 14 days. Ulcers that fail to heal within this time need referral to exclude other causes.
- ② Painless ulcers. These can indicate sinister pathology, especially if the patient is older than 50 years. In addition, it is likely that the ulcer will have been present for some time before the patient presented to the pharmacy.
- ③ Numerous ulcers. Crops of 5 to 10 or more ulcers are rare in MAUs. Referral is necessary to determine the cause.
- ④ Major ulcer or candidiasis. See Fig. 7.9 for a primer on the differential diagnosis of oral thrush.

Evidence base for over-the-counter medication

A wide range of products are used for the temporary relief and treatment of mouth ulcers. These products contain corticosteroids, local anaesthetics, antibacterials, astringents and antiseptics.

Corticosteroids

Topical corticosteroids are recommended as one of the mainstays of treatment for patients with MAU; however, most products are not available OTC in the UK.

Hydrocortisone mucoadhesive buccal tablets

Only one trial conducted by Truelove and Morris-Owen (1958) could be found. The authors recruited 52 patients suffering from various forms of oral ulceration and found that 23 patients were suffering from minor aphthous ulceration. They stated that 22 of the 23 patients obtained rapid relief of pain, and the healing rate of the ulcers was accelerated.

Antibacterial agents

A number of randomized controlled trials have investigated antibacterial mouthwashes containing chlorhexidine gluconate. Data from some but not all studies have found that they may reduce the frequency and duration of recurrent ulcers and may reduce the pain and severity of each episode of ulceration. However, like topical corticosteroids, the evidence for antibacterial agents is of poor quality.

Products containing anaesthetic or analgesics

There is very little evidence to support the pain-relieving effect of anaesthetics or analgesics in MAUs, apart from choline salicylate and benzydamine. However, these preparations are clinically effective in other painful oral conditions. It is therefore not unreasonable to expect some relief of symptoms when using these products to treat MAUs.

Choline salicylate

Choline salicylate has been shown to exert an analgesic effect in a number of small studies. However, only one study by Reedy (1970) involving 27 patients evaluated choline salicylate in the treatment of oral aphthous ulceration. No significant differences were found between choline salicylate and placebo in ulcer resolution, but choline salicylate was found to be significantly superior to placebo in relieving pain.

Benzydamine

Benzydamine mouthwash has been studied in a small, low-quality trial for its effect in managing recurrent aphthous stomatitis. (Taylor 2018) The study found that benzydamine was not significantly different from placebo in terms of ulcer severity or ulcer pain. However, nearly 50% of patients preferred benzydamine because of its transient topical analgesic effect.

Protectorants

Pastes that contain gelatin, pectin, and carmellose sodium stick when in contact with wet mucosal surfaces. These have been advocated, but there is a paucity of data to support their efficacy.



Table 7.3
Practical prescribing: Summary of medicines for ulcers

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
Corticosteroid	>12 years	None	None	None	OK
Choline salicylate	>16 years	None	None	None	OK
Lidocaine	>7 years (Iglu) ^a	Can cause sensitization reactions	None	None	OK
Benzocaine	>12 years				
Chlorhexidine	>12 years	None	None	None	OK
Benzydamine	>12 years	May cause stinging	None	None	OK

^aChildren should not be given products routinely because ulcers are rare in this age group.

HINTS AND TIPS BOX 7.1: ULCERS

Protectorant products Apply after food because food is likely to rub off these products.

Practical prescribing and product selection

Prescribing information relating to the medicines used for ulcers is reviewed in Table 7.3; useful tips relating to patients presenting with ulcers are given in Box 7.1.

Hydrocortisone tablets

Each tablet contains 2.5 mg hydrocortisone in the form of the ester hydrocortisone sodium succinate. The dose for adults and children over 12 is one pellet to be dissolved in close proximity to the ulcers four times a day for up to 5 days. It does not interact with any medicines, can be taken by all patient groups, has no side effects, and appears to be safe in pregnancy and breastfeeding.

Antibacterial agents

Chlorhexidine (e.g., Corsodyl) mouthwash is indicated as an aid in the treatment and prevention of gingivitis and in the maintenance of oral hygiene, which includes the management of aphthous ulceration. Ten millilitres of the mouthwash should be rinsed around the mouth for about 1 minute twice a day. It can be used by all patient groups, including those who are pregnant and breastfeeding. Side effects associated with its

use include reversible tongue and tooth discolouration, burning of the tongue, and taste disturbances.

Choline salicylate

Adults and children older than 16 years should apply the these gels (Bonjela Cool, Bonjela Adult) using a clean finger over the ulcer every 3 hours when needed. It is a safe medicine and can be given to all patient groups. It is not known to interact with any medicines or cause any side effects.

Local anaesthetics

All local anaesthetics have a short duration of action; frequent dosing is therefore required to maintain the anaesthetic effect. They are thus best used on an as-needed basis, although the upper limit on the number of applications allowed varies, depending on the concentration of anaesthetic included in each product. They appear to be free from any drug interactions, have minimal side effects, and can be given to most patients. A small percentage of patients might experience a hypersensitivity reaction with lidocaine (Anbesol range, Iglu gel, Medijel) or benzocaine (Orajel range); this appears to be more common with benzocaine.

Benzydamine

For dosing and administration of the oral rinse, see page 34.

Protectorants

These can be applied as frequently as required. There are no interactions, and they can be used in all patient groups.

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Websites

- Behçet's Syndrome Society: <https://behcets.org.uk/>
- Oral health foundation (formerly the British Dental Health Foundation): <https://www.dentalhealth.org/>

Oral thrush

Background

Oropharyngeal candidiasis (oral thrush) is an opportunistic mucosal infection that is unusual in healthy adults. If oral thrush is suspected in this population, community pharmacists should determine whether any identifiable risk factors are present. A healthy adult with no risk factors generally requires referral to the doctor.

Prevalence and epidemiology

The very young (neonates) and the very old are most likely to suffer from oral thrush. It has been reported that 14% of infants at 4 weeks and 10% of debilitated older patients suffer from oral thrush. It is associated with underlying pathology such as diabetes, xerostomia (dry mouth) and patients who are immunocompromised, or an attributable risk factor such as recent antibiotic therapy, inhaled corticosteroids or ill-fitting dentures is present.

Aetiology

It is reported that *Candida albicans* is found in the oral cavity of 30% to 60% of healthy people in developed countries

(Gonsalves et al., 2007). Prevalence in denture wearers is even higher. Changes to the normal environment in the oral cavity allow *C. albicans* to proliferate.

Arriving at a differential diagnosis

Oral thrush is not difficult to diagnose, and the role of the pharmacist is to eliminate underlying pathology and exclude risk factors. A number of other conditions need to be considered (Table 7.4) and asking a number of specific questions of the patient will aid the differential diagnosis (Table 7.5). After questioning, the pharmacist should inspect the oral cavity to help confirm the diagnosis.

Table 7.4
Causes of oral lesions and their relative incidence in community pharmacy

Incidence	Cause
Most likely	Thrush
Likely	Minor aphthous ulcers, medicine-induced thrush, ill-fitting dentures
Unlikely	Lichen planus, underlying medical disorders, such as diabetes, xerostomia (dry mouth), and immunosuppression, major and herpetiform ulcers, herpes simplex
Very unlikely	Leukoplakia, squamous cell carcinoma



Table 7.5
Specific questions to ask the patient: Oral thrush

Question	Relevance
Size and shape of lesion	Typically patients with oral thrush present with patches. They tend to be irregularly shaped and vary in size from small to large.
Associated pain	Thrush almost always causes some degree of discomfort. Painless patches, especially in people >50 years, should be referred to exclude sinister pathology, such as leukoplakia.
Location of lesions	Oral thrush often affects the tongue and cheeks, although if precipitated by inhaled steroids, the lesions appear on the pharynx.

Clinical features of oral thrush

The classic presentation of oral thrush is with creamy white, soft, elevated patches that can be wiped off, revealing underlying erythematous mucosa (Fig. 7.7). Burning or irritation is associated with the infection rather than true pain. Lesions can occur anywhere in the oral cavity but usually affect the tongue, palate, lips and cheeks. Patients sometimes complain of malaise and loss of appetite. In neonates, spontaneous resolution can occur but can take a few weeks.

Conditions to eliminate

Likely causes

Minor aphthous ulcers

Mouth ulcers are covered earlier in this chapter; please refer to this section for the differential diagnosis of these from oral thrush.

Medicine-induced thrush

Inhaled corticosteroids and antibiotics are often associated with causing thrush. In addition, medicines that cause dryness of the mouth can also predispose people to thrush. Always take a medicine history to determine whether medicines could be a cause of the symptoms.



Fig. 7.7 Oral candidiasis. From Forbes, C. D., & Jackson, W. F. (2004). *Illustrated pocket guide to clinical medicine* (2nd ed.). St Louis: Mosby.

Denture wearers

Wearing dentures, especially if they are not taken out at night, not kept clean, or do not fit well can predispose people to thrush.

Unlikely causes

Lichen planus

Lichen planus is a dermatological condition with lesions similar in appearance to plaque psoriasis. In about 50% of people, the oral mucous membranes are affected. The cheeks, gums, or tongue develop white, slightly raised painless lesions that resemble a spider's web. Other symptoms can include soreness of the mouth and a burning sensation. Occasionally, lichen planus of the mouth occurs without any skin rash.

Underlying medical disorders

As stated previously, oral thrush is unusual in the adult population. Patients are at greater risk of developing thrush if they suffer from medical conditions such as diabetes or xerostomia (dry mouth) or are immunocompromised.

Other forms of ulceration

Major and herpetiform ulcers and herpes simplex are covered in more detail in the mouth ulcer section of this chapter; see these sections for the differential diagnosis from oral thrush.

Very unlikely causes

Leukoplakia

Leukoplakia is predominantly a white lesion of the oral mucosa that is a diagnosis based on exclusion (Fig. 7.8). It is often associated with smoking and is a precancerous lesion,



Fig. 7.8 Leukoplakia. From Forbes, C. D., & Jackson, W. F. (2004). *Illustrated pocket guide to clinical medicine* (2nd ed.). St Louis: Mosby.

although epidemiological data have suggested that the annual transformation rate to squamous cell carcinoma is approximately 1%. Patients present with a symptomless white patch mainly on the buccal mucosa but also on the tongue, which develops over a period of weeks. The lesion cannot be wiped off, unlike oral thrush. Most cases are seen in people over the age of 40 and is more common in men.

Squamous cell carcinoma

Squamous cell carcinoma is covered in more detail under mouth ulcers and the reader is referred to this section for differential diagnosis from oral thrush.

Fig. 7.9 will aid the differentiation of thrush from other oral lesions.

! TRIGGER POINTS indicative of referral: Oral thrush

Symptoms/signs	Possible danger/reason for referral	Urgency of referral
Diabetic patients	May indicate poor diabetic control	As soon as practicable
Duration > 3 weeks	Unlikely to be thrush and needs further investigation by a doctor	
Immuno-compromised patients	Likely to have severe and extensive involvement; outside community pharmacist's remit	Urgent possible same-day referral
Painless lesions	Sinister pathology	

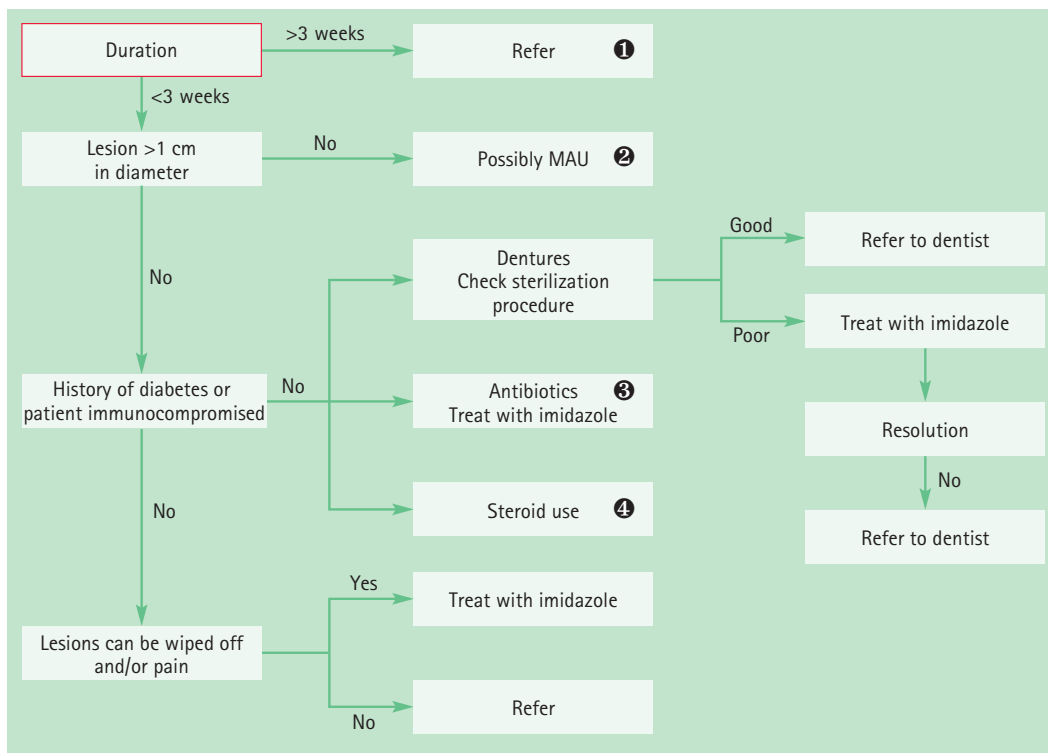


Fig. 7.9 Primer for the differential diagnosis of oral thrush.

① Duration. Any lesion lasting more than 3 weeks must be referred to exclude sinister pathology.

② Minor aphthous ulcers (MAUs). See Fig. 7.6 for a primer on the differential diagnosis of mouth ulcers.

③ Antibiotics. Broad-spectrum antibiotics, such as amoxicillin and macrolides, can precipitate oral thrush by altering the normal flora of the oral cavity.

④ Inhaled corticosteroids. High-dose inhaled corticosteroids can cause oral thrush. Patients should be encouraged to use a spacer and wash their mouth out after inhaler use to minimize this problem.

Evidence base for over-the-counter medication

Only Daktarin oral gel (miconazole) is available OTC to treat oral thrush. It has proven efficacy and appears to have clinical cure rates between 80% and 90%. In comparative trials, Daktarin appears to have superior cure rates than the prescription-only medication (POM) nystatin (Hoppe & Hahn 1996; Hoppe, 1997).

Practical prescribing and product selection

Prescribing information relating to Daktarin Oral gel is discussed and summarized in [Table 7.6](#); useful tips relating to the application of Daktarin are given in 'Hints and Tips' in [Box 7.2](#).

The dosage of the gel is four times a day in all age groups, although the volume administered varies, depending on the age of the patient. For those aged between 4 and 24 months, 1.25 mL (¼ measuring spoon) of gel should be applied; for adults and children older than 2 years, 2.5 mL (½ measuring spoon) of gel is applied.

It can cause nausea and vomiting, dry mouth and oral discomfort. The manufacturers state that it can interact with a number of medicines; namely mizolastine, cisapride, triazolam, midazolam, quinidine, pimozone, HMG-CoA reductase inhibitors (statins) and anticoagulants. However, there is a lack of published data to determine how clinically significant

these interactions are except with warfarin. Co-administration of warfarin with miconazole increases warfarin levels markedly, and the patient's INR (internationalized normalized ratio) should be monitored closely. The manufacturers advise that Daktarin should be avoided in pregnancy, but published data do not support an association between miconazole and congenital defects. It appears to be safe to use while breastfeeding.

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Table 7.6
Practical prescribing: Summary of medicine for oral thrush

Name of medicine	Use in children	Very common (≥1/10) or common (≥1/100) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
Daktarin	>4 months (unlicensed under 4 months but Clinical Knowledge Summaries (CKS) advocates its use to GPs as first-line treatment)	Nausea and vomiting, dry mouth	Warfarin	None	OK

HINTS AND TIPS BOX 7.2: DAKTARIN

Application of Daktarin	Patients should be advised to hold the gel in the mouth for as long as possible to increase contact time between the medicine and the infection. For denture wearers, the dentures should be removed at night and brushed with the gel.
Duration of treatment	Treatment should be continued for up to 2 days after the symptoms have cleared to prevent relapse and reinfection.
Patient acceptability	The gel is flavoured orange to make retention in the mouth more acceptable to patients.

Gingivitis

Background

Gingivitis simply means inflammation of the gums; it is usually caused by an excess buildup of plaque on the teeth. The condition is entirely preventable if regular and correct toothbrushing is undertaken.

Prevalence and epidemiology

It is estimated 50% of the UK population is affected by gum disease, and more than 85% of people older than 40 years will experience gingival disease. Men are affected slightly more than women.

Aetiology

After toothbrushing, the teeth soon become coated in a mixture of saliva and gingival fluid, known as *pellicle*. Oral bacteria and food particles adhere to this coating and begin to proliferate, forming plaque; subsequent brushing of the teeth removes this plaque buildup. However, if plaque is allowed to build up for 3 or 4 days, bacteria begin to undergo internal calcification, producing calcium phosphate, better known as *tartar* (or *calculus*). This adheres tightly to the surface of the tooth and retains bacteria in situ. The bacteria release enzymes and toxins that invade the gingival mucosa, causing inflammation of the gingiva (gingivitis). If the plaque is not removed, the inflammation travels downwards, involving the periodontal ligament and associated tooth structures (periodontitis). A pocket forms between the tooth and gum and, over a period of years, the root of the tooth and bone are eroded until the tooth becomes loose and is lost. This is the main cause of tooth loss in people over 40 years of age.

A number of risk factors are associated with gingivitis and periodontitis; these include diabetes mellitus, cigarette smoking, poor nutritional status and poor oral hygiene. Gingivitis also worsens during pregnancy.

Arriving at a differential diagnosis

Gingivitis often goes unnoticed because symptoms can be very mild and painless. This often explains why a routine checkup at the dentist reveals more severe gum disease than patients thought they had. A dental history needs to be taken from the patient, in particular details of his or her toothbrushing routine and technique, as well as the frequency of visits to the dentist. The mouth should be inspected for tell-tale signs of gingival inflammation. A number of



Table 7.7
Specific questions to ask the patient: Gingivitis

Question	Relevance
Toothbrushing technique	Overzealous toothbrushing can lead to bleeding gums and gum recession. Make sure the patient is not 'overcleaning' his or her teeth. An electric toothbrush might be helpful for people who apply too much force when brushing teeth.
Bleeding gums	Gums that bleed without exposure to trauma and is unexplained or unprovoked need referral to exclude underlying pathology.

gingivitis-specific questions should always be asked of the patient to aid in the differential diagnosis (Table 7.7).

Clinical features of gingivitis

Gingivitis is characterized by swelling and reddening of the gums, which bleed easily with slight trauma; for example, when brushing teeth. Plaque might be visible, especially on teeth that are difficult to reach when toothbrushing. Halitosis might also be present.

Periodontitis

If gingivitis is left untreated, it will progress into periodontitis. Symptoms are similar to those of gingivitis but the patient will experience spontaneous bleeding, taste disturbances, halitosis and difficulty while eating. Periodontal pockets might be visible, and the patient might complain of loose teeth. Referral to a dentist is needed for evaluation.

Medicine-induced gum bleeding

Medicines such as warfarin, heparin, and NSAIDs might produce gum bleeding. It is also worth noting that a number of medicines can cause gum hypertrophy, notably phenytoin and ciclosporin. It has also been seen in patients taking nifedipine. If medicine-induced gum hypertrophy is suspected, the patient should have at minimum 1- to 3-month history of taking the medicine.

Spontaneous bleeding

A number of conditions can produce spontaneous gum bleeding; for example, agranulocytosis and leukaemia. Other

symptoms should be present, such as progressive fatigue, weakness and signs of a systemic illness such as fever. In agranulocytosis, the patient will have a history of taking medicines that decrease granulocyte production.

Oral lichen planus

This commonly manifests on the gingiva. It presents with nonswollen red gingiva with white, plaque-type lesions. For more information see the oral thrush section.

! TRIGGER POINTS indicative of referral: Gingivitis

Symptoms and signs	Possible danger and reason for referral	Urgency of referral
Foul taste associated with gum bleeding Loose teeth	Suspect periodontitis	As soon as practicable to a dentist
Spontaneous gum bleeding	Suspect periodontitis or more sinister pathology	Immediate referral to either a dentist or doctor
Signs of systemic illness	Indicator of more serious underlying pathology	As soon as practicable to a doctor

Evidence base for over-the-counter medication

Put simply, there is no substitute for good oral hygiene. Prevention of plaque buildup is the key to healthy gums and teeth. *Twice-daily brushing is recommended to maintain oral hygiene at adequate levels.* Brushing teeth with a fluoride

toothpaste to prevent tooth decay should preferably take place after eating. Flossing is recommended three times a week to access areas that a toothbrush might miss; this is associated with less gum bleeding compared with toothbrushing alone (Sambunjak et al., 2019).

A Cochrane review concluded that powered toothbrushes (with rotation oscillation action, where the brush heads rotate in one direction and then in the opposite direction) are more effective than manual brushing for plaque removal (Yaacob et al., 2014).

There is a plethora of oral hygiene products marketed to the public. These products should be reserved for established gingivitis or those patients who have a poor toothbrushing technique.

Mouthwashes contain chlorhexidine, hexetidine and hydrogen peroxide. Of these, chlorhexidine has high-quality evidence for reducing dental plaque and gingivitis, regardless of its concentration (James et al., 2017).

Practical prescribing and product selection

Prescribing information relating to the medicines used for gingivitis is discussed and summarized in [Table 7.8](#); useful tips relating to products for oral care are given in 'Hints and Tips' in [Box 7.3](#).

All mouthwashes have minimal side effects and can be used by all patient groups. They are rinsed around the mouth for 30 to 60 seconds and spat out.

Chlorhexidine gluconate mouthwash (e.g., Corsodyl)

This is suitable for adults and children older than 12 years, with a standard dose of 10 mL twice a day. Although chlorhexidine is free from side effects, patients should be warned that prolonged use (>4 weeks) may stain the tongue and brown the teeth. This can be reduced or removed by brushing teeth before use. If this fails to remove the staining, it can be



Table 7.8
Practical prescribing: Summary of medicines for gingivitis

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
Chlorhexidine	>12 years	Staining of teeth and tongue. Mild irritation	None	None	OK
Hexetidine	>6 years	Mild irritation or numbness of tongue			
Hydrogen peroxide	>6 years	None			

HINTS AND TIPS BOX 7.3: TOOTH PROTECTION

- Dental flossing** A piece of floss about 8 inches long should be wrapped around the ends of the middle fingers of each hand, leaving 2 to 3 inches between the first finger and thumb. The floss should be placed between two teeth and curved into a C shape around one tooth, slid up between the gum and tooth until resistance is felt, and then moved vertically up and down several times to remove plaque.
- Using fluoride** Fluoride does reduce dental caries. Drinking water in some parts of the UK contains measurable concentrations of fluoride. Therefore, fluoride toothpastes or fluoride supplementation is not needed. However, most people in Britain require fluoride supplementation, which is normally obtained through toothpaste. Most packs of toothpaste state how many parts per million (ppm) of fluoride the toothpaste contains: 00 ppm is a low level, 1000–1500 ppm is a high level. A low-dose toothpaste should be used for children <7 years to avoid dental fluorosis, which causes tooth discolouration. Oral fluoride supplements can also be given where fluoride in the water is less than 0.7 ppm (see British National Formulary for dosing).

removed by a dentist. It is also available in spray and gel (1%) formulations, with both also only licensed for adults and children older than 12 years.

Hexetidine (Oraldene)

Adults and children older than 6 years should use a 15-mL dose of hexetidine (Oraldene) two or three times a day.

Hydrogen peroxide (e.g., Peroxyl)

Adults and children older than 6 years should use 10 mL rinsed around the mouth up to four times a day. It can cause mucosal irritation, but is rare.

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Dyspepsia**Background**

Confusion surrounds the terminology associated with upper abdominal symptoms, and the term *dyspepsia* is used by different authors to mean different things. It is therefore an umbrella term generally used by health care professionals

to refer to a group of upper abdominal symptoms categorized as the following:

- Functional dyspepsia, nonulcer dyspepsia (indigestion)
- Gastro-oesophageal reflux disease (GORD, heartburn)
- Gastritis
- Duodenal ulcers
- Gastric ulcers

Prevalence and epidemiology

The exact prevalence of dyspepsia is unknown. This is largely because of the number of people who self-medicate or do not report mild symptoms to their doctor. However, it is clear that dyspepsia is extremely common. Between 25% and 40% of the general population in the West are reported to suffer from dyspepsia symptoms each year. Prevalence increases with age and has been reported to be higher in women than in men.

Aetiology

The aetiology of dyspepsia differ depending on the cause. Decreased muscle tone leads to lower oesophageal sphincter incompetence (often as a result of medicines or overeating) and is the principal cause of GORD. Increased acid production results in inflammation of the stomach (gastritis) and is usually attributable to *Helicobacter pylori* infection, or acute alcohol indigestion. The presence of *H. pylori* is central to duodenal and gastric ulceration; *H. pylori* is present in 95% of duodenal ulcers and 80% of gastric ulcers. The exact mechanism whereby it causes ulceration is still unclear but the bacteria produce toxins that stimulate the inflammatory cascade.

Finally, when no specific cause can be found for a patient's symptoms, the complaint is referred to as *functional dyspepsia* and is thought to be multifactorial, with motility, acid secretion and infection all contributing to symptoms.

Arriving at a differential diagnosis

Overwhelmingly, patients who present in a community pharmacy with dyspepsia are likely to be suffering from GORD, gastritis or functional dyspepsia (Table 7.9). Research has shown that even patients who meet National Institute for Health and Care Excellence (NICE) guidelines for endoscopic investigation are found to have gastritis/hiatus hernia (30%), oesophagitis (10%–17%) or no abnormal findings (30%).

Despite this a thorough medical and drug history should be taken to enable the community pharmacist to rule out serious pathology. A number of dyspepsia-specific questions should always be asked of the patient to aid in differential diagnosis (Table 7.10). Patients exhibiting ALARM

Table 7.9
Causes of upper gastrointestinal symptoms and their relative incidence in community pharmacy

Incidence	Cause
Most likely	Functional dyspepsia
Unlikely	Medicine-induced, ulcers, irritable bowel syndrome, biliary disease
Very unlikely	Gastric and oesophageal cancers, atypical angina

symptoms (see Trigger points for referral and Fig. 7.10) need referring for further investigation.

Clinical features of dyspepsia

Patients with dyspepsia present with a range of symptoms commonly involving the following:

- Vague abdominal discomfort (aching) above the umbilicus associated with belching
- Bloating
- Flatulence
- A feeling of fullness
- Nausea and/or vomiting
- Heartburn

Although dyspeptic symptoms are a poor predictor of disease severity or underlying pathology, retrosternal heartburn is the classic symptom of GORD.

Conditions to eliminate

Unlikely causes

Peptic ulceration

Ruling out peptic ulceration is probably the main consideration for community pharmacists when assessing patients with symptoms of dyspepsia. Ulcers are categorized as gastric or duodenal. They occur most commonly in patients from 30 to 50 years old. Typically, the patient will have well-localized, midepigastic pain described as constant, annoying, gnawing or boring. With gastric ulcers, the pain comes on whenever the stomach is empty, usually 30 minutes after eating, and is generally relieved by antacids or food and aggravated by alcohol and caffeine. Gastric ulcers are also more commonly associated with weight loss and GI bleeds than duodenal ulcers. Patients can experience weight loss of 5 to 10 kg and, although this could indicate carcinoma, especially in people older than 40 years, a benign gastric ulcer is found most of the time on investigation. NSAID



Table 7.10
Specific questions to ask the patient: Dyspepsia

Question	Relevance
Age	Young adults are likely to suffer from dyspepsia with no specific pathological condition, unlike patients >50 years, in whom a specific pathological condition becomes more common.
Location	Dyspepsia is experienced as pain above the umbilicus and centrally located (epigastric area). Pain below the umbilicus will not be due to dyspepsia. Pain experienced behind the sternum (breastbone) is likely to be heartburn. If the patient can point to a specific area of the abdomen, it is unlikely to be dyspepsia.
Nature of pain	Pain associated with dyspepsia is described as aching or discomfort. Pain described as gnawing, sharp or stabbing is more likely to be ulcer-related.
Radiation	Pain that radiates to other areas of the body is indicative of more serious pathology, and the patient must be referred. The pain might be cardiovascular in origin, especially if the pain is felt down the inside aspect of the left arm.
Severity	Pain described as debilitating or severe must be referred to exclude more serious conditions.
Associated symptoms	Persistent vomiting with or without blood is suggestive of ulceration or even cancer and must be referred. Black and tarry stools indicate a bleed in the gastrointestinal tract and must be referred.
Aggravating or relieving factors	Pain shortly after eating (1–3 hours) and relieved by food or antacids are classic symptoms of ulcers. Symptoms of dyspepsia are often brought on by certain types of food; for example, caffeine-containing products and spicy food.
Social history	Bouts of excessive drinking are commonly implicated in dyspepsia. Likewise, eating food on the move or too quickly is often the cause of the symptoms. A person's lifestyle is often a good clue to whether these are contributing to the symptoms.
Risk factors for GORD	Stress, smoking, being overweight, and taking medicines that decrease lower oesophageal sphincter tone predispose people to GORD.
<i>GORD</i> , Gastro-oesophageal reflux disease.	

use is associated with a three- to fourfold increase in gastric ulcers.

Duodenal ulcers tend to be more consistent in symptom presentation. Pain occurs 2 to 3 hours after eating, and pain that awakens a person at night is highly suggestive of a duodenal ulcer.

The peak incidence of duodenal ulcers is between 45 and 64 years, whereas the incidence of gastric ulcers increases with age. If ulcers are suspected, referral to the GP is necessary because peptic ulcers can only be conclusively diagnosed by endoscopy.

Medicine-induced dyspepsia

A number of medicines can cause gastric irritation, leading to or provoking GI discomfort, or they can decrease lower oesophageal sphincter tone, resulting in reflux. Aspirin and NSAIDs are very often associated with dyspepsia and can

affect up to 25% of patients. [Table 7.11](#) lists other medicines commonly implicated in causing dyspepsia.

Irritable bowel syndrome

Patients younger than 50 years who have uncomplicated dyspepsia, lower abdominal pain, and altered bowel habits are likely to have irritable bowel syndrome (IBS). For further details on IBS, see later in this chapter.

Biliary disease

Acute cholecystitis (inflammation of the gallbladder) and cholelithiasis (presence of gallstones in the bile ducts, also called *biliary colic*) typically present with sudden persistent colicky and severe epigastric pain. Pain usually lasts 30 minutes but can last hours; it starts a few hours after a meal, frequently awakening the patient in the early hours of the morning. The pain can radiate to the tip of the right

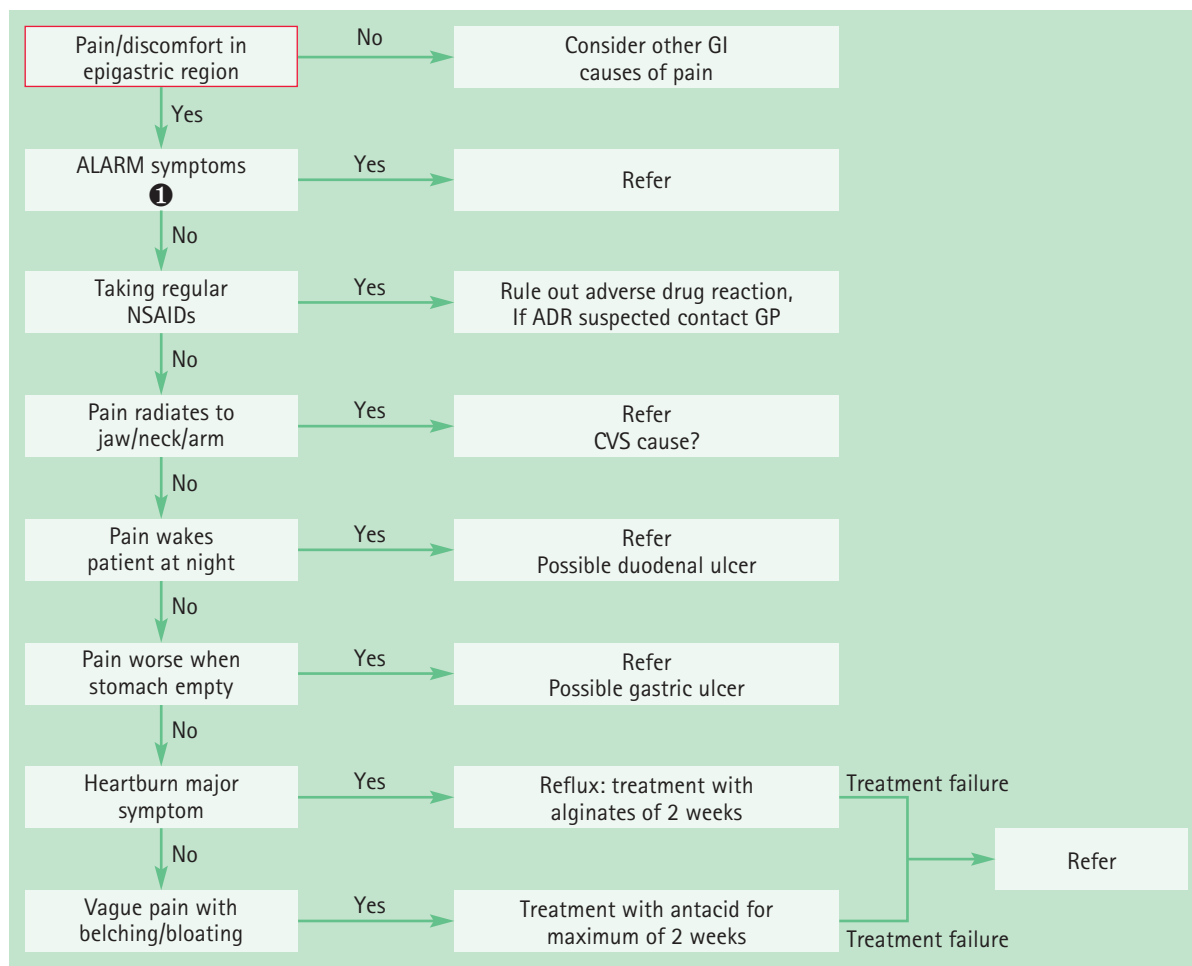


Fig. 7.10 Primer for the differential diagnosis of dyspepsia. 1, ALARM symptoms. These include anaemia (signs can include tiredness and pale complexion), loss of weight, anorexia, dark stools, difficulty in swallowing and vomiting blood. *GI*, Gastrointestinal; *GP*, general practitioner; *NSAIDs*, nonsteroidal antiinflammatory drugs.

scapula (see Fig. 7.18). Fatty foods often aggravate the pain. Nausea and vomiting are common. The incidence increases with increasing age and is most common in people older than 50 years. It is also more prevalent in women than in men.

Very unlikely causes

Gastric carcinoma

Gastric carcinoma is the third most common GI malignancy after colorectal and pancreatic cancers. However, only 2% of patients who are referred by their GP for an endoscopy have malignancy. It is therefore a rare condition, and community pharmacists are extremely unlikely to encounter a patient with carcinoma. One or more ALARM symptoms should be present, plus symptoms such as nausea and vomiting.

Oesophageal carcinoma

In its early stages, oesophageal carcinoma might go unnoticed. Over time, however, because the oesophagus becomes constricted, patients will complain of difficulty in swallowing and experience a sensation of food sticking in the oesophagus. As the disease progresses, weight loss becomes prominent, and anaemia may occur.

Atypical angina

Not all cases of angina have the classic textbook presentation of pain in the retrosternal area with radiation to the neck, back, or left shoulder that is precipitated by temperature changes or exercise. Patients can complain of dyspepsia-like symptoms and feel generally unwell. These symptoms might be brought on by a heavy meal. In such cases, antacids will fail to relieve symptoms, and referral is needed.



Table 7.11
Medicines that commonly cause dyspepsia/
abdominal discomfort

Acarbose (1%–10%)
Antibiotics (e.g., macrolides, tetracyclines)
Anticoagulants
Angiotensin-converting enzyme (ACE) inhibitors
Alcohol (in excess)
Bisphosphonates
Calcium antagonists
Iron
Metformin
Metronidazole
Nitrates
Oestrogens
Orlistat (>10%)
Potassium supplements
Selective serotonin reuptake inhibitors
Sildenafil (1%–10%)
Steroids
Theophylline

Other conditions

Coeliac disease, Crohn's disease, and pancreatitis can exhibit dyspepsia-like symptoms, although these will not be the major presenting symptoms. Symptoms such as diarrhoea and pain will be much more prominent.

Fig. 7.10 will aid in the differentiation of the causes of dyspepsia.



TRIGGER POINTS indicative of referral: Dyspepsia

Symptoms/signs	Possible danger/ reason for referral	Urgency of referral
ALARM signs and symptoms ● Anaemia (signs include tiredness,	Symptoms requiring further investigation	Urgent referral to GP

pale complexion, shortness of breath)

- Loss of weight
- Anorexia
- Recent onset of progressive symptoms
- Melaena, dysphagia, and haematemesis

Pain described as severe, debilitating or that awakens the patient at night
Persistent vomiting

Suggests ulceration

As soon as practicable

Referred pain

Possible cardiovascular or biliary cause

Evidence base for over-the-counter medication

The National Institute for Health and Care Excellence (NICE) has issued guidance on the management of dyspepsia and GORD in adults in primary care (2014). These guidelines have specific information on pharmacist management of dyspepsia, and specific reference is made to this guidance. In accordance with NICE guidelines, the group of patients that should be treated by pharmacists are classed as having 'uninvestigated dyspepsia' (i.e., those who have not had endoscopic investigation). OTC treatment options consist of antacids, H₂ antagonists, alginates and proton pump inhibitors (PPIs). Before treatment is initiated, lifestyle advice should be given where appropriate. Although there is no strong evidence that dietary changes will lessen dyspepsia symptoms, a general healthier lifestyle will have wider health benefits. Recommendations should include the following:

- Change diet to a lower fat diet.
- Keep alcohol intake to recommended levels.
- Stop smoking.
- Decrease weight.
- Reduce caffeine intake.

It might also be possible to identify factors that precipitate or worsen symptoms. Commonly implicated foods that

precipitate dyspepsia are spicy or fatty foods, caffeine, chocolate and alcohol. Bending is also said to worsen symptoms.

Antacids

Antacids have been used for many decades to treat dyspepsia and have proven efficacy in neutralizing stomach acid. However, the neutralizing capacity of each antacid varies, depending on the metal salt used. In addition, the solubility of each metal salt differs, which affects their onset and duration of action. Sodium and potassium salts are the most highly soluble, which enables them to have a quicker onset, but are shorter acting. Magnesium and aluminium salts are less soluble, so these have a slower onset, but longer duration of action. Calcium salts have the advantage of being quick acting and have a prolonged action.

It is therefore common for manufacturers to combine two or more antacid ingredients together to ensure a quick onset (generally sodium salts; e.g., sodium bicarbonate) and prolonged action (aluminium, magnesium or calcium salts).

Alginates

Alginate products are promoted as *first-line treatment for patients suffering from GORD*. When in contact with gastric acid the alginate precipitates out, forming a spongelike matrix that floats on top of the stomach contents. Alginate preparations are also commonly combined with antacids to help neutralize stomach acid. In clinical trials, alginate-containing products have demonstrated superior symptom control compared with placebo and antacids, although the evidence of greater efficacy is limited.

H₂ antagonists

Just one H₂ antagonist is currently available OTC in the UK, ranitidine. Cimetidine and famotidine were also available OTC but have been withdrawn by the manufacturer; nizatidine has exemption from POM control but currently there is no marketed product.

There is a paucity of publicly available trial data supporting their use at nonprescription doses.

The inhibitory effects of OTC doses of ranitidine on gastric acid have been investigated in healthy volunteers. Trials showed conclusively that ranitidine and its comparator drug famotidine significantly raised intragastric pH compared with placebo, although antacids (calcium carbonates) had a significantly quicker onset of action but with shorter duration.

Controlled studies have consistently shown H₂ antagonists to be superior to placebo (Moayyedi et al., 2006). However, the same review found only two head to head studies comparing H₂ antagonists with antacids, and the results showed no significant difference in symptom scores.

Proton pump inhibitors

A number of trials have compared PPIs with H₂ antagonists for nonulcer dyspepsia and GORD-like symptoms (Talley et al., 2002; Sigterman et al., 2013; Pinto-Sanchez et al., 2017). Results indicated that PPIs, even at half the standard POM dose, are generally superior to H₂ antagonists in treating dyspeptic symptoms.

Summary

Antacids will work for most people presenting at the pharmacy with mild dyspeptic symptoms. They can be used as first-line therapy unless heartburn predominates; then an alginate or alginate-antacid combination can be used. H₂ antagonists appear to be equally as effective as antacids but are considerably more expensive. PPIs are most effective and could be considered first-line, especially for those patients who suffer from moderate to severe or recurrent symptoms. Like H₂ antagonists, they are expensive in comparison to simple antacids and might influence patient choice or the pharmacist's recommendation.

Practical prescribing and product selection

Prescribing information relating to the medicines used for dyspepsia is discussed and summarized in [Table 7.12](#). A small number of products are licensed for children younger than 16 years but should not be recommended because dyspepsia symptoms in children are uncommon.

Antacids

Most antacids marketed are combination products containing two, three or even four constituents. The rationale for combining different salts together appears to be twofold:

- First, to ensure the product has quick onset (containing sodium or calcium) and a long duration of action (containing aluminium or calcium)
- Second, to minimize any side effects that might be experienced from the product

For example, magnesium salts tend to cause diarrhoea, and aluminium salts tend to cause constipation; however, if both are combined in the same product, neither side effect is noticed. Useful tips relating to antacids are given in 'Hints and Tips' in [Box 7.4](#).

Antacids can affect the absorption of a number of medications via the mechanisms of chelation and adsorption. Commonly affected medicines include tetracyclines, quinolones, imidazoles, phenytoin, penicillamine and bisphosphonates. In addition, the absorption of enteric-coated preparations can be affected due to antacids increasing the



Table 7.12
Practical prescribing: Summary of medicines for dyspepsia

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
Antacids					
Sodium only	>12 years	None	None	Patients with heart disease	OK
Calcium only		Constipation	Tetracyclines, quinolones, imidazoles, phenytoin, penicillamine and bisphosphonates	None	OK
Magnesium only		Diarrhoea			
Aluminium only		Constipation			
Alginates	>12 years ^a	None	None	Patients with heart disease	OK
Ranitidine	>16 years	None	None	None	Experience has shown them to be OK; reported diarrhoea with famotidine during breastfeeding
PPIs					
Omeprazole, esomeprazole	>18 years	Headache, diarrhoea, constipation, nausea and vomiting, abdominal pain, insomnia, dizziness, dry mouth, rash	Azole antifungals, clopidogrel, diazepam, fluvoxamine, cilostazol, atazanavir	None	Manufacturers advise avoidance but limited information indicates that maternal PPI doses produce low levels in milk and would not be expected to cause any adverse effects in breastfed infants
Pantoprazole		As for other PPIs, plus fatigue			
<p><i>PPIs</i>, Proton pump inhibitors. ^aCertain products can be given to children but dyspepsia is unusual in children and it might be prudent to refer such patients to their GP.</p>					

stomach pH. Most of these interactions are easily overcome by leaving a minimum gap of 1 hour between the respective doses of each medicine.

Most patient groups can take antacids, although patients on salt-restricted diets (e.g., patients with coronary heart disease) should ideally avoid sodium-containing antacids.

Alginates

Products containing alginates (e.g., the Gaviscon range) are combination preparations that contain an alginate with antacids. They are best given after each main meal and before bedtime, although they can be taken on an as-needed basis. They can be given during pregnancy and breastfeeding and

HINTS AND TIPS BOX 7.4: ANTACIDS

Type of formulation?	Ideally, antacids should be given in the liquid form because the acid-neutralizing capacity and speed of onset is greater than that of tablet formulations.
Overuse of antacids	Misuse and chronic use of antacids will result in significant systemic absorption, leading to various unwanted medical conditions. Milk-alkali syndrome has been reported with chronic abuse of calcium-containing antacids, as has osteomalacia with aluminium-containing products. Antacid therapy should ideally not be longer than 2 weeks. If symptoms have not resolved in this time, other treatments and/or evaluation from the GP should be recommended.
When is the best time to take antacids?	Antacids should be taken after food because gastric emptying is delayed in the presence of food. This allows antacids to exert their effect for up to 3 hours.
Salt (sodium) content	Be aware that some antacid preparations contain significant amounts of sodium; for example, Gaviscon Advance contains 4.6 mmol of sodium/10 mL. UK Medicines Information (UKMi) has produced a document detailing medicines with high sodium content. ^a
Older adults	Avoid constipating products because older adults are prone to constipation.
Possible solutions to minimize symptoms	Simple suggestions such as eating less but eating more often or eating smaller meals might help control symptoms. Avoid eating late at night and lying flat at night; use a pillow to prop up the person.

^aSpecialist Pharmacy Service. What is the sodium content of medicines? 2019.
<https://www.sps.nhs.uk/articles/what-is-the-sodium-content-of-medicines-2>

to most patient groups but, as with antacids, patients on salt-restricted diets should ideally avoid sodium-containing alginate preparations. They are reported not to cause side effects or interactions with other medicines.

Ranitidine

Sales of ranitidine (e.g., Zantac, Gavilast, Ranicalm) are restricted to adults and children older than 16 years. It possesses no clinically important drug interactions, and side effects are rare. Evidence suggests that it can be used in pregnancy and breastfeeding, although manufacturers advise patients to speak to their doctor or pharmacist before taking. One tablet (75 mg) should be taken straight away but, if symptoms persist, another tablet should be taken 1 hour later. The maximum dose is 300 mg (four tablets) in 24 hours. The General Sales List versions of ranitidine (Zantac 75 Relief and Ranicalm) cannot be used for the prevention of heartburn, and the maximum dose is only two (150-mg) tablets in 24 hours.

Proton pump inhibitors

These are only available to adults and those aged 18 years and older. If symptoms have not been controlled within 2 weeks, the patient should be referred to the doctor.

Omeprazole (Dexcel Heartburn Relief Tablets, Boots Acid Reflux Tablets)

This is marketed for the relief of reflux-like symptoms (e.g., heartburn) associated with acid-related dyspepsia.

Omeprazole can cause a number of common side effects (>1 in 100; see Table 7.12). Drug interactions with omeprazole are possible because it is metabolized in the liver by cytochrome P450 isoenzymes. These include azole antifungals (decreased azole bioavailability), diazepam (enhanced diazepam side effects), fluvoxamine (increased omeprazole levels), cilostazol (increased cilostazol levels) and clopidogrel (reduced clopidogrel levels). Other interactions listed in the manufacturer's literature include phenytoin and warfarin, but their clinical significance appears low.

It appears to be safe in pregnancy and excreted in only small amounts of breast milk; it is not contraindicated when used as a POM medicine. However, product licences for pharmacy use state that it should not be recommended.

Esomeprazole (Nexium Control)

Nexium Control is indicated for the short-term treatment of reflux symptoms (e.g., heartburn and acid regurgitation) in adults. The recommended dose is 20 mg (one tablet) once daily with its side effects and cautions in use being the same as for omeprazole.

Pantoprazole

Pantoprazole (Pantoloc Control) has a license for the short-term symptomatic treatment of GORD-like symptoms (e.g., heartburn). The dosage is one 20-mg tablet daily. Manufacturers advise avoidance in pregnancy and breastfeeding women. However, limited data in breastfeeding indicate that maternal pantoprazole doses of 40 mg daily produce low levels in milk and would not be expected to cause any adverse effects in breast-fed infants. Like other PPIs, pantoprazole is associated with a number of side effects, interactions, and cautions.

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- GutsUK: <https://gutscharity.org.uk/>
- New Zealand Society of Gastroenterology: <https://nzsg.org.nz/>

Diarrhoea

Background

Diarrhoea can be defined as an increase in frequency of the passage of soft or watery stools relative to the usual bowel habit for that individual. The World Health Organization (2017) defines this as the passage of three or more loose or liquid stools per day. It is not a disease but a sign of an underlying problem, such as an infection or gastrointestinal disorder. It can be classified as acute (<14 days), persistent (>14 days), or chronic (lasting longer than a month). Most patients will present to the pharmacy with a self-diagnosis of acute diarrhoea. It is necessary to confirm this self-diagnosis because patients' interpretations of their symptoms might not match closely with the medical definition of diarrhoea.

Prevalence and epidemiology

The exact prevalence and epidemiology of diarrhoea are not well known. This is probably due to the number of patients who do not seek care or who self-medicate. However, acute diarrhoea does generate high medical consultation rates. It has been reported that children under the age of 5 years have between one and three bouts of diarrhoea per year and adults, on average, just under one episode of diarrhoea per year. Many of these cases are thought to be food-related.

Aetiology

The aetiology of diarrhoea depends on its cause. Acute gastroenteritis, the most common cause of diarrhoea in all age groups, is usually viral in origin. Commonly implicated viruses

are the rotaviruses (now vaccine preventable) and noroviruses. Viruses tend to cause diarrhoea by blunting the villi of the upper small intestine, decreasing the absorptive surface. Bacterial causes of diarrhoea are normally a result of eating contaminated food or drink, which cause diarrhoea by a number of mechanisms. For example, enterotoxigenic *Escherichia coli* produces enterotoxins that affect gut function with secretion and loss of fluids, enteropathogenic *E. coli* interferes with normal mucosal function, and enteroinvasive *E. coli*, *Shigella*, and *Salmonella* spp. cause injury to the mucosa of the small intestine and deeper tissues.

Other organisms – for example, *Staphylococcus aureus* and *Bacillus cereus* – produce preformed enterotoxins, which on ingestion stimulate the active secretion of electrolytes into the intestinal lumen.

Arriving at a differential diagnosis

The most common causes of diarrhoea are viral and bacterial infections (Table 7.13), and the community pharmacist can appropriately manage the vast majority of cases. The main priority is identifying patients that need referral and how quickly they need to be referred. Dehydration is the main complicating factor, especially in the very young and very old. A number of diarrhoea-specific questions should always be asked of the patient to aid in the differential diagnosis (Table 7.14).

Table 7.13
Causes of diarrhoea and their relative incidence in community pharmacy

Incidence	Cause
Most likely	Viral and bacterial infection
Likely	Medicine-induced
Unlikely	Irritable bowel syndrome, giardiasis, faecal impaction
Very unlikely	Ulcerative colitis, Crohn's disease, colorectal cancer, malabsorption syndromes

Clinical features of acute diarrhoea

Symptoms are normally rapid in onset, with the patient having a history of prior good health. Nausea and vomiting might be present before or during the bout of acute diarrhoea. Abdominal cramping, flatulence and tenderness are also often present. If rotavirus is the cause, the patient might also experience viral prodromal symptoms such as cough and cold. Acute infective diarrhoea is usually watery in nature, with no blood present. Complete resolution of symptoms should be observed in 2 to 4 days.



Table 7.14
Specific questions to ask the patient: Diarrhoea

Question	Relevance
Nature of the stools	Diarrhoea associated with blood and mucus (dysentery) requires referral to eliminate invasive infection such as <i>Shigella</i> , <i>Campylobacter jejuni</i> , <i>Salmonella</i> , <i>Clostridium difficile</i> and <i>Escherichia coli</i> O157. Bloody stools are also associated with conditions such as inflammatory bowel disease.
Periodicity	A history of recurrent diarrhoea of no known cause should be referred for further investigation.
Duration	A person who presents with a history of chronic diarrhoea should be referred. The most frequent causes of chronic diarrhoea are irritable bowel syndrome (IBS), inflammatory disease, and colon cancer.
Onset of symptoms	Ingestion of bacterial pathogens can give rise to symptoms in a matter of a few hours (toxin-producing bacteria) after eating contaminated food or up to 3 days later. It is therefore important to ask about food consumption over the last few days, establish if anyone else ate the same food, and check the status of his or her health.
Timing of diarrhoea	Patients who experience diarrhoea first thing in the morning might have underlying pathology such as IBS.
Recent change of diet	Changes in diet can cause changes to bowel function; for example, when away on holiday. If the person has recently been to a non-Western country, giardiasis is a possibility.
Signs of dehydration	Mild (<5%) dehydration can be vague but includes tiredness, anorexia, nausea and light-headedness. Moderate (5%–10%) dehydration is characterized by dry mouth, sunken eyes, decreased urine output, moderate thirst and decreased skin turgor (pinch test of 1–2 seconds or longer).

Conditions to eliminate

Likely causes

Medicine-induced diarrhoea

Many medicines can induce diarrhoea (Table 7.15). If medication is suspected as the cause of the diarrhoea, the patient's doctor should be contacted and an alternative suggested.

Unlikely causes

Irritable bowel syndrome

Patients younger than 50 years who have had abdominal pain and discomfort, bloating, or a change in bowel habit for 6 months are likely to have IBS. For further details on IBS, see later in this chapter.

Giardiasis

Giardiasis, a protozoan infection of the small intestine, is contracted through drinking contaminated drinking water. It is an uncommon cause of diarrhoea in the West. However, with more people taking foreign holidays to non-Western countries, enquiry about recent travel should be made. The patient will present with watery and foul-smelling diarrhoea, accompanied with symptoms of bloating, flatulence, and epigastric pain. If giardiasis is suspected, the patient must be referred to the doctor for confirmation and appropriate antibiotic treatment.

Faecal impaction

Faecal impaction is usually seen in older adults and those with poor mobility. Patients might present with continuous



Table 7.15
Examples of medicines known to cause diarrhoea^a

Alpha blocker	Prazosin
ACE inhibitor	Lisinopril, perindopril
Angiotensin receptor blocker	Telmisartan
Acetylcholinesterase inhibitor	Donepezil, galantamine, rivastigmine
Antacid	Magnesium salts
Antibacterial	All
Antidiabetic	Metformin, acarbose
Antidepressant	SSRIs, clomipramine, venlafaxine
Antiemetic	Aprepitant, dolasetron
Antiepileptic	Carbamazepine, oxcarbazepine, tiagabine, zonisamide, pregabalin, levetiracetam
Antifungal	Caspofungin, fluconazole, flucytosine, nystatin (in large doses), terbinafine, voriconazole
Antimalarial	Mefloquine
Antiprotozoal	Metronidazole, sodium stibogluconate
Antipsychotic	Aripiprazole
Antiviral	Abacavir, emtricitabine, stavudine, tenofovir, zalcitabine, zidovudine, amprenavir, atazanavir, indinavir, lopinavir, nelfinavir, saquinavir, efavirenz, ganciclovir, valganciclovir, adefovir, osetamivir, ribavirin, fosamprenavir
Beta blocker	Bisoprolol, carvedilol, nebivolol
Bisphosphonate	Alendronic acid, disodium etidronate, ibandronic acid, risedronate, sodium clodronate, disodium pamidronate, tiludronic acid
Cytokine inhibitor	Adalimumab, infliximab
Cytotoxic	All classes of cytotoxics

Continued



Table 7.15
Examples of medicines known to cause diarrhoea (Continued)

Alpha blocker	Prazosin
Dopaminergic	Levodopa, entacapone
Growth hormone antagonist	Pegvisomant
Immunosuppressant	Cyclosporin, mycophenolate, leflunomide
NSAIDs	All
Ulcer healing	Proton pump inhibitors
Vaccines	Pediacel, <i>Haemophilus</i> , meningococcal
Miscellaneous	Calcitonin, strontium ranelate, colchicine, dantrolene, olsalazine, anagrelide, nicotinic acid, pancreatin, eplerenone, acamprosate

ACE, Angiotensin-converting enzyme; NSAIDs, nonsteroidal antiinflammatory drugs; SSRIs, selective serotonin reuptake inhibitors.

^aFrequently defined as very common (>10%) or common (1%–10%).

Adapted from Whittlesea C. Hodson K. *Clinical Pharmacy and Therapeutics*. 6th ed. London: Churchill Livingstone; 2018.

soiling as a result of liquid passing around hard stools and mistakenly believe they have diarrhoea. On questioning, the patient might describe the passage of regular, poorly formed hard stools that are difficult to pass. Referral is needed because manual removal of the faeces is often required.

Very unlikely causes

Ulcerative colitis and Crohn's disease

Both conditions are characterized by chronic inflammation at various sites in the GI tract and follow periods of remission and relapse. They can affect any age group, although peak incidence is in those between 20 and 30 years. In mild cases of both conditions, bloody diarrhoea is one of the major presenting symptoms. Patients often have left lower quadrant abdominal pain and suffer from urgency, nocturnal diarrhoea and early morning rushes. In the acute phase, patients will appear unwell and have malaise.

Malabsorption syndromes

Lactose intolerance is often diagnosed in infants under 1 year old. In addition to more frequent loose bowel movements, symptoms such as fever, vomiting, perianal excoriation and a failure to gain weight might occur.

Celiac disease has a bimodal incidence; first, in early infancy, when cereals become a major constituent of the diet, and second, during the fourth and fifth decades. It can present with a wide range of clinical symptoms and should be

suspected in individuals with persistent GI symptoms such as steatorrhea (fatty, frothy or floating stools in the toilet), bloating and abdominal pain. Fatigue and weight loss are also observed.

Colorectal cancer

Approximately 40 000 new cases of colorectal cancer are registered each year in the UK and represent the second most common cause of cancer deaths. Occurrence is strongly related to age, with almost 75% of cases occurring in people aged 65 years and older. Colorectal carcinomas are rare in patients younger than 40 years, but any middle-aged patient presenting with signs of anaemia (e.g., fatigue, pale skin, shortness of breath) and a change in bowel habits should be viewed with suspicion. Persistent diarrhoea accompanied by a feeling that the bowel has not really been emptied is suggestive of neoplasm. This is especially true if weight loss is also present. However, weight loss, a classic textbook sign of colon cancer, is common but observed only in the later stages of the disease. Therefore, a patient is unlikely to have noticed a marked weight loss when visiting a pharmacy early in the disease progression.

Further information on symptoms that are suggestive of lower GI tract cancers is provided by NICE (<https://cks.nice.org.uk/gastrointestinal-tract-lower-cancers-recognition-and-referral#!diagnosisSub>).

Fig. 7.11 will aid in the differentiation of diarrhoeal cases that require referral.

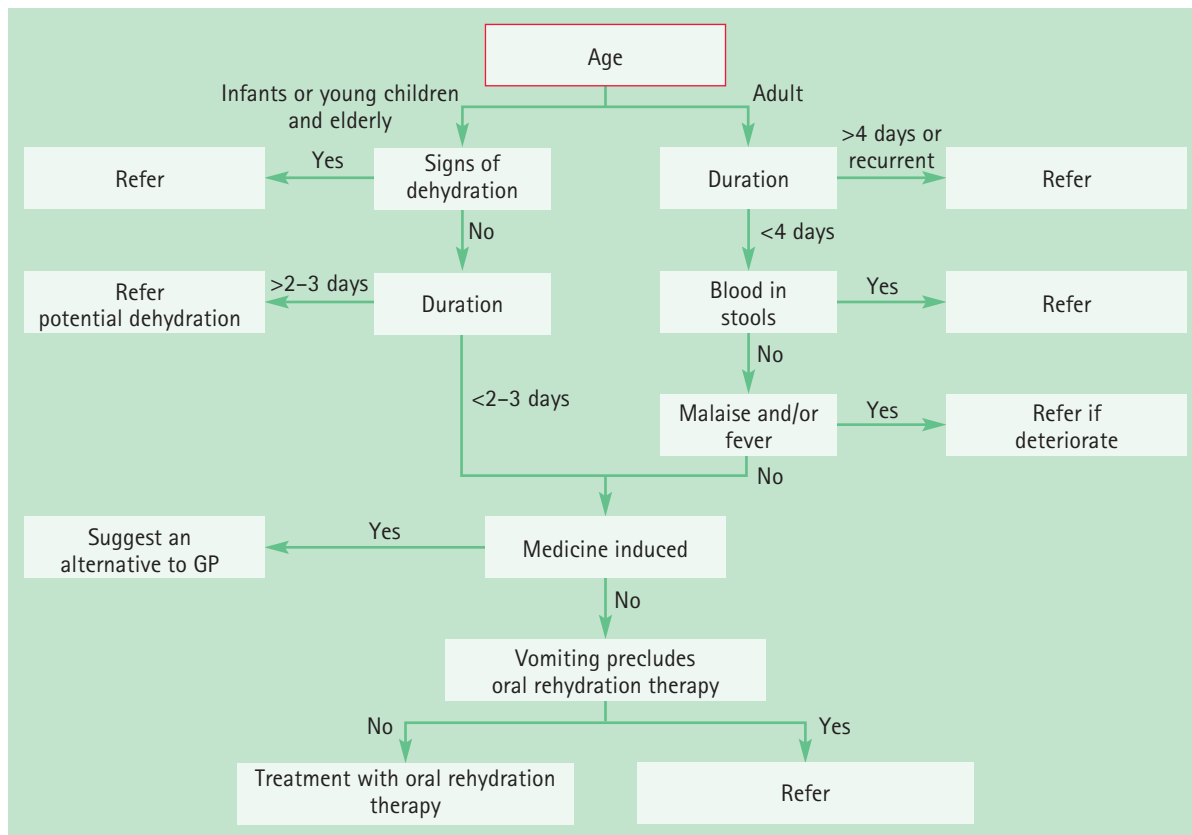


Fig. 7.11 Primer for the differential diagnosis of diarrhoea.

! TRIGGER POINTS indicative of referral: Diarrhoea

Symptoms/signs	Possible danger/ reason for referral	Urgency of referral
Duration longer than 2–3 days in children and older adults Patients unable to drink fluids	At risk of dehydration and associated complications	Same-day referral
Diarrhoea following recent travel to tropical or subtropical climate	Giardiasis?	As soon as practicable
Change in bowel habit (long-term) >40 years	Sinister pathology?	

Presence of blood or mucous in the stool	
Suspected faecal impaction in older adults	Outside scope of community pharmacist
Severe abdominal pain	
Steatorrhoea	Malabsorption syndrome?

Evidence base for over-the-counter medication

Acute infectious diarrhoea still remains one of the leading causes of death in developing countries, despite advances in its treatment. In developed and Western countries, diarrhoeal disease is primarily of economic and socially disruptive significance. Goals of OTC treatment are therefore concentrated on the relief of symptoms. Given that most

causes of diarrhoea only last 24 to 48 hours, the main aim of treatment should be to reduce any potential dehydration caused by fluid loss. Agents that change the motility of the gut to reduce diarrhoea (e.g., loperamide) should be reserved for situations where staying at home and resting would be impractical or inconvenient.

Before considering treatment, it is important to stress to patients the importance of hand washing. Interventions that promote hand washing can reduce diarrhoea episodes by about one third (Ejemot-Nwadiaro et al., 2015).

Oral rehydration solution

Oral rehydration solution (ORS) represents one of the major advances in medicine. It has proved to be a simple, highly effective treatment, which has decreased mortality and morbidity associated with acute diarrhoea in developing countries. The formula recommended by the World Health Organization (WHO) contains glucose (75 mmol/L), sodium (75 mmol/L), potassium (20 mmol/L), chloride (65 mmol/L) and citrate (10 mmol/L) in an almost isotonic fluid. Until recently, the WHO oral rehydration solution contained 90 mmol/L sodium but a systematic review (Hahn et al., 2002) concluded that ORS, with a reduced osmolarity compared with the standard WHO formula, was associated with fewer complications in children with mild to moderate diarrhoea. Based on this and other findings, the WHO oral rehydration solution now has a reduced osmolarity of 245 mmol/L, which contains 75 mmol/L of sodium. A number of similar preparations are available commercially in the form of sachets that require reconstitution in clean water before use; however, commercially available solutions in the UK contain lower sodium concentrations (60 mmol/L of sodium) because diarrhoea tends to be isotonic, and therefore replacement of large quantities of sodium is less important.

Rice-based oral rehydration solution

In many developing countries, a glucose substitute was added to electrolytes because of glucose unavailability. Clinical trials showed these rice-based ORS to be highly efficacious, well tolerated and potentially more effective than conventional ORS.

Loperamide

Loperamide is a synthetic opioid analogue that is thought to exert its action via opiate receptors. It slows intestinal tract time increasing the water resorbing capacity of the gut. It has been extensively researched, with many published trials investigating its effectiveness in acute infectious diarrhoea. Most well-designed, double-blind, placebo-controlled trials have consistently shown it to be significantly better than

placebo and comparable to diphenoxylate in terms of reducing the duration of diarrhoea, but with longer duration of action. Loperamide is also available compounded with simethicone. However, there is little evidence of better efficacy in terms of diarrhoeal symptoms with this combination.

Bismuth subsalicylate

Bismuth-containing products have been used for many decades. Their use has declined over time as other products have become more popular. Bismuth subsalicylate has been shown to be effective in treating *traveller's diarrhoea*. A review paper by Steffen (1990) concluded that bismuth subsalicylate was clinically superior to placebo, decreasing the number of unformed stools and increasing the number of patients who were symptom-free. However, two of the trials reviewed showed bismuth subsalicylate to be significantly slower in symptom resolution than its comparator drug, loperamide.

Kaolin and morphine

The constipating side effect of opioid analgesics can be used to treat diarrhoea. However, kaolin and morphine products have no evidence of efficacy and should not be recommended. It remains a popular home remedy, especially with older adults.

Rotavirus vaccine

From 2013, the rotavirus vaccine was added to the routine UK childhood vaccination schedule. The oral vaccine is given as two doses, the first at 2 months and the second at 3 months, alongside other routine childhood vaccinations. Since its introduction, cases of rotavirus have decreased by more than 80% (Soares-Weiser et al., 2019).

Summary

Because diarrhoea results in fluid and electrolyte loss, it is important to reestablish the normal fluid balance, so ORS is first-line treatment for all age groups, especially children and frail older adults. Loperamide is a useful adjunct in reducing the number of bowel movements but should be reserved for those patients who will find it inconvenient to use a toilet.

Practical prescribing and product selection

Prescribing information relating to the medicines used for diarrhoea is discussed and summarized in [Table 7.16](#); useful tips relating to patients presenting with diarrhoea are given in 'Hints and Tips' in [Box 7.5](#).



Table 7.16
Practical prescribing: Summary of medicines for diarrhoea

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
ORS (oral rehydration salts)	Infants and older	None	None	None	OK
Loperamide	>12 years	Headache, flatulence, nausea	None	None	OK
Bismuth	>16 years	Black stools or tongue	Quinolone antibiotics	None	Avoid in breastfeeding if possible because it has a salicylate content and risk of association with Reye's syndrome.
Morphine salts	>12 years	None	None	None	OK

HINTS AND TIPS BOX 7.5: DIARRHOEA

Rough guidelines for referral for children	<1 year old: refer if duration >1 day. <3 years old: refer if duration >2 days. >3 years old: refer if duration >3 days.
Kaolin and morphine	Subject to abuse. Store out of sight.
Alternative to oral rehydration salts	Patients can be advised to increase their intake of fluids, particularly fruit juices with their glucose and potassium content and soups because of their sodium chloride content.

Oral rehydration salts

Oral rehydration salts (Dioralyte, Dioralyte Relief [rice-based]) can be given to all patient groups and has no side effects or drug interactions. The volume of solution given is dependent on how much fluid is lost. Because infants and older adults are more at risk of developing dehydration, they should be encouraged to drink as much ORS as possible. In adults, 2 L of ORS should be given in the first 24 hours, followed by unrestricted normal fluids, with 200 mL of rehydration solution per loose stool. The solution is best sipped every 5 to 10 minutes rather than drunk in large quantities less frequently. In infants, 1 to 1.5 times the usual feed volume should be given.

Loperamide (e.g., *Diah-Limit*, *Dioraleze*, *Imodium range*)

The dose is two capsules immediately, followed by one capsule after each further bout of diarrhoea. It has minimal central nervous system (CNS) side effects, although CNS depressant

effects and respiratory depression have been reported at high doses. OTC doses are therefore limited to 16 mg/day and cannot be used in children under 12. Loperamide has an excellent safety record and has few common side effects (see Table 7.16). It is available in a range of formulations, such as dispersible tablets, melt tabs and liquid.

Bismuth

Bismuth (Pepto-Bismol Liquid, 87.6 mg/5 mL bismuth subsalicylate and chewable tablet, 262.5 mg) should only be given to people over the age of 16. The dose is 30 mL or two tablets taken every 30 to 60 minutes, when needed, with a maximum of eight doses in 24 hours. Bismuth subsalicylate is well tolerated and has a favourable side-effect profile, although black stools are commonly observed (caused by unabsorbed bismuth compound). Occasional use is not known to cause problems during pregnancy and breastfeeding, but the manufacturers' state it should not be used. Bismuth can decrease the bioavailability of quinolone antibiotics; therefore, a minimum 2-hour gap should be left between doses of each medicine.

Morphine (e.g., Kaolin and morphine, J Collis Browne's mixture)

Morphine is generally well tolerated at OTC doses, with no side effects reported. The products can be given to all patient groups, including pregnant and breastfeeding women. There are no drug interactions of note. The standard dose for adults and children older than 12 years is 5 to 10 mL every 6 hours.

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Constipation

Background

Constipation, like diarrhoea, is a symptom rather than a condition. Constipation arises when the patient experiences a reduction in his or her normal bowel habits accompanied with more difficult defecation and/or hard stools.

Prevalence and epidemiology

Constipation is very common, although its prevalence is not well established, probably because of underreporting due to high levels of self-treatment by patients. It occurs in all age groups but is especially common in older adults. It has been estimated that 25% to 40% of all people over the age of 65 have constipation. Many older adults have normal frequency of bowel movements but strain at stool. This is probably a result of a sedentary lifestyle, a decreased fluid intake, poor nutrition, avoidance of fibrous foods and chronic illness. Women are two to three times more likely to suffer from constipation than men, and 40% of women in late pregnancy experience constipation.

Aetiology

The normal function of the large intestine is to remove water and various salts from the colon and drying and expelling the faeces. Any process that facilitates water resorption will generally lead to constipation. The most common cause of constipation is decrease in intestinal tract transit time of food, which allows greater water resorption from the large bowel, leading to harder stools that are more difficult to pass. This is usually caused by a deficiency in dietary fibre, a change in lifestyle and/or environment, and medication. Occasionally, patients ignore the defecation reflex because it may be inconvenient for them to defecate.

Arriving at a differential diagnosis

The first thing a pharmacist should do is to establish the patient's current bowel habit compared with normal. Questioning should then concentrate on determining the cause. Constipation does not usually have sinister pathology; the most common cause in the vast majority of nonelderly adults will be a lack of dietary fibre (Table 7.17). However, constipation can be caused by medication, many disease states, including neurological disorders (e.g., multiple sclerosis, Parkinson disease), metabolic and endocrine conditions (e.g., diabetes, hypothyroidism) and psychological causes (e.g., depression, eating disorders). A number of

Table 7.17
Causes of constipation and their relative incidence in a community pharmacy

Incidence	Cause
Most likely	Eating habits, lifestyle
Likely	Medication
Unlikely	Irritable bowel syndrome, pregnancy, depression, functional disorders (children)
Very unlikely	Colorectal cancer, hypothyroidism

constipation-specific questions should always be asked of the patient to aid in the differential diagnosis (Table 7.18).

Clinical features of constipation

Besides the inability to defecate, patients might also have abdominal discomfort and bloating. In children, parents might also notice that the child is more irritable and has a decreased appetite. Specks of blood in the toilet might be present and are usually due to straining at stool. In the vast majority of cases, blood in the stool does not indicate sinister pathology. Patients presenting with acute constipation with no other symptoms apart from very small amounts of bright red blood can be managed in the pharmacy; however, if blood loss is substantial (stools appear tarry, red or black), referral is needed.



Table 7.18
Specific questions to ask the patient: Constipation

Question	Relevance
Change of diet or routine	Constipation usually has a social or behavioural cause. There will usually be some event that has precipitated the onset of symptoms.
Pain on defecation	Associated pain when going to the toilet is usually due to a local anorectal problem. Constipation is often secondary to the suppression of defecation because it induces pain. These cases are best referred for physical examination.
Presence of blood	Bright red specks in the toilet or smears on toilet tissue suggest haemorrhoids or a tear in the anal canal (fissure). However, if blood is mixed in the stool (melaena), referral to the doctor is necessary. A stool that appears black and tarry is suggestive of an upper gastrointestinal bleed.
Duration (chronic or recent?)	If a patient suffers from long-standing constipation and has been previously seen by the doctor, treatment could be given. However, cases >14 days with no identifiable cause or previous investigation by the doctor should be referred.
Lifestyle changes	For example, changes in job or marital status can precipitate depressive illness that can manifest with physiological symptoms, such as constipation.

Conditions to eliminate

Likely causes

Medicine-induced constipation

Many medicines are known to cause constipation. Most exert their action by decreasing gut motility, although opioids tend to raise sphincter tone and reduce sensitivity to rectal distension. A detailed medication history should always be sought from the patient; Table 7.19 lists the commonly implicated medicines that cause constipation.

Unlikely causes

Irritable bowel syndrome

Patients younger than 50 years who have had abdominal pain and discomfort, bloating or a change in bowel habit for 6 months are likely to have IBS. For further details, see later in this chapter.

Pregnancy

Constipation is common in pregnancy, especially in the third trimester. A combination of increased circulating progesterone, displacement of the uterus against the colon by the foetus, decreased mobility and iron supplementation all contribute to an increased incidence of constipation while pregnant. Most patients complain of hard stools rather than a decrease in bowel movements. If a laxative is used, a bulk-forming laxative should be recommended.

Depression

Upwards of 20% of the population will suffer from depression at some time. Many will present with physical as well as emotional symptoms. It has been reported that one-third of all patients suffering from depression present with



Table 7.19
Examples of medicines known to cause constipation^a

Alpha blocker	Prazosin
Antacid	Aluminium and calcium salts
Anticholinergic	Trihexyphenidyl, hyoscine, oxybutynin, procyclidine, tolterodine
Antidepressant	Tricyclics, SSRIs, reboxetine, venlafaxine, duloxetine, mirtazapine
Antiemetic	Palonosetron, dolasetron, aprepitant
Antiepileptic	Carbamazepine, oxcarbazepine
Antipsychotic	Phenothiazines, haloperidol, pimozide and atypical antipsychotics such as amisulpride, aripiprazole, olanzapine, quetiapine, risperidone, zotepine, clozapine
Antiviral	Foscarnet
Beta blocker	Oxprenolol, bisoprolol, nebivolol; other beta-blockers tend to cause constipation more rarely
Bisphosphonate	Alendronic acid
CNS stimulant	Atomoxetine
Calcium channel blocker	Diltiazem, verapamil
Cytotoxic	Bortezomib, buserelin, cladribine, docetaxel, doxorubicin, exemestane, gemcitabine, irinotecan, mitoxantrone, pentostatin, temozolomide, topotecan, vinblastine, vincristine, vindesine, vinorelbine
Dopaminergic	Amantadine, bromocriptine, cabergoline, entacapone, tolcapone, levodopa, pergolide, pramipexole, quinagolide
Growth hormone antagonist	Pegvisomant
Immunosuppressant	Basiliximab, mycophenolate, tacrolimus
Lipid-lowering agent	Cholestyramine, colestipol, rosuvastatin, atorvastatin (other statins uncommon), gemfibrozil
Iron	Ferrous sulphate
Metabolic disorders	Miglustat
Muscle relaxant	Baclofen
NSAID	Meloxicam; other NSAIDs, e.g., aceclofenac and COX-2 inhibitors reported as uncommon
Smoking cessation	Bupropion
Opioid analgesic	All opioid analgesics and derivatives
Ulcer healing	All proton pump inhibitors, sucralfate

CNS, Central nervous system; COX-2, cyclooxygenase-2; NSAIDs, nonsteroidal antiinflammatory drugs.

^aFrequently defined as very common(>10%) or common (1%–10%).

Adapted from Whittlesea, C., Hodson, K. (2018). *Clinical pharmacy and therapeutics* (6th ed.). London: Churchill Livingstone.

gastrointestinal complaints in a primary care setting. Core symptoms of persistent low mood and loss of interest in most activities should trigger referral.

Functional causes in children

Constipation in children is common, and the cause can be varied. Constipation is not normally a result of organic disease but stems from poor diet or a traumatic experience associated with defecation; for example, unwillingness to defecate due to association of prior pain on defecation.

Very unlikely causes

Colorectal cancer

Any patient older than 40 years presenting for the first time with a marked change in bowel habit should be referred.

For further information on colorectal cancer, see earlier in this chapter (diarrhoea entry).

Hypothyroidism

The signs and symptoms of hypothyroidism are often subtle and insidious in onset. Patients might experience weight gain, lethargy, cold intolerance, coarse hair, menstrual irregularities, dry skin and constipation. Hypothyroidism affects 10 times more women than men, and peak incidence is in the fifth or sixth decade. Constipation is often less pronounced than lethargy and cold intolerance.

Fig. 7.12 will aid in the differentiation among common causes of constipation and more serious causes.

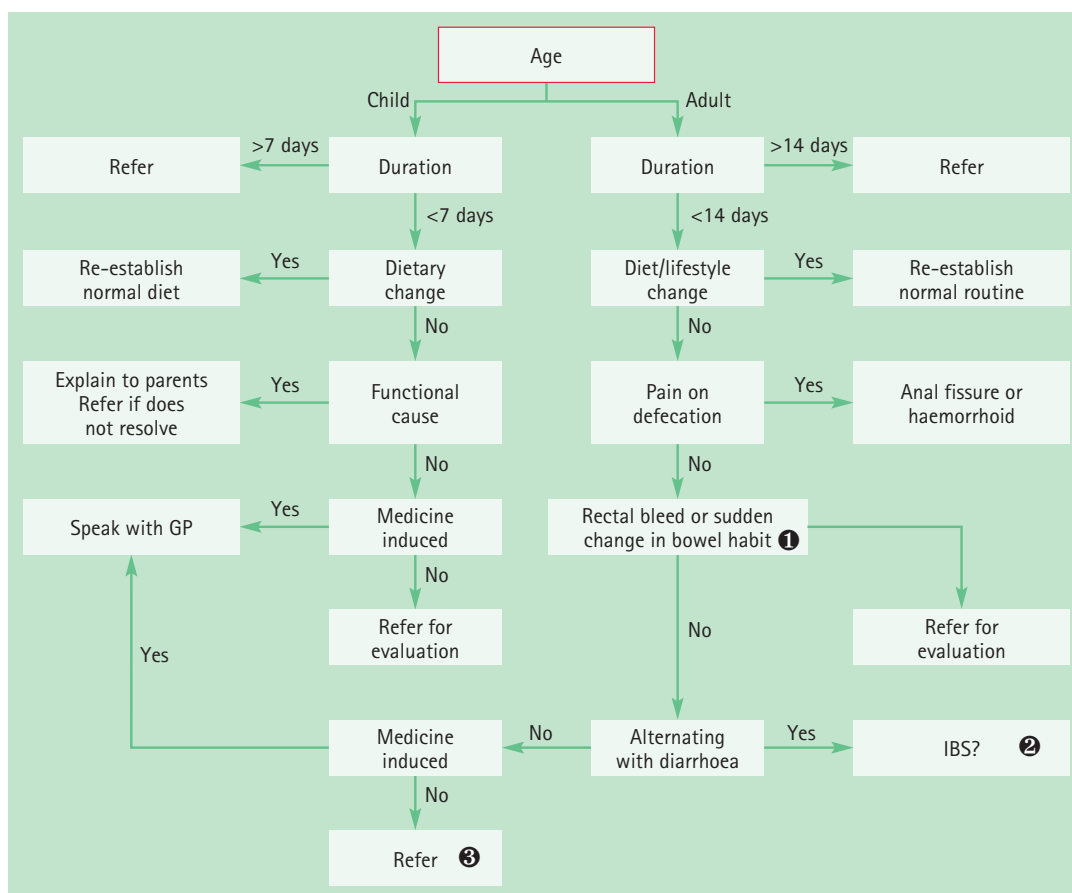


Fig. 7.12 Primer for the differential diagnosis of constipation.

① Patients with unexplained constipation of recent onset accompanied with rectal bleeding should be referred for further investigation; most likely a colonoscopy or sigmoidoscopy and stool culture to eliminate carcinoma.

② See Fig. 7.13 for a primer on the differential diagnosis of irritable bowel syndrome (IBS).

③ If no obvious cause of constipation can be found, referral to the GP is needed for further evaluation.



TRIGGER POINTS indicative of referral

Symptoms/signs	Possible danger/ reason for referral	Urgency of referral
Patients >40 years with a marked change in bowel habits with no obvious cause	Suspect rectal carcinoma	Same-day referral
Longer than 14 days' duration, with no identifiable cause	This requires further investigation to rule out more sinister causes	As soon as practicable
Tiredness	Check for anaemia or thyroid dysfunction	
Pain on defecation that might cause the patient to suppress the defecation reflex	Check for anal fissure	

Evidence base for over-the-counter medication

For uncomplicated constipation, nondrug treatment is advocated as first-line treatment for all patient groups because simple dietary and lifestyle modifications (increasing exercise) will relieve most acute cases of constipation. Advice includes increasing fluid and fibre intake. Dietary fibre increases stool bulk, stool water content, and colonic bacterial load. Fibre intake should be increased to approximately 30 g/day in the form of fruit, vegetables, cereals, grain foods, and whole-grain bread. It is important to remind patients that adequate fluid intake (2 L/day) is needed when following a high-fibre diet; patients might experience excessive gas production, colicky abdominal pain, and bloating. Effects of a high-fibre diet are usually seen in 3 to 5 days.

If medication is required, four classes of OTC laxatives are available—bulk-forming agents, stimulants, osmotics, and stool softeners. Despite their widespread use, surprisingly few well-designed trials have substantiated clinical efficacy.

A systematic review in 1997 identified 36 trials involving 1815 participants who met their inclusion criteria; it involved 25 different laxatives representing all four classes (Tramonte et al., 1997). Twenty of the trials compared laxative against placebo or regular diet, 13 of which

demonstrated statistically significant increases in bowel movement. The remaining 16 trials compared different types of laxatives with each other. The review concluded that laxatives do increase the number of bowel movements and, in 9 of 11 trials studying overall symptom control, laxatives performed significantly better than placebo. Unfortunately, because of a lack of comparative trial data, the review could not conclude which laxative was most efficacious. A more recent review of both stimulant and nonstimulant laxatives in functional constipation also found that all laxative classes are superior to placebo (Paré & Fedorak, 2014). However, comparisons between classes could not be made, with the authors finding only one small study ($N = 40$) that compared stimulant and nonstimulant laxatives.

Summary

Laxatives do work but deciding on which class is more superior over another is not possible, and factors such as the patient's health status, side-effect profile of the medicine and its cost will influence choice.

Practical prescribing and product selection

Prescribing information relating to the medicines used for constipation is discussed and summarized in [Table 7.20](#); useful tips relating to these medicines are given in 'Hints and Tips' in [Box 7.6](#).

OTC products are licensed for use in young children but, in accordance with good practice, children younger than 6 years who have failed to respond to dietary intervention should be referred to their doctor. The discussion that follows does, however, make reference to dosing in children younger than 6 years as some products can be used in this age group.

Bulk-forming laxatives

Bulk-forming laxatives (e.g., ispaghula [psyllium] husk, methylcellulose, sterculia) exert their effect by mimicking increased fibre consumption, swelling in the bowel and increasing faecal mass. In addition, they encourage the proliferation of colonic bacteria, and this helps further increase faecal bulk and stool softness. Patients should be advised to increase their fluid intake while taking bulk-forming medicines. The effect is usually seen in 12 to 36 hours but can take as long as 72 hours. Side effects commonly experienced include flatulence and abdominal distension. They are well tolerated in pregnancy and breastfeeding and have no teratogenic effects. They appear to have no drug interactions of any note.



Table 7.20
Practical prescribing: Summary of medicines for constipation

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
Bulk forming					
Ispaghula (psyllium) husk	>6 years	Flatulence, abdominal bloating	None	None	OK
Methylcellulose	>12 years				
<i>Sterculia</i>	>6 years				
Stimulant					
Senna	>2 years ^a	Abdominal pain	None	None	OK, but use other laxatives in preference to stimulants in pregnancy and breastfeeding
Glycerol	Infants and older ^a				
Sodium picosulfate	>10 years				
Bisacodyl	>4 years ^a				
Osmotic					
Lactulose	Infants and older ^a	Flatulence, abdominal pain, colic	None	None	OK
Magnesium hydroxide	Not recommended				
Stool softeners					
Docusate	>6 months ^a	None reported	None	None	OK

^aIf prescribing to children <6 years, the pharmacist must be competent in prescribing laxatives for children.

Ispaghula husk (Fybogel)

Ispaghula husk has to be reconstituted with water before taking. Adults should take one sachet or two level, 5-mL spoonful twice daily; for children between 6 and 12 years, ½ to one, 5-mL spoonful twice daily.

Methylcellulose

Methylcellulose is only available as Celevac tablets. The adult dose is three to six tablets twice daily, and each dose should be taken with at least 300 mL of liquid.

Sterculia (Normacol and Normacol Plus granules or sachets)

Both *Sterculia* products contain 62% *Sterculia*, but Normacol Plus also contains 8% *Frangula*. The dose for both products is

the same. Adults and children older than 12 years should take one or two sachets or heaped 5-mL spoonful once or twice daily after meals. For children between 6 and 12 years, the dose is half that of the adult dose.

The granules should be placed dry on the tongue and swallowed immediately with plenty of water or a cool drink. They can also be sprinkled onto and taken with soft food, such as yoghurt.

Stimulant laxatives

Stimulant laxatives (e.g., bisacodyl, glycerol, senna, sodium picosulfate) increase GI motility by directly stimulating the colonic nerves. It is this action that presumably causes abdominal pain and is the main side effect associated with stimulant laxatives. Additionally, stimulant laxatives are associated with the possibility of nerve damage with long-term use

HINTS AND TIPS BOX 7.6: CONSTIPATION

Administration of suppositories	<ol style="list-style-type: none"> 1. Wash your hands. 2. Lie on one side with your knees pulled up towards your chest. 3. Gently push the suppository, pointed end first, into your back passage with your finger. 4. Push the suppository in as far as possible. 5. Lower your legs, roll over onto your stomach, and remain still for a few minutes. If you feel your body trying to expel the suppository, try to resist this. Lie still and press your buttocks together. 6. Wash your hands. <p>NOTE: For some suppositories, such as glycerol, it is recommended that the suppository be dipped in water before insertion.</p>
Sachets containing ispaghula husk	Once the granules have been mixed with water, the drink should be taken as soon as the effervescence subsides because the drink sets and becomes undrinkable.
Prolonged use of lactulose	In children, this can contribute to the development of dental caries. Patients should be instructed to pay careful attention to dental hygiene.
Lactulose taste	The sweet taste is unpalatable to many patients, especially if high doses need to be taken.
Bisacodyl	Bisacodyl tablets are enteric-coated, and patients should be told to avoid taking antacids and milk at the same time because the coating can be broken down, leading to dyspepsia and gastric irritation.
Laxative abuse	Some people, especially young women, use laxatives as a slimming aid. Any very slim person who is regularly purchasing laxatives should be politely asked about why they are taking the laxatives. An opening question could be phrased, 'We've noticed that you have been buying quite a lot of these, and we are concerned that you should be better by now. Is there anything we can do for you to help?'
Onset of action	Stimulants are the quickest-acting laxative, usually within 6–12 hours. Lactulose and bulk-forming laxatives may take 48–72 hours before an effect is seen. Stool softeners are the slowest in onset, taking up to 3 days or more to have an effect.
Which laxative to use in pregnancy?	Fibre supplementation and bulk-forming agents are considered to be safe and should therefore be first-line treatments wherever possible. Stimulant laxatives and macrogols also appear to be safe in pregnancy. Stimulant laxatives are more effective than bulk-forming laxatives but are more likely to cause diarrhoea and abdominal pain.
Avoid drinks with caffeine	These can act as a diuretic and serve to make constipation worse.
Combining laxatives	There is little evidence on the beneficial effect of combining different classes of laxatives. However, in refractory cases, this approach might be justifiable.

and are the most commonly abused laxatives. Their onset in action is quicker than other laxative classes, with patients experiencing a bowel movement in 6 to 12 hours when taken orally. They can be taken by all patient groups, have no drug interactions, and are safe in pregnancy and breastfeeding. However, because of their ability to cause muscle contractions, they are best avoided in pregnancy, if possible.

Bisacodyl (*Dulcolax*)

Bisacodyl is available as tablets or suppositories and can be given to patients older than 4 years. The dose for children is

5 mg (one paediatric suppository) and, for adults and children older than 10 years, the dose is 5 to 10 mg (one or two tablets or one Dulcolax 10-mg suppository).

Glycerol suppositories

Glycerol suppositories are normally used when a bowel movement is needed quickly. The patient should experience a bowel movement in 15 to 30 minutes. Varying sizes are made to accommodate use for different ages. The 1-g suppositories are designed for infants, the 2-g for children and the 4-g for adults.

Senna (e.g., Senokot, Ex-Lax Senna)

Senna is available as syrup, tablets, or granules. Dosing of proprietary products differs from those recommended in the British National Formulary (BNF) and BNF for children (BNF-C). Proprietary products tend to have lower dosing schedules than those advocated in the BNF/BNF-C. These are as follows: adults and children older than 12 years should take 15 mg each day (two tablets or 10 mL), preferably at bedtime; children older than 6 years should take half the adult dose (7.5 mg, one tablet, or 5 mL) and those from 2 to 6 years, 3.75 to 7.5 mg (half-tablet to one 5-mL tablet).

Sodium picosulfate (e.g., Dulcolax Pico)

Adults and children over 10 years should take 5 to 10 mg (5–10 mL) at night. In children older than 4 years, the dose is 2.5 to 5 mg (2.5–5 mL).

Osmotic laxatives

These (e.g., lactulose, macrogol [polyethylene glycol] and magnesium salts) act by retaining fluid in the bowel by osmosis or by changing the pattern of water distribution in the faeces. Flatulence, abdominal pain and colic are frequently reported. They can be taken by all patient groups, have no drug interactions and are safely used in pregnancy and breastfeeding.

Lactulose

Lactulose is given twice daily for all ages. The dose for adults is initially 15 mL (adjusted upwards depending on response), for children between 5 and 17 years, the dose is 5 to 20 mL, for those between 1 and 4 years, the dose is 2.5 to 10 mL and for children younger than 1 year, the dose is 2.5 mL. It has been reported that up to 20% of patients experience troublesome flatulence and cramps, although these often settle after a few days. It may take 48 hours or longer to have an effect.

Magnesium salts

Magnesium, when used as a laxative, is usually given as magnesium hydroxide. The adult dose ranges between 30 to 45 mL, when needed. It is commonly prescribed for older adults.

Stool softeners (liquid paraffin and docusate sodium)

Liquid paraffin has traditionally been used to treat constipation. However, the adverse side effect profile of liquid paraffin now means that it should not be recommended because other, safer medicines are available.

Docusate sodium

Docusate sodium is a nonionic surfactant that has stool-softening properties, which allow penetration of intestinal fluids into the faecal mass. It also has weak stimulant properties. Docusate is available as capsules (DulcoEase, Dioctyl) or solution. It can be given to children aged 6 months and older. Children between the age of 6 months and 2 years should take 12.5 mg (5 mL of Docusal paediatric solution) three times a day. For children aged between 2 and 12 years, the dose is 12.5 to 25 mg (5–10 mL) three times a day. Adults and children older than 12 years should take up to 500 mg daily in divided doses. In contrast to liquid paraffin, docusate sodium seems to be almost free of any side effects. Docusate sodium can be given to all patient groups.

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Irritable bowel syndrome

Background

Irritable bowel syndrome (IBS) is one of the most common GI tract conditions seen in primary care. It can be defined as a functional bowel disorder (i.e., absence of abnormality) in which abdominal pain and bloating are associated with a change in bowel habits. The diagnosis is suggested by the presence of long-standing colonic symptoms, without any deterioration in the patient's general health.

Prevalence and epidemiology

Adult prevalence rates in Western countries are reported to be between 10% and 20% and has been increasing. Approximately twice as many women than men are affected. It most commonly affects people between 20 and 30 years old, and onset after the age of 50 years is unusual.

Aetiology

There are no specific anatomical, biochemical or microbiological factors to explain the aetiology of IBS, but it is now clearly understood to be multifactorial. Many factors can contribute to disease expression and include motility dysfunction, diet and genetics. In a small proportion of

cases, symptoms appear after bacterial gastroenteritis. Psychological factors also influence symptom reporting and consultation, and some studies have shown that patients who suffer from higher levels of stress or depression experience worse symptoms compared with other patients. Flare-up of symptoms has also been associated with periods of increased stress. Symptoms of diarrhoea and constipation appear to be linked with hyperactivity of the small intestine and colon in response to food ingestion and parasympathomimetic drugs. Excessive parasympathomimetic activity might account for mucus associated with the stool.

Arriving at a differential diagnosis

IBS is essentially a diagnosis of exclusion, and a careful and thorough history of the patient's symptoms is essential. A number of IBS-specific questions should always be asked of the patient to aid in the differential diagnosis (Table 7.21).

Clinical features of irritable bowel syndrome

IBS is characterized by abdominal pain or discomfort, located especially in the left lower quadrant of the abdomen, which is often relieved by defecation or the passage of wind. Altered defecation, constipation or diarrhoea, with associated bloating is also normally present. People with IBS can present with 'diarrhoea-predominant', 'constipation-predominant', or alternating symptom profiles. During bouts of diarrhoea,



Table 7.21
Specific questions to ask the patient: Irritable bowel syndrome (IBS)

Question	Relevance
Age	IBS usually affects people <45 years. Particular care is required in labelling middle-aged (i.e., >45 years old) and older patients with IBS when presenting with bowel symptoms for the first time. Prevalence of organic bowel disease is more common after the age of 45.
Periodicity	IBS tends to be episodic. The patient might have a history of being well for a number of weeks or months in between bouts of symptoms. Often, patients can trace their symptoms back many years, even to childhood.
Presence of abdominal pain	The nature of pain experienced by patients with IBS is very varied, ranging from localized and sharp to diffuse and aching. It is therefore not very discriminatory; however, the patient will probably have experienced similar abdominal pain in the past. Any change in the nature and severity of the pain is best referred for further evaluation.
Location of pain	Pain from IBS is normally located in the left lower quadrant. For further information on other conditions that cause pain in the lower abdomen, see the abdominal pain section.
Diarrhoea and constipation	Patients with IBS do not have textbook definitions of constipation or diarrhoea, but bowel function will be different than normal. Constipation-predominant IBS is more common in women.

mucus tends to be visible on the stools. Patients might also complain of increased stool frequency but pass normal or pellet-like stools. Diarrhoea on awakening and shortly after meals is also observed in many patients. IBS is likely if the patient has had any of the following symptoms for 6 months:

- Abdominal pain or discomfort
- Bloating
- Change in bowel habit

Conditions to eliminate

Constipation and diarrhoea

Because the major presenting symptom of IBS is an alteration in defecation, it is necessary to differentiate IBS from constipation and diarrhoea. For further information on differentiating these conditions from IBS, please see earlier in this chapter.

Fig. 7.13 will aid in the differentiation of IBS from other abdominal conditions.

! TRIGGER POINTS indicative of referral: IBS		
Symptoms/signs	Possible danger/ reason for referral	Urgency of referral
Blood in the stool	The presence of blood in the stool is unusual in IBS and can suggest inflammatory bowel disease	As soon as practicable
Fever Nausea and/or vomiting Severe abdominal pain	Not usually associated with IBS; suggests origin of symptoms from other abdominal causes	
Children < 16 years Patients > 45 years with recent changes to bowel habit	IBS is unusual in these age groups. Refer for further investigation	
Steatorrhoea	Associated with malabsorption syndromes	

Evidence base for over-the-counter medication

Before medicines are recommended, it might be useful to discuss if stress is a factor and if this can be avoided. In addition, dietary modification has shown to be effective for some patients (see 'Hints and Tips' in Box 7.7). If diet is deemed a major contributor towards symptoms, food avoidance can be tried. Suspected food products must be excluded from the diet for a minimum of 2 weeks and then gradually reintroduced to determine whether the food item triggers symptoms.

Antispasmodics are considered first-line pharmacological intervention for IBS, although the evidence base for them is weak; these include mebeverine, alverine, hyoscine and peppermint oil. In addition, bulk-forming and stimulant laxatives can be used to treat constipation-predominant IBS and loperamide for diarrhoea-predominant IBS. Both laxatives and diarrhoeals can be taken on a regular basis using the lowest effective dose. The following section only concentrates on the evidence for products specifically marketed for the treatment of IBS.

Antispasmodics

A Cochrane review (Ruepert et al., 2011) concluded that antispasmodics as a class of medicines compared with placebo provide a statistically significant benefit for abdominal pain, global assessment and IBS symptom scores. However, as the authors acknowledged, antispasmodics are pharmacologically diverse and, in their review, it was not possible to include all compounds (due to a limited number of studies) at subgroup analysis. Therefore, in this review, it was not possible to determine the individual effectiveness of certain OTC antispasmodics. No data were reviewed for alverine, and only one trial was included that considered mebeverine. In that trial (Kruis et al., 1986), no statistically significant effect for improvement of global assessment was found. This was also the case for hyoscine. The only OTC product for which the review found evidence of efficacy was peppermint oil. For peppermint oil, a statistically significant effect for improvement of global assessment and for improvement of IBS symptom score was found.

Alternative treatments

Herbal remedies

Herbal remedies for IBS have been subject to a Cochrane review (Liu et al., 2006). In this report, 75 trials were reviewed, involving 71 different herbal medicines versus placebo or conventional pharmacological treatment. When compared against placebo, STW 5 (iberogast) and STW5-II, Padma Lax, Ton Gxie Yao Fang and Ayurvedic preparations showed significant improvement of global symptoms. Compared with conventional therapy (in 65 trials testing 51 different herbal medicines), 22 herbal medicines demonstrated

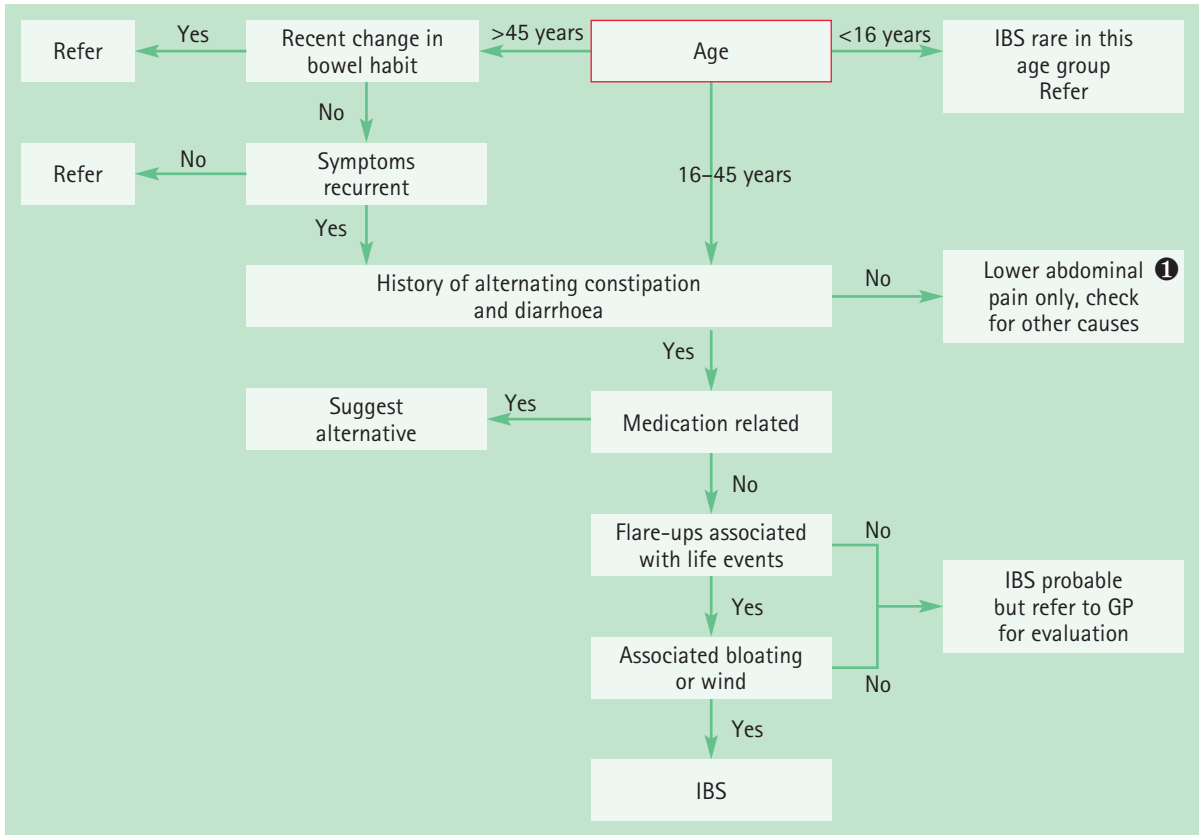


Fig. 7.13 Primer for differential diagnosis of irritable bowel syndrome.

❶ Lower abdominal pain. See Fig. 7.29 for a primer on the differential diagnosis of abdominal pain.

HINTS AND TIPS BOX 7.7: IRRITABLE BOWEL SYNDROME

Dietary advice ^a	<p>Have regular meals and avoid missing meals.</p> <p>Drink at least eight cups of fluid per day, especially noncaffeinated drinks.</p> <p>Reduce intake of alcohol and fizzy drinks.</p> <p>Consider limiting intake of high-fibre food.</p> <p>Reduce intake of so-called resistant starch often found in processed or recooked foods.</p> <p>Limit fresh fruit to three portions per day.</p>
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^aAdapted from National Institute for Health and Care Excellence (NICE) Guidelines. Taken from NICE CG61. <https://www.nice.org.uk/guidance/cg61>

a statistically significant benefit for symptom improvement. Most trials were, however, deemed to be of poor methodological quality and the authors concluded that findings should be interpreted with caution.

Probiotics

Probiotics, such as *Lactobacillus* and *Bifidobacterium*, have also been promoted for IBS. A systematic review identified 18 studies using probiotics alone or in combination for the

treatment of IBS (Moayyedi et al., 2010). The results suggested that probiotics significantly improved IBS symptoms, and there was no apparent difference across the probiotics. However, the authors noted that there was potential publication bias in the review, with an overrepresentation of small positive studies; therefore, these estimates of efficacy were likely to be overestimates. The authors concluded that probiotics appear to be effective in IBS; however, the size of the effect and the effectiveness of individual probiotics is still to be established. Conclusions from a recent systematic review by the British Dietetic Association (McKenzie et al., 2016) recommended that although probiotics are unlikely to provide substantial benefits, if individuals choose to try them, they should try one at a time and for a minimum of 4 weeks before switching or stopping.

Relaxation therapy and cognitive behavioural therapy
A 2009 Cochrane review concluded that cognitive-behavioural therapy might be effective, although studies included in the review were of poor quality (Zijdenbos et al., 2009).

Hypnotherapy

Hypnotherapy might be effective in treating IBS symptoms, including abdominal pain, but studies reviewed were of poor quality and small size, so the findings need to be interpreted with caution (Webb et al., 2007).

Practical prescribing and product selection

Prescribing information relating to the medicines used for IBS is discussed and summarized in [Table 7.22](#); useful tips

relating to the treatment of patients with IBS are given in 'Hints and Tips' in [Box 7.7](#).

All marketed products can be given to children (see individual entries) but anyone younger than 16 years suspected of having IBS should be referred to a doctor because IBS in this age group is unusual.

Hyoscine butyl bromide (Buscopan IBS Relief, Buscopan Cramps)

The recommended starting dose for adults is one tablet, three times a day, although this can be increased to two tablets, four times a day, if necessary. Buscopan Cramps can be given to children over the age of 6 (one tablet, three times a day). It is a quaternary derivative of hyoscine, so it does not readily cross the blood-brain barrier; therefore, sedation is not normally experienced, although it might cause dry mouth and skin rash, but these are uncommon. Because of its anticholinergic effects, it is best avoided with other medicines that also have anticholinergic effects; for example, antihistamines, tricyclic antidepressants, neuroleptics and disopyramide. It can be given during pregnancy and breastfeeding but avoided if possible. It should also be avoided in patients with glaucoma, myasthenia gravis and prostate enlargement.

Mebeverine

Adults should take one tablet, three times a day, preferably 20 minutes before meals. Mebeverine (Colofac IBS) is not



Table 7.22

Practical prescribing: Summary of irritable bowel syndrome (IBS) medicines

Name of medicine	Use in children ^a	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
Hyoscine	>6 years	None	Tricyclic antidepressants, neuroleptics, antihistamines, disopyramide	Glaucoma, myasthenia gravis, prostate enlargement	Avoid if possible, although single doses in breastfeeding are acceptable
Mebeverine	>18 years	None	None	None	OK
Peppermint oil	>15 years	None	None	None	OK in pregnancy; try to avoid in breastfeeding because it may reduce milk supply
Alverine	>12 years	None	None	None	OK

^aIrritable bowel syndrome (IBS) is unusual in children. Any person <16 years presenting with IBS-like symptoms should be referred for further evaluation.

known to interact with other medicines, has no cautions in its use, and can be given in pregnancy and breastfeeding, although there is a lack of detailed studies. It is associated with very few side effects, although allergic reactions have been reported, but their frequency has not been established.

Alverine

Adults and children over 12 years should take one or two capsules, three times a day. Like mebeverine, alverine (Spasmonal) is not known to interact with other medicines, has no cautions in its use, and can be given in pregnancy and whilst breastfeeding. It has no interactions with other medicines and can be used by all patient groups. Rash, nausea, headache, dizziness, itching and allergic reactions have been reported but their incidence is unknown.

Peppermint oil

Adults and children older than 15 years can take peppermint oil (Colpermin IBS Relief). The dosage is one capsule, three times a day, before food, which can be increased to two capsules, three times a day, for severe symptoms. It can cause heartburn and allergic rashes but the incidence of these are difficult to determine. It is safe to use in pregnancy but, in theory, can decrease breast milk production. It has no drug interactions and can be used by all patient groups.

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Websites

- IBS therapists specialising in hypnotherapy: <http://www.ibs-register.co.uk>
- Irritable Bowel Syndrome Self Help and Support Group: <http://www.ibsgroup.org>

Haemorrhoids

Background

Haemorrhoids (piles) are the most common problem affecting the anorectal region. Patients might feel embarrassed talking about symptoms, and it is therefore important that any requests for advice are treated sympathetically and away from others to avoid embarrassing the patient.

Prevalence and epidemiology

The exact prevalence of haemorrhoids is unknown but it is very common. Reports vary, but upwards of one in two people will experience at least one episode at some point during their lives. Haemorrhoids can occur at any age but are rare in children and adults younger than 20 years. It affects both sexes equally and is more common with increasing age, especially in people from 45 to 65 years. There is a high incidence of haemorrhoids in pregnant women.

Aetiology

The cause of haemorrhoids is probably multifactorial, with anatomical (degeneration of elastic tissue), physiological (increased anal canal pressure) and mechanical (straining at stool) processes implicated. Haemorrhoids have been traditionally described as engorged veins of the haemorrhoidal plexus. The analogy of varicose veins of the anal canal is often used but is misleading. Current thinking favours the theory of prolapsed anal cushions. Anal cushions maintain fine continence; these are submucosal vascular structures suspended in the canal by a connective tissue framework derived from the internal anal sphincter and longitudinal muscle. Within each of the three cushions is a venous plexus fed by an arteriovenous blood supply. Veins in these cushions fill with blood when sphincters inside them relax and empty when the sphincters contract. Fragmentation of the connective tissue supporting the cushions leads to their descent. The prolapsed anal cushion has impaired venous return, resulting in venous stasis and inflammation of the cushion's epithelium.

Haemorrhoids are classified as internal or external. This distinction is an anatomical one. Superior to the anal sphincter, there is an area known as the *dentate line*. At this junction, epithelial cells change from squamous to columnar epithelial tissue. Above the dentate line, haemorrhoids are classified as internal and below, external. Furthermore, internal haemorrhoids are graded according to severity: grade I,

do not prolapse out of the anal canal; grade II, prolapse on defecation but reduce spontaneously; grade III, require manual reduction; and grade IV, cannot be reduced.

Arriving at a differential diagnosis

In the first case, most patients with anorectal symptoms will self-diagnose haemorrhoids and often self-treat. Bleeding tends to cause the greatest concern and often motivates the patient to seek help. Invariably, rectal bleeding is of little consequence but should be thoroughly investigated to exclude other pathology (Table 7.23). A number of haemorrhoid-specific questions should always be asked (Table 7.24).

Table 7.23
Causes of rectal bleeding and their relative incidence in community pharmacy

Incidence	Cause
Most likely	Haemorrhoids
Likely	Anal fissure
Unlikely	Ulcerative colitis and Crohn's disease
Very unlikely	Upper GI bleeds, colorectal and anal cancers, diverticulitis



Table 7.24
Specific questions to ask the patient: Haemorrhoids

Question	Relevance
Duration	Patients with haemorrhoids tend to have had symptoms for some time before requesting advice. However, patients with symptoms that have been constantly present for >3 weeks should be referred.
Pain	Pain, if experienced, tends to occur on defecation but is also noticed at other times for example when sitting. Pain is usually described as a dull ache. Sharp or stabbing pain at the time of defecation can suggest an anal fissure or tear.
Rectal bleeding	Slight rectal bleeding is often associated with haemorrhoids. Blood appears bright red and might be visible on the toilet bowl, surface of the stool or pink-coloured water in the toilet bowl. Rectal bleeding is usually a direct referral sign but if due to haemorrhoids referral is usually not necessary unless the patient is unduly anxious. Blood mixed in the stool has to be referred to eliminate a GI bleed. Large volumes of blood or blood loss not associated with defecation must be referred to eliminate possible carcinoma.
Associated symptoms	Symptoms associated with haemorrhoids are usually localized; for example, anal itching. Other symptoms such as nausea, vomiting, loss of appetite and altered bowel habits should be viewed with caution and underlying pathology suspected. Referral would be needed.
Diet	A lack of dietary fibre that leads to constipation is a contributory factor to haemorrhoids. The passage of hard stools and straining during defecation can cause haemorrhoids. Find out about the patient's diet and current bowel habits.

GI, Gastrointestinal.

Clinical features of haemorrhoids

Symptoms experienced by the patient are dependent on the severity or type of haemorrhoid. Bright red painless rectal bleeding is the most common symptom. Blood is usually seen as spotting around the toilet, streaking on toilet tissue or visible on the surface of the stool. Itching and irritation are also commonly observed. Symptoms are often intermittent, and each episode usually lasts from a few days to a few weeks. Internal haemorrhoids are rarely painful, whereas external haemorrhoids can cause pain due to the cushion becoming thrombosed. Pain is described as a dull ache that increases in severity when the patient defecates, leading to patients ignoring the urge to defecate. This can then lead to constipation, which in turn will lead to more difficulty in passing stools and further increase the pain associated with defecation.

Conditions to eliminate

Dermatitis-related conditions

Localized anal itching can result from dermatitis or even threadworm infection. If pruritus is the major presenting symptom, contact dermatitis should be considered and is often caused by toiletries.

Medication

Because constipation is a contributory factor in the manifestation of haemorrhoids, medicines that are prone to causing constipation should, if possible, be avoided. Table 7.19 lists medicines that are commonly known to cause constipation.

Conditions causing rectal bleeding

A number of conditions can present with varying degrees of rectal bleeding. However, other symptoms should be present, which will allow them to be excluded.

Anal fissure

Anal fissures are common, with the 15- to 40-year-old age group most affected; they are also often experienced during pregnancy. Symptoms often follow a period of constipation and are normally caused by straining at stool. Pain always occurs with defecation, which can be severe and sharp, with pain lasting for a number of hours after defecation. Bright red blood is commonly seen. Nonurgent referral is necessary for confirmation of the diagnosis.

Ulcerative colitis and Crohn's disease

In mild cases of both conditions, bloody diarrhoea is one of the major presenting symptoms. However, other symptoms are usually present and are described on page 185.

Upper gastrointestinal bleeds

Erosion of the stomach wall or upper intestine is normally responsible for GI bleeds and is often associated with NSAID intake. The colour of the stool is related to the rate of bleeding. Stools from GI bleeds can be tarry (indicating a bleed of 100–200 mL of blood) or black (indicating a bleed of 400–500 mL of blood). Urgent referral is needed.

Colorectal and anal cancer

Rectal bleeding is observed in both cancers but bleeding can depend on the site of the tumour; for example, sigmoid tumours lead to bright red blood in or around the stool. Rectal bleeding tends to be persistent and steady though slight for all tumours. Any patient older than 40 years presenting for the first time with a marked change in bowel habit should be referred. For further information on colorectal cancer, see under diarrhoea.

Diverticular disease

This is usually associated with intermittent left lower abdominal pain, bloating and changes in bowel habits. However, it may present with painless rectal bleeding. Its incidence increases with increasing age.

Fig. 7.14 will aid in the differentiation of haemorrhoids.



TRIGGER POINTS indicative of referral: Haemorrhoids

Symptoms/signs	Possible danger/reason for referral	Urgency of referral
Persistent or marked change in bowel habit in patients >40 years Unexplained rectal bleeding	Sinister pathology?	Urgent to doctor
Blood mixed in the stool Fever	Suspect GI bleeds or inflammatory bowel disease	
Patients who have to reduce their haemorrhoids manually	OTC treatment will not help	As soon as practicable
Severe pain associated with defecation	Anal fissure?	

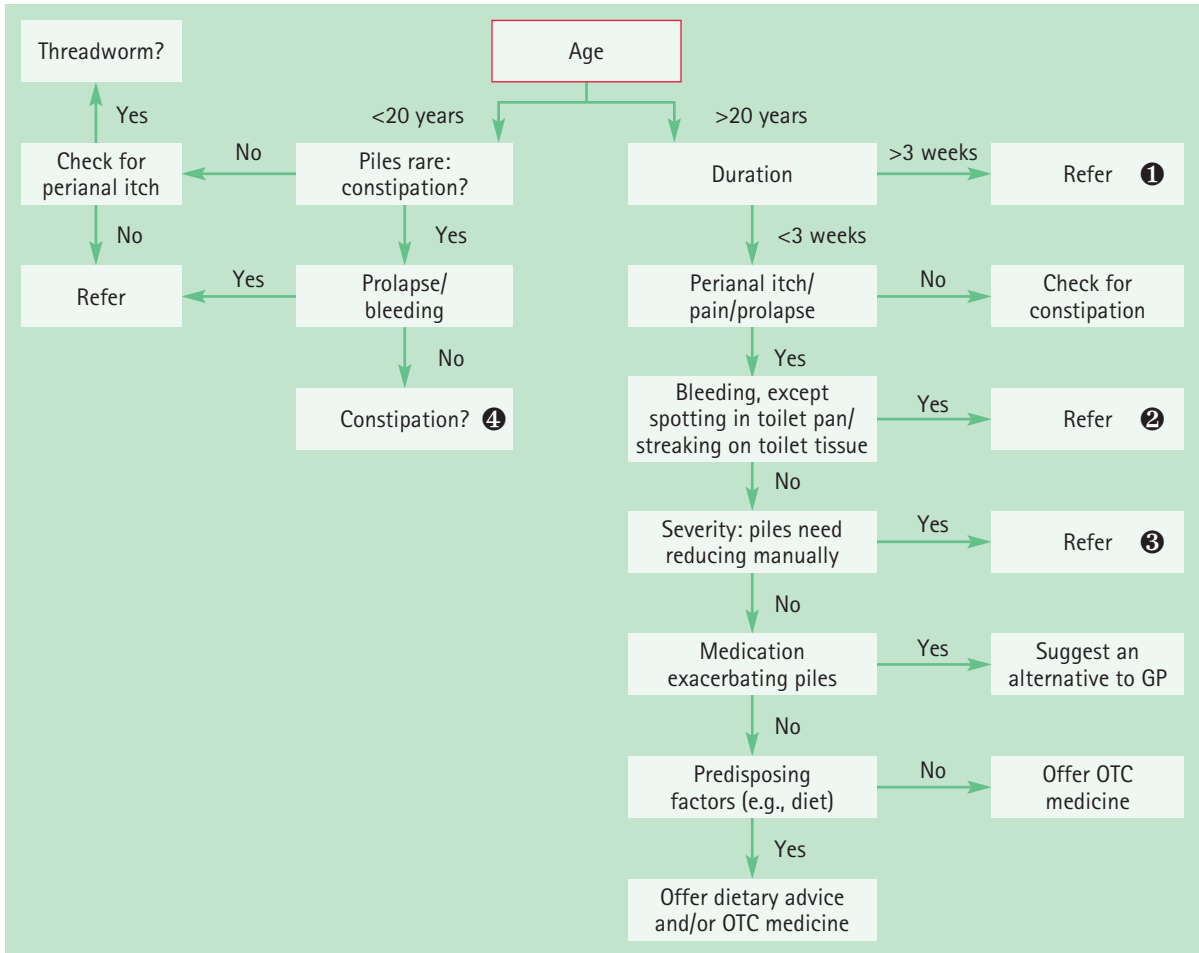


Fig. 7.14 Primer for the differential diagnosis of haemorrhoids.

- ① Duration. Patients with long-standing symptoms that have not been seen previously by the GP should be referred to eliminate any underlying pathology. In the vast majority of cases, no sinister findings will result.
- ② Rectal bleeding. In most cases, rectal bleeding is a sign of referral. However, in cases where sinister pathology has been

excluded and only mild local bleeding has occurred, the pharmacist could instigate treatment.

- ③ Severity. Medication is unlikely to help any patient who has to reduce haemorrhoids manually. Referral for other treatments is recommended.

- ④ Constipation. See Fig. 7.12.

Evidence base for over-the-counter treatment and pharmacological medications

Diet

Reviews by Alonso-Coello et al. (2005, 2006) have concluded that general measures to prevent constipation will help decrease straining during defecation, ease the symptoms of haemorrhoids, and reduce recurrence. Patients should therefore be asked about their normal diet to determine fibre

intake. Those with diets low in fibre should be encouraged to increase their fibre and fluid intake because this will help produce softer stools and reduce constipation. Patients should try to eat more fruit, vegetables, bran and whole-grain bread. If this is not possible, fibre supplementation with a bulk-forming laxative could be recommended. Bulk-forming laxatives will take 2 to 3 days to relieve constipation and may take up to 6 weeks to improve symptoms of haemorrhoids.

Pharmacological intervention

Numerous products are marketed for the relief and treatment of haemorrhoids. These include a wide range of therapeutic agents and commonly include anaesthetics, astringents, antiinflammatories and protectorants. Most products contain a combination of these agents.

The inclusion of such a diverse range of chemical entities appears to be based largely on theoretical grounds rather than any evidence base. Extensive literature searching found only one published trial regarding the efficacy of any marketed product (Ledward, 1980); however, this trial suffered from serious methodological flaws.

Anaesthetics

Few studies in English appear to have been published using local anaesthetics (e.g., lidocaine) to treat and relieve symptoms of haemorrhoids. A small study ($N = 89$) comparing two commercial ointment and suppository preparations containing hydrocortisone and cinchocaine (Uniroid, Proctosedyl) found that both products improved pain and itching (Smith & Moodie, 1988). Although the authors concluded that they were efficacious in most patients, given the poor quality of the trial design (e.g., open label) and the lack of placebo comparator, it is difficult to draw any conclusions about their efficacy. However, anaesthetics have proven efficacy when used on other mucosal surfaces; their use could therefore be justifiably recommended. Their action is short-lived and will produce temporary relief from perianal itching and pain. They require frequent application and might therefore cause skin sensitization.

Astringents (allantoin, bismuth, zinc, Peru balsam)

Astringents are included in haemorrhoid preparations on the theoretical basis that they precipitate surface proteins, thus producing a protective coat over the haemorrhoid. However, there appears to be no evidence to support this theory. Certain proprietary products only contain astringents and, at best, will provide a placebo effect.

Antiinflammatory drugs

Steroids (e.g., hydrocortisone) have proven effectiveness in reducing inflammation and would therefore be useful in reducing haemorrhoidal swelling; however, trials with OTC products containing hydrocortisone appear not to have been undertaken.

Protectorants (e.g., shark liver oil)

Protectorants are claimed to provide a protective coating over the skin and thus produce temporary relief from pain and perianal itch. These claims cannot be substantiated and, as with

astringents, any benefit conveyed by a protectorant is probably a placebo effect. In addition, there is an ethical dimension to using a product with no efficacy sourced from sharks.

Other agents

Sclerosing agents (e.g., lauromacrogol), and wound-healing agents (e.g., yeast cell extract) can also be found in some products. There is no evidence supporting their effectiveness.

Flavonoids

Dietary supplementation with flavonoids is a common alternative treatment that is popular in continental Europe and the Far East. As an adjunct, their use has been shown to reduce acute symptoms and secondary haemorrhage after haemorrhoidectomy.

Summary

With so little data available on their effectiveness, it is impossible to say whether any product is a credible treatment for haemorrhoids, and many medical authorities regard them as little more than placebos. It seems prudent to recommend products containing a local anaesthetic or hydrocortisone because they do have proven effectiveness in other similar conditions.

Treatment should only be recommended to patients with mild haemorrhoids. Any person complaining of prolapsing haemorrhoids, which need reducing by the patient, should be referred because these patients might require nonsurgical intervention with sclerotherapy or rubber band ligation. If these fail to effect a cure, a haemorrhoidectomy might be performed.

Practical prescribing and product selection

Prescribing information relating to the medicines used for haemorrhoids is discussed and summarized in [Table 7.24](#). The licenses of products for haemorrhoids allow them to be used in all patient groups, except children under 12 years of age. (NOTE: good practice dictates that people under 20 years suspected of haemorrhoids should be referred.) They do not interact with any other medicines and can be used in pregnancy and breastfeeding. The standard dose for any formulation is twice daily, plus an application after each bowel movement. Minimal side effects have been reported but are usually limited to slight irritation. Products that contain hydrocortisone are subject to several licensing restrictions; they are restricted to use in patients over a certain age (Perinal spray, 14 years; Germoloids spray, 16 years; Anusol range, 18 years), no longer than 1 week's duration, and not for use in pregnant or lactating women.



Table 7.25
Practical prescribing: Summary of haemorrhoid products

Product	Form	Anaesthetics	Astringents	Steroids	Protectorants
Anacal ^a	Ointment	No	No	No	No
Anodesyn	Ointment or suppository	Yes	Yes	No	No
Anusol	Cream, ointment or suppository	No	Yes	No	No
Anusol Plus HC; Anusol Soothing Relief	Ointment or suppository	No	Yes	Yes	No
Germoloids	Cream, ointment or suppository	Yes	Yes	No	No
Germoloids HC	Spray	Yes	No	Yes	No
Hemocane	Cream	Yes	No	No	No
Perinal	Spray	Yes	No	Yes	No
Preparation H ^b	Ointment	No	No	No	Yes
Preparation H	Gel	No	Yes	No	No

^aContains a sclerosing agent.

^bContains yeast cell extract.

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Further reading

- Sneider, E. B., & Maykel, J. A. (2010). Diagnosis and management of symptomatic hemorrhoids. *The Surgical Clinics of North America*, 90(1), 17–32.

Abdominal pain

Background

Abdominal pain is a symptom of many different conditions, ranging from acute self-limiting problems to life-threatening conditions such as ruptured appendix and bowel obstruction. The overwhelming majority of cases seen in a community pharmacy will be of a nonserious nature, self-limiting and not require medical referral. The most common conditions that present to community pharmacies are dyspepsia affecting the upper abdomen, primary dysmenorrhoea, and IBS affecting the lower abdomen. These are covered in more detail elsewhere in this chapter. However, other conditions will present with abdominal pain (Table 7.25); these are covered more thoroughly in this section. This book takes a *four-quadrant approach* to describe the location of signs and symptoms (Fig. 7.15).

Prevalence and epidemiology

The prevalence and epidemiology of abdominal pain within the population are determined by those conditions that cause it. Because so many conditions can give rise to abdominal

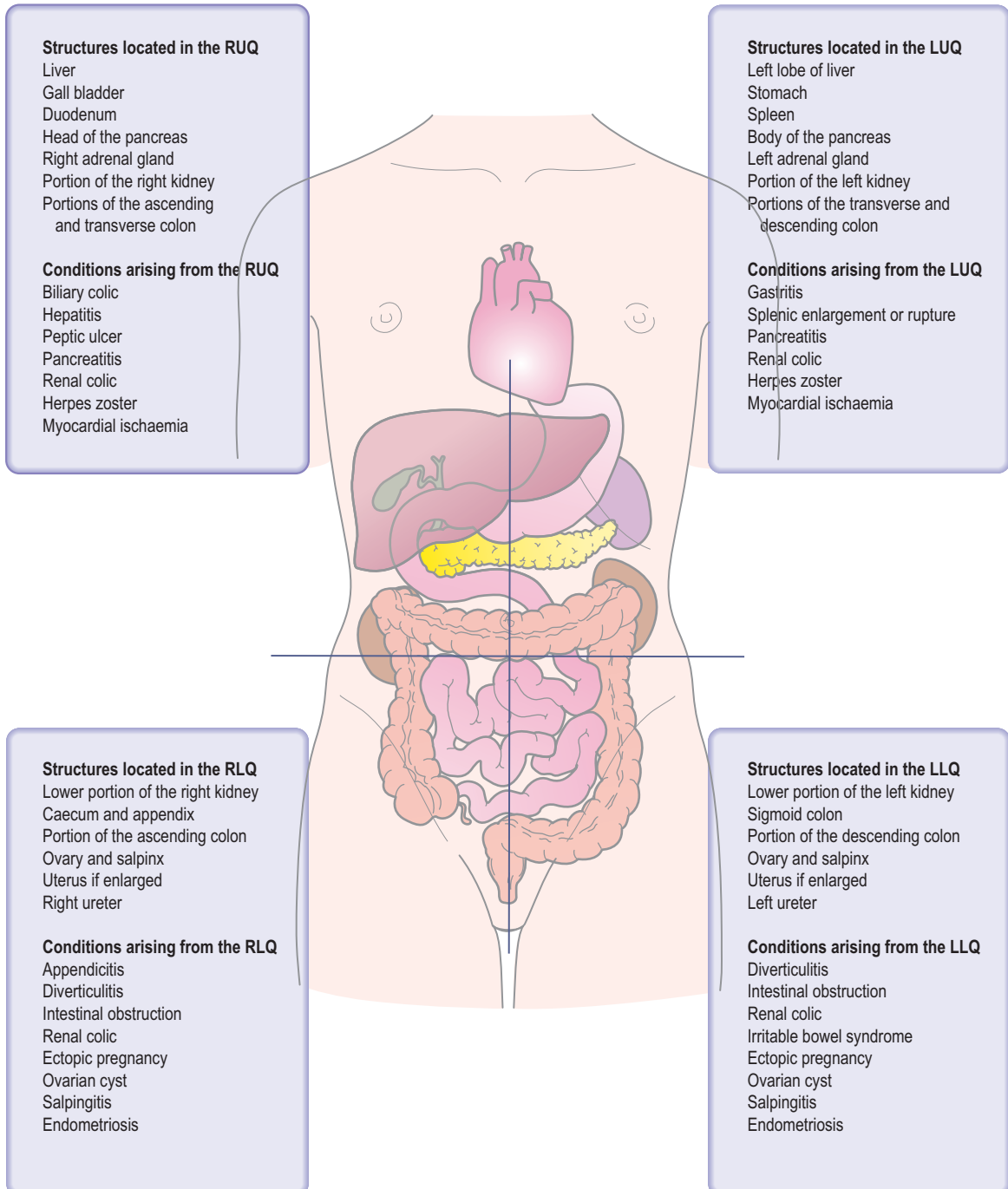


Fig. 7.15 Anatomical location of organs and conditions that can cause abdominal pain. *LLQ*, Left lower quadrant; *LUQ*, left upper quadrant; *RLQ*, right lower quadrant; *RUQ*, right upper quadrant.

pain, it is likely that most of the population will, at some point, suffer from abdominal pain. For example, one study found that 40% of the UK population had suffered from dyspepsia during the previous 12 months.

Aetiology

Abdominal pain not only arises from the GI tract but also from the cardiovascular and musculoskeletal systems

Table 7.26
Causes of abdominal pain

Probability	Cause		
	Upper abdomen	Lower abdomen	Diffuse
Most likely	Dyspepsia	Irritable bowel syndrome, primary dysmenorrhoea	Gastroenteritis
Likely	Peptic ulcers	Diverticulitis (older patient)	Not applicable
Unlikely	Cholecystitis, cholelithiasis, renal colic	Appendicitis, endometriosis, renal colic	Not applicable
Very unlikely	Splenic enlargement, hepatitis, myocardial infarction	Ectopic pregnancy, salpingitis, intestinal obstruction	Pancreatitis, peritonitis

(Table 7.26). Therefore, abdominal pain is dependent on its cause. GI tract causes, include poor muscle tone leading to reflux (e.g., lower oesophageal sphincter incompetence), infections that cause peptic ulcers (from *H. pylori*), and mechanical blockages causing renal and biliary colic. Cardiovascular causes include angina and myocardial infarction, whereas musculoskeletal problems often involve tearing of abdominal muscles.

Arriving at a differential diagnosis

The main role of the community pharmacist is to identify symptoms in patients that suggest more serious pathology so that patients can be further evaluated. This is not easy because many abdominal conditions do not present with

classic textbook symptoms, and patients tend to present to the pharmacist early in the course of the disease, often before the presenting symptoms have assumed the more usual textbook description. The low prevalence of serious disease and overlapping symptoms with minor illness make the task even more difficult. Single symptoms are poor predictors of final diagnosis (except for reflux oesophagitis, in which the presence of heartburn is highly suggestive). It is therefore important to look for symptom clusters and to use knowledge of the incidence and prevalence of conditions to determine whether referral is needed. This necessitates taking a very careful history and not relying on a single symptom to label a patient with a particular problem. Specific questions relating to abdominal pain should be asked (Table 7.27).



Table 7.27
Specific questions to ask the patient: Abdominal pain

Question	Relevance
Location of pain	Knowing the location of major organs and associated structures is extremely helpful in differential diagnosis (see Fig. 7.13) because pain in many conditions will be concentrated where the organ is situated.
Nature of the pain	Heartburn is typically associated with a retrosternal burning sensation. Cramplike pain is seen in diverticulitis, IBS, salpingitis and gastroenteritis. Colicky pain (pain that comes and goes) has been used to describe the pain of appendicitis, biliary and renal colic, and intestinal obstruction. Gnawing pain is associated with pancreatitis and pancreatic cancer and boring pain with ulceration.
Radiating pain	Abdominal pain that moves from its original site should be viewed with caution. Pain that radiates to the jaw, face and arm could be cardiovascular in origin. Pain that moves from a central location to the right lower quadrant could suggest appendicitis. Pain radiating to the back may suggest peptic ulcer or pancreatitis.
Severity of pain	Nonserious causes of abdominal pain generally do not give rise to severe pain. Pain scores should be used to try and quantify severity. For example, 0 indicates no pain, and 10 the worst pain imaginable. Scores higher than 6 suggest a high degree of pain and need to be referred.

Continued



Table 7.27
Specific questions to ask the patient: Abdominal pain (Continued)

Question	Relevance
Age of patient	With increasing age, abdominal pain is more likely to have an identifiable and serious organic cause. Appendicitis is the only serious abdominal condition that is much more common in young patients.
Onset and duration	In general, if no identifiable cause can be found, abdominal pain with a sudden onset is generally a symptom of more serious conditions; for example, peritonitis, appendicitis, ectopic pregnancy, renal and biliary colic. Pain that lasts >6 hours is suggestive of underlying pathology.
Aggravating or ameliorating factors	Biliary colic can be aggravated by fatty foods. Vomiting tends to relieve pain in gastric ulcers. Pain in duodenal ulcer is relieved after ingestion of food. Pain in salpingitis and appendicitis is often made worse by movement.
Associated symptoms	Vomiting, weight loss, melaena, altered bowel habits and haematemesis are all symptoms that suggest more serious pathology and require referral.

Conditions affecting the upper abdomen

Left upper quadrant pain

Dyspepsia and gastritis

Patients with dyspepsia present with a range of symptoms that commonly involve vague abdominal discomfort (aching) above the umbilicus (Fig. 7.16) associated with belching, bloating, flatulence, a feeling of fullness and heartburn. It is normally relieved by antacids and aggravated by certain foods or excessive caffeine. Vomiting is unusual. For further information on dyspepsia, see earlier section in this chapter.

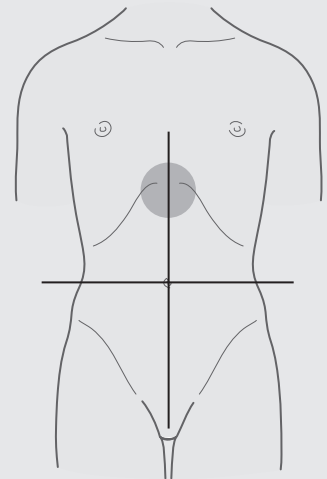


Fig. 7.16 The position of pain in gastritis and dyspepsia.

Splenic enlargement or rupture

If the spleen is enlarged, generalized left upper quadrant pain associated with abdominal fullness and early feeding satiety is observed (Fig. 7.17). Referred pain to the left shoulder is sometimes seen. The condition is rare and is nearly always secondary to another primary cause, which might be an infection, a result of inflammation or haematological in origin.

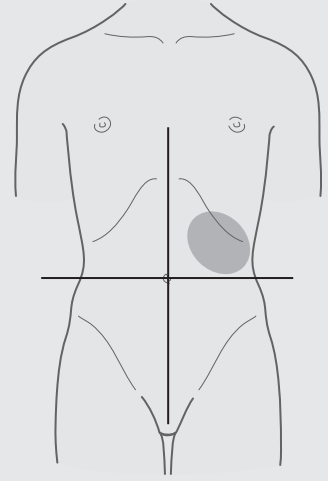


Fig. 7.17 The position of pain associated with splenic enlargement.

Right upper quadrant pain***Acute cholecystitis and cholelithiasis***

Cholelithiasis (presence of gallstones in the bile ducts, also called *biliary colic*) is the more common presentation (Fig. 7.18). Typically, the pain lasts for more than 30 minutes, but less than 8 hours and is colicky in nature and often severe. Nausea and vomiting are often present. Typically, the onset is sudden, starts a few hours after a meal and frequently awakens the patient in the early hours of the morning. In acute cholecystitis (inflammation of the gallbladder), symptoms are similar but are also associated with fever and abdominal tenderness. The pain may radiate to the tip of the right scapula. The incidence of both increases with increasing age and is most common in people older than 50 years. It is also more prevalent in women than in men.

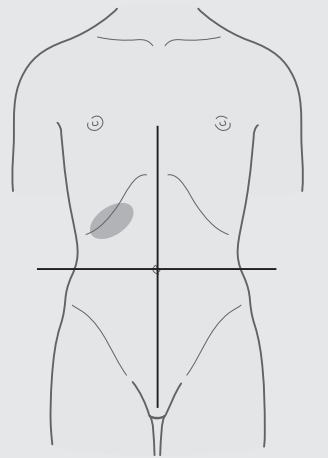


Fig. 7.18 The position of pain associated with acute cholecystitis and cholelithiasis.

Hepatitis

Liver enlargement from any type of hepatitis will cause discomfort or dull pain around the right rib cage (Fig. 7.19). Associated early symptoms are general malaise, tiredness, skin rash (pruritus) and nausea. On examination, there is normally hepatic tenderness.

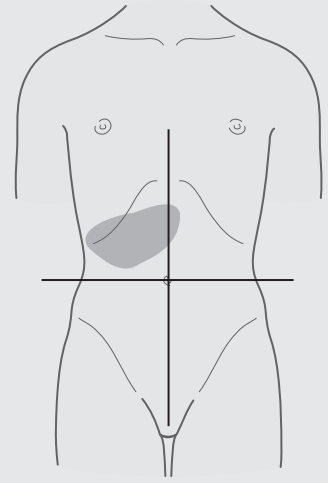


Fig. 7.19 The position of pain associated with hepatitis.

Ulcers

Pain of ulcers are localized midepigastria pain (Fig. 7.20) described as constant, annoying and/or gnawing and boring. For more information on peptic ulcers, please see earlier in this chapter.

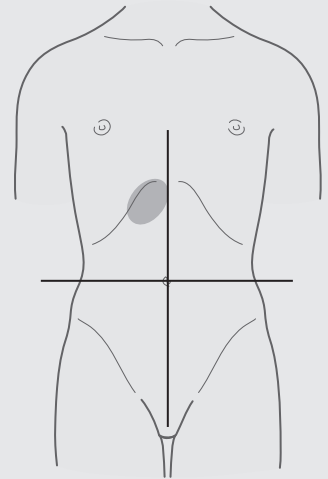


Fig. 7.20 The position of pain associated with ulcers.

Pain affecting right and left upper quadrants**Acute pancreatitis**

Pain of pancreatitis develops suddenly and is described as agonizing and constant, with the pain being centrally located (epigastric) that often radiates into the back (Fig. 7.21). Pain reaches its maximum intensity within minutes and can last hours or days. Vomiting is common but does not relieve the pain. Early in the attack, patients might get relief from the pain by sitting forwards. It is commonly seen in those that misuse alcohol (25% of cases) or suffer from gallstones (50% of cases). Patients are very unlikely to present in a community pharmacy due to the severity of the pain, but a mild attack could present with steady epigastric pain that is sometimes centred close to the umbilicus and can be difficult to distinguish from other causes of upper quadrant pain.

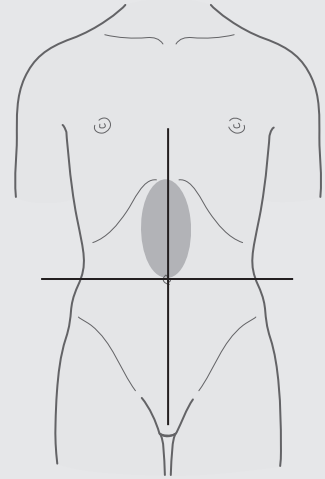


Fig. 7.21 The position of pain associated with pancreatitis.

Renal colic

Urinary calculi (stones) can occur anywhere in the urinary tract, although usually stones get lodged in the ureter. Pain begins in the loin, radiating around the flank into the groin, sometimes down the inner side of the thigh (Fig. 7.22). Pain is very severe and colicky in nature. Attacks are spasmodic and tend to last minutes to hours; they often leave the person prostrate with pain, who is restless and cannot lie still. Symptoms of nausea and vomiting might also be present. It is twice as common in men than in women and usually occurs between the ages of 40 and 60 years.

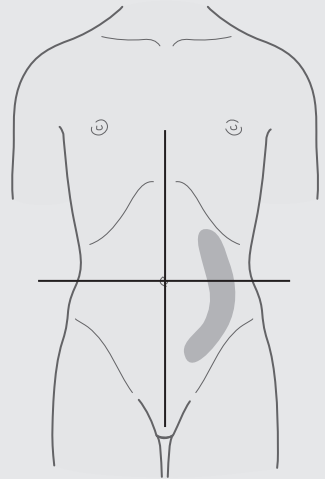


Fig. 7.22 The position of pain in renal colic.

Myocardial ischaemia

Angina and myocardial infarction (MI) cause chest pain that can be difficult to distinguish initially from epigastric or retrosternal pain caused by dyspepsia (Fig. 7.23). However, pain of cardiovascular origin often radiates to the neck, jaw and inner aspect of the left arm. Typically, angina pain is precipitated by exertion and subsides after a few minutes once at rest. Pain associated with MI will present with characteristic deep crushing pain. The patient will appear pale, display weakness and be tachycardic. Cardiovascular pain should respond to sublingual glyceryl trinitrate therapy.

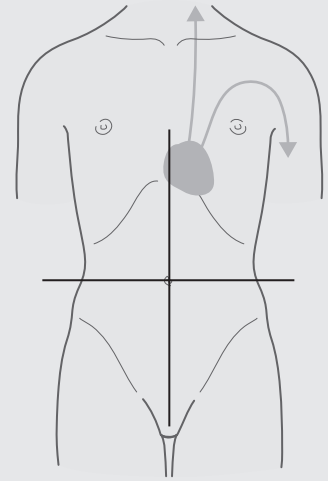


Fig. 7.23 The position of pain associated with myocardial ischaemia.

Herpes zoster (shingles)

Pain associated with herpes zoster typically occurs once the rash has erupted, although prodromal symptoms are usually present; these include tingling sensations, malaise and headache. Pain is described as an intense burning, aching or stabbing (Fig. 7.24).

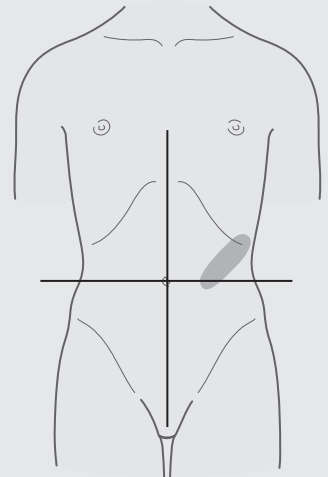


Fig. 7.24 The position of pain in herpes zoster.

Conditions affecting the lower abdomen

The most common causes of lower abdominal pain are muscle strains, IBS, appendicitis and dysmenorrhoea in women. Apart from appendicitis, all these conditions can present in either quadrant.

Irritable bowel syndrome

Pain is most often observed in the left lower quadrant (Fig. 7.25); however, the discomfort can be vague and diffuse, and about one-third of patients exhibit upper abdominal pain. The pain is described as cramplike and is recurrent. Patients younger than 50 years who have had abdominal pain or discomfort, bloating or a change in bowel habits for 6 months are likely to have IBS. For further details on IBS, see that section earlier in this chapter.

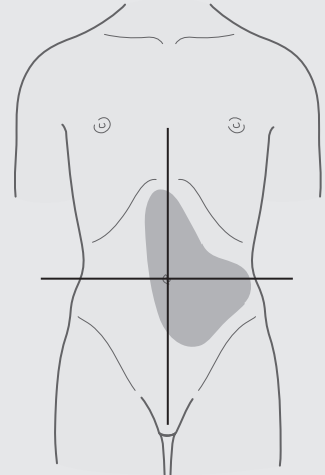


Fig. 7.25 The position of pain associated with irritable bowel syndrome.

Diverticulitis

Pain is more commonly seen in the left lower quadrant (Fig. 7.26) but can be suprapubic and occasionally in the right lower quadrant. Pain tends to be cramplike in nature, with local tenderness and associated fever. Altered bowel habits are usual, with diarrhoea more common than constipation. The incidence of diverticulitis increases with increasing age.

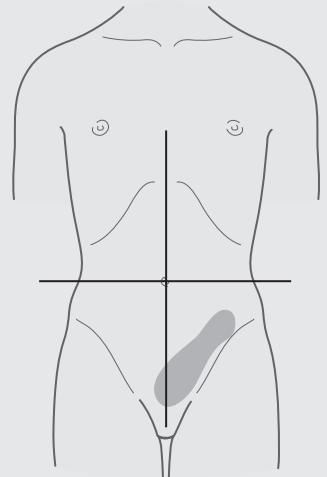


Fig. 7.26 The position of pain associated with diverticulitis.

Appendicitis

Typically, the pain starts in the midabdominal region, around the umbilicus, before migrating to the right lower quadrant after a few hours (Fig. 7.27), although right-sided pain is experienced from the outset in about 50% of patients. The pain of appendicitis is described as colicky or cramplike but, after a few hours, becomes constant. Movement tends to aggravate the pain and vomiting might also be present. Appendicitis is most common during the early teenage years, especially in males.

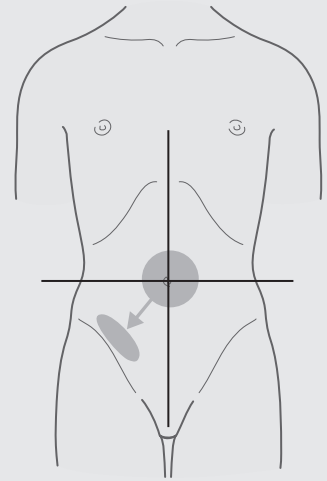


Fig. 7.27 The position of pain associated with appendicitis.

Conditions affecting women (other than period pain)

Generalized lower abdominal pain (Fig. 7.28) can be experienced in a number of gynaecological conditions. These are as follows:

- Ectopic pregnancy: These are usually experienced between weeks 5 and 14 of the pregnancy. Patients suffer from persistent moderate to severe pain that is sudden in onset. Referred pain to the tip of the scapula is possible. Most patients (80%) experience bleeding that ranges from spotting to the equivalent of a menstrual period. Diarrhoea and vomiting are often also present.
- Salpingitis (inflammation of the fallopian tubes): This occurs predominantly in young, sexually active women, especially those fitted with an intrauterine device (IUD). Pain is usually bilateral, low and cramping. Pain starts shortly after menstruation and can worsen with movement. Malaise and fever are common.
- Endometriosis: Patients experience lower abdominal aching pain that usually starts 5 to 7 days before menstruation begins and can be constant and severe. The pain often worsens at the onset of menstruation. Referred pain into the back and down the thighs is also possible.

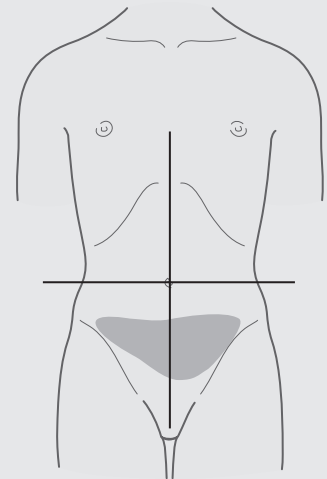


Fig. 7.28 The position of pain associated with gynaecological conditions.

Other conditions

Intestinal obstruction

Intestinal obstruction is most prevalent in people over the age of 50. It has a sudden and acute onset. The pain is described as colicky, which can come and go and be experienced anywhere in the lower abdomen. Constipation and vomiting are prominent features.

Diffuse abdominal pain

A number of conditions will present with diffuse abdominal pain over the four quadrants. The most common cause of diffuse pain seen by the pharmacist is gastroenteritis. Other causes include peritonitis and pancreatitis.

Gastroenteritis

Other symptoms of nausea, vomiting and diarrhoea will be more prominent in gastroenteritis than abdominal pain. The patient might also have a fever and suffer from general malaise.

Peritonitis

Severe pain in the upper abdomen is present. This is accompanied by intense rigidity of the abdominal wall producing a boardlike appearance; fever and vomiting might also be present. Urgent referral is required.

Fig. 7.29 will aid in the differentiation of the different types of abdominal pain.

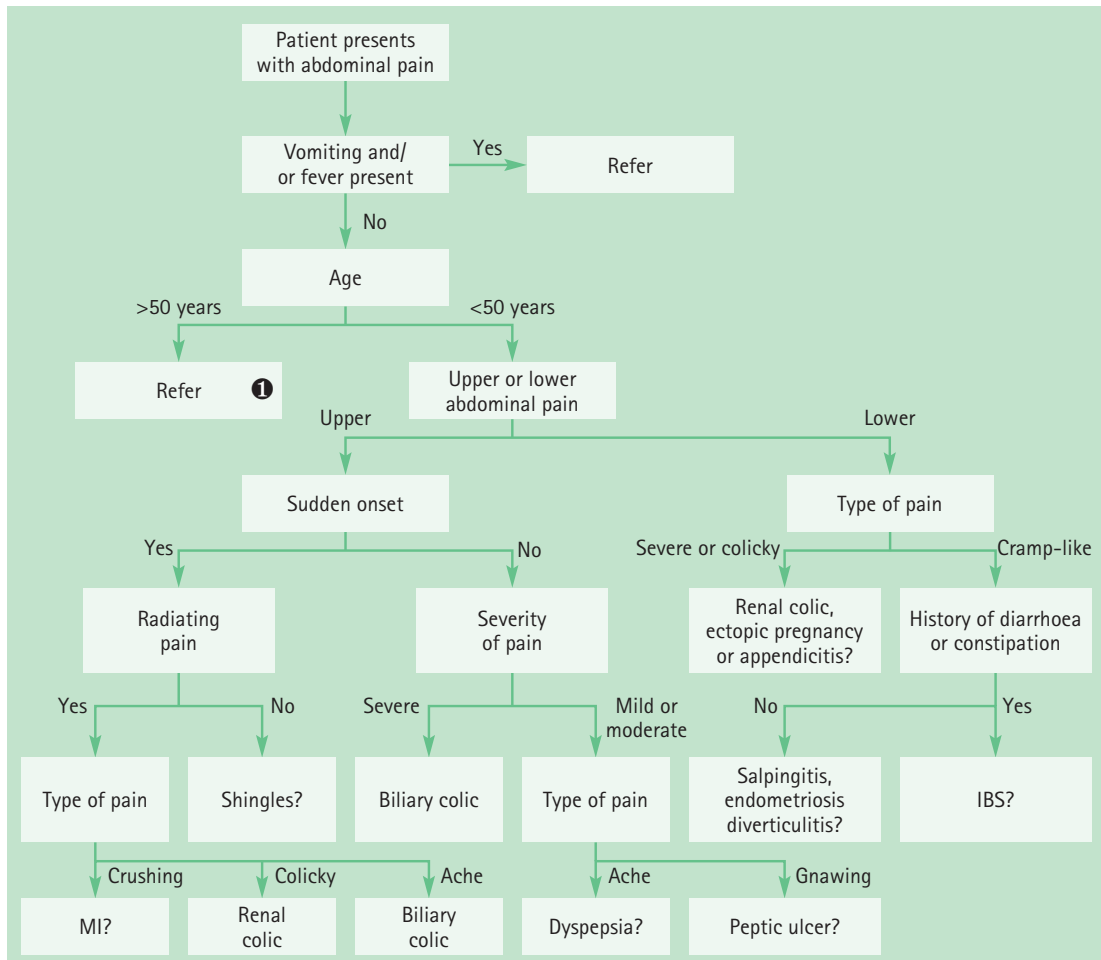


Fig. 7.29 Primer for the differential diagnosis of abdominal pain.

① Organic disease is more likely to be the cause of abdominal pain in patients older than 50 years, especially if symptoms are new or more severe than normal.

**TRIGGER POINTS** indicative of referral:
Abdominal pain

Symptoms/signs	Possible danger/ reason for referral	Urgency of referral
Severe pain or pain that radiates with or without vomiting	Suggests conditions such as peritonitis, pancreatitis, appendicitis, or renal or biliary colic	Immediate referral to GP
Lower abdominal pain in pregnancy	Ectopic pregnancy?	
Abdominal pain with fever	Suggests potential diverticulitis, peritonitis, biliary colic or salpingitis	As soon as possible
Older adults	Diverticulitis and obstruction more common	

Evidence base for over-the-counter medication and practical prescribing and product selection

The three conditions that have abdominal pain and discomfort as one of the major presenting symptoms and can be treated OTC are dyspepsia, IBS and dysmenorrhoea. For further information on products used to treat these conditions, see other sections in this chapter.

Further reading

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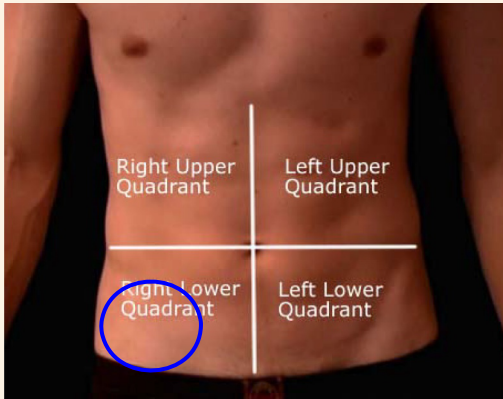
Self-assessment questions

The following questions are intended to supplement the text. Two levels of questions are provided, multiple choice questions and case studies. The multiple-choice questions are designed to test knowledge and application of knowledge, and the case studies allow this knowledge to be put in context in patient scenarios.

Multiple-choice questions

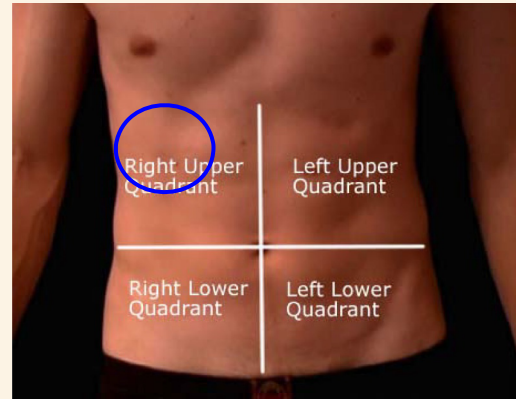
- 7.1 A 69-year-old woman asks for your advice about her dentures; they do not seem to fit properly. You perform a visual inspection and observe a white patch near the base of her tongue. She has no pain. Based on this information, what is the most likely diagnosis?
- Leukoplakia
 - Lichen planus
 - Major aphthous ulcers
 - Minor aphthous ulcers
 - Trauma-related ulcers
- 7.2 Miss Kandola presents with diarrhoea that she has had for 3 days. She complains of epigastric pain and bloating. You suspect giardiasis. Which question would be most appropriate to help determine whether giardiasis was the cause?
- Recent foreign travel
 - Ingestion of different food
 - Contact with people suffering from diarrhoea
 - Recent history of blood in diarrhoea
 - Diarrhoea in the early morning
- 7.3 In the treatment of constipation, which one of the following statements is true?
- Bulk-forming laxatives usually act within 12 to 24 hours.
 - Senna tablets should be avoided in nursing mothers.
 - Fybogel is not suitable for a patient with coeliac disease.
 - Lactulose should not be taken by diabetics.
 - Liquid paraffin has been linked as a cause of lipid pneumonia.
- 7.4 An adult patient presents with symptoms of abdominal pain and discomfort in the epigastric area. Which of the following conditions is the least likely cause?
- Oesophagitis
 - Duodenal ulcer
 - Gastric ulcer
 - Angina
 - Gastritis
- 7.5 A 41-year-old woman who has been diagnosed with irritable bowel syndrome has seen an advertisement for Buscopan IBS Relief. She asks for more information about the side effects of this product. Which of the following is the least common side effect experienced with Buscopan IBS Relief?
- Dry mouth
 - Tachycardia
 - Allergic skin reaction
 - Urinary retention
 - Anaphylactic reactions
- 7.6 Which of the following symptoms is most indicative of renal colic?
- Loin pain radiating to the groin
 - Left lower quadrant pain radiating to loin area
 - Right lower quadrant pain radiating to loin area
 - Back pain radiating to loin area
 - Localized loin pain only
- 7.7 Which of the following patient groups is most likely to suffer from oral thrush?
- Denture wearers
 - Well-controlled diabetics
 - Middle-aged adults
 - Young children
 - Asthmatics using low-dose corticosteroids
- 7.8 Mrs Singh, 37 years old, asks for an indigestion remedy. She says she has been getting discomfort (points towards the area in the epigastric area) over the last few days. She has not noticed any other symptoms apart from a bit of wind. What would be the most likely diagnosis?
- Reflux
 - Gastric ulcer
 - Duodenal ulcer
 - Nonulcer dyspepsia
 - Irritable bowel syndrome

7.9 Based solely on location, what is a likely diagnosis for this 25-year-old patient?



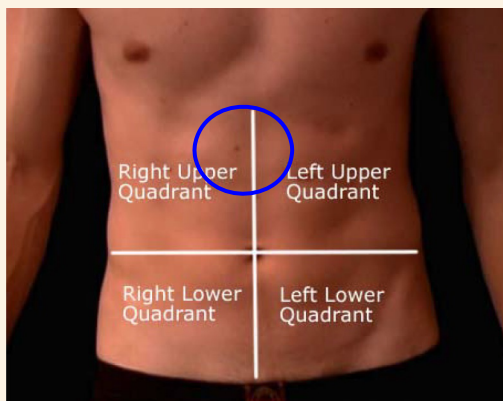
- a. IBS
- b. Peptic ulcer
- c. Renal colic
- d. Appendicitis
- e. Gallstones

7.11 Based solely on location, what is a likely diagnosis for this patient?



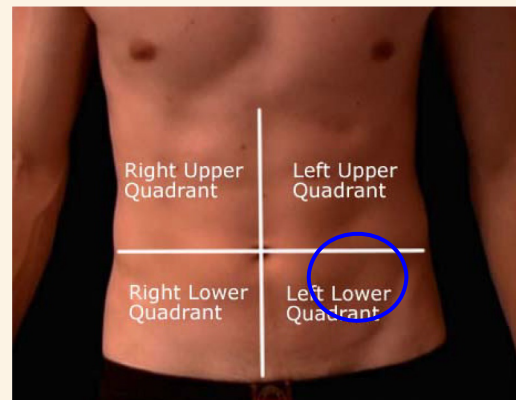
- a. IBS
- b. Peptic ulcer
- c. Renal colic
- d. Appendicitis
- e. Gall stones

7.10 Based solely on location, what is a likely diagnosis for this patient?



- a. IBS
- b. Peptic ulcer
- c. Renal colic
- d. Appendicitis
- e. Gallstones

7.12 Based solely on location, what is a likely diagnosis for this patient?



- a. IBS
- b. Peptic ulcer
- c. Pancreatitis
- d. Appendicitis
- e. Gallstones

7.13 A 14-year-old boy and his mother ask for your advice about his sore mouth. You perform a visual inspection and observe two small circular lesions on the inside of the gums. They are painful. Based on this information, what is the most likely diagnosis?

- a. Leukoplakia
- b. Lichen planus
- c. Major aphthous ulcers
- d. Minor aphthous ulcers
- e. Trauma-related ulcers

7.14 Mr FT has come into your pharmacy with previously diagnosed haemorrhoids. Which one of the following symptoms would indicate referral to the doctor?

- a. Bright red blood on the surface of the stool
- b. Stools that are tarry
- c. Perianal itching
- d. Mucous discharge
- e. Dull ache on defecation

7.15 Epigastric discomfort would be most closely associated with which of the following conditions?

- a. Appendicitis
- b. Gastric ulcer
- c. Diverticulitis
- d. Irritable bowel syndrome
- e. Renal colic

Questions 7.16 to 7.21 concern the following conditions:

- A. Irritable bowel syndrome
- B. Giardiasis
- C. Pyelonephritis
- D. Haemorrhoids
- E. Reflux
- F. Ulcerative colitis
- G. Salpingitis
- H. Appendicitis
- I. Dyspepsia

Select, from A to I, which of the above is most associated with the following statements:

7.16 Nocturnal diarrhoea is sometimes seen.

7.17 Tenderness is felt in the loin area.

7.18 Is associated with retrosternal pain.

7.19 Is associated with right lower quadrant pain.

7.20 Is associated with left lower quadrant pain.

7.21 Pain usually starts centrally and then moves to the right lower quadrant.

Questions 7.22 to 7.25 concern the following laxatives

- A. Lactulose
- B. Docusate sodium
- C. Senna tablets
- D. Macrogol oral powder
- E. Ispaghula husk
- F. Sterculia

Select, from A to F, which statement is most appropriate:

7.22 Has the quickest onset of action?

7.23 Can be given to children younger than 4 months?

7.24 Is most associated with abdominal pain?

7.25 Is indicated only for chronic constipation?

Answers

7.1 Answer: a

Rationale: Based on the observation that the lesion is painless, this eliminates minor (c) and major (d) ulcers as well as trauma-related ulcers (e). Based on the description as a patch and the age of the person, this points to leukoplakia (a) as the correct answer.

7.2 Answer: a

Rationale: Giardiasis is a protozoan infection almost always contracted from subtropical climates. Therefore, enquiring about recent foreign travel (a) in this case would be most helpful; (b, food ingestion) and (c, close contact with others) could be helpful for establishing food poisoning; blood in diarrhoea (d) and early morning rushes (e) would be more useful for irritable bowel disease (IBD).

7.3 Answer: e

Rationale: Bulk-forming laxatives (a) have a slow onset of action and have no restrictions in use with coeliac patients (c); senna (b) is excreted in the breast milk but has not been shown to have any detrimental effects. Although lactulose (d) is a sugar, the dose normally used in constipation should not pose a problem for diabetics. However, there are reports of lipid pneumonia with liquid paraffin.

7.4 Answer: d

Rationale: All could present with pain in this area. Oesophagitis (a) and gastritis (e) are common causes of epigastric pain. Ulcers (b and c) are less common, but angina (d) would be the least likely.

7.5 Answer: d

Rationale: Dry mouth (a), tachycardia (b) and allergic skin reactions (c) are uncommon; anaphylactic shock (e) is stated to be less than uncommon; urinary retention is rare (d).

7.6 Answer: a

Rationale: Loin pain is associated with renal colic and typically radiates away from this area, so options b, c and d can be discounted. Typically, the pain radiates away from the loin area, so e can also be eliminated.

7.7 Answer: a

Rationale: Thrush can be precipitated with steroid inhalers (e) but is not common with low-dose inhalers; infants rather than young children (d) are predisposed to thrush; thrush is rare in healthy adults, such as well-controlled diabetics (b) and middle-aged individuals (c).

7.8 Answer: a

Rationale: All listed conditions, other than irritable bowel syndrome (e), present with epigastric symptoms. Reflux (a) is associated with a burning pain and ulcers (b and c) are not associated with wind. Therefore, d is the most appropriate answer.

7.9 Answer: d

Rationale: Right lower quadrant pain is typically seen in renal colic (c) and appendicitis (d). The person is young, so this suggests appendicitis as the answer, more than renal colic.

7.10 Answer: b

Rationale: Pain experienced with IBS (a), renal colic (c) and appendicitis (d) would usually be lower quadrant. Gallstones (e) tend to be more right upper quadrant rather than central.

7.11 Answer: e

Rationale: See answer to 7.10.

7.12 Answer: a

Rationale: Pain experienced with IBS (a), pancreatitis (c) and appendicitis (d) would usually be lower quadrant. Appendicitis would be right lower quadrant and pancreatitis would be seen in both quadrants.

7.13 Answer: d

Rationale: Options a and b are seen as patches rather than circular lesions; in c, major ulcers are large, and e are irregular in shape.

7.14 Answer: b

Rationale: Blood mixed in stool should be referred to the GP to eliminate GI bleed. Slight rectal bleeding is often associated with haemorrhoids and can be visible in the

toilet or on the surface of the stool. Usually, blood on the stool is a direct referral sign but, if the cause is haemorrhoids, this can be treated. The other symptoms—c, d and e—are typical of haemorrhoids.

7.15 Answer: B

Rationale: Right lower quadrant would be a; c and d would be lower quadrant; loin pain would be e.

7.16 Answer: F

Rationale: Diarrhoea is observed in IBS (A), giardiasis (B), and ulcerative colitis (F). IBS and giardiasis show no discernible times of the day where diarrhoea would be experienced.

7.17 Answer: C

Rationale: Pain felt in the loin area is often associated with kidney problems. From the list given, the only option consistent with pain in this region is pyelonephritis (C).

7.18 Answer: E

Rationale: Pain is a key feature in IBS (A), pyelonephritis (C), reflux (E), salpingitis (G), and appendicitis (H). Right lower quadrant pain is most closely associated with appendicitis because IBS is left lower quadrant, pyelonephritis is loin pain and salpingitis tends to be diffuse.

7.19 Answer: H

Rationale: See answer 7.18.

7.20 Answer: A

Rationale: See answer 7.18.

7.21 Answer: H

Rationale: See answer 7.18.

7.22 Answer: C

Rationale: Stimulant laxatives are the quickest acting laxatives; only senna, C, from the list is a stimulant laxative.

7.23 Answer: B

Rationale: Only docusate and lactulose have licences for children younger than 1 year; docusate can be given to infants from 6 months of age and older.

7.24 Answer: C

Rationale: Flatulence is experienced with most laxatives but stimulant laxatives are well recognized to cause abdominal pain.

7.25 Answer: D

Rationale: Macrogol and docusate have licences for chronic use, but docusate can also be used to prevent chronic constipation.

Self-assessment questions

The following questions are intended to supplement the text. Two levels of questions are provided: multiple choice questions and case studies. The multiple choice questions are designed to test knowledge and application of knowledge, and the case studies allow this knowledge to be put in context in patient scenarios.

Multiple choice questions

- 7.1** Which one of the following symptoms is most indicative of renal colic
- Back pain radiating to loin area
 - Left lower quadrant pain radiating to loin area
 - Localized loin pain only
 - Loin pain radiating to the groin
 - Right lower quadrant pain radiating to loin area
- 7.2** In the treatment of constipation, which one of the following statements is true?
- Bulk-forming laxatives usually act within 12 to 24 hours
 - Fybogel is not suitable for a patient with coeliac disease
 - Lactulose should not be taken by diabetics
 - Liquid paraffin has been linked with causing lipid pneumonia
 - Senna tablets should be avoided in nursing mothers
- 7.3** A man asks for the best thing to stop diarrhoea as he is going on holiday and he doesn't want to be caught short. Which of the following is the first-line treatment to be recommended?
- Antibiotics
 - Antispasmodics
 - Kaolin and morphine
 - Loperamide
 - Rehydration solution
- 7.4** Antacids that contain aluminium, calcium or magnesium salts inhibit the intestinal absorption of which of the following?
- Cephalexin
 - Chloramphenicol
 - Erythromycin
 - Phenoxymethylpenicillin
 - Tetracycline
- 7.5** What condition predisposes patients to oral thrush?
- Asthma
 - Diabetes mellitus
 - Heart failure
 - Hyperlipidaemia
 - Parkinson's disease
- 7.6** Abdominal pain that starts centrally then moves to the right lower quadrant is indicative of?
- Appendicitis
 - Irritable bowel syndrome
 - Pancreatitis
 - Pyelonephritis
 - Renal colic
- 7.7** Which condition is least likely to cause rectal bleeding?
- Anal fissure
 - Colorectal cancer
 - Crohn's disease
 - Haemorrhoids
 - Irritable bowel syndrome
- 7.8** Mrs Jones, a 52-year-old woman, asks for advice on a spot on the inside of her cheek. Based solely on the sex and age of the patient, what is the most likely diagnosis?
- Herpes simplex ulcers
 - Leukoplakia
 - Lichen planus
 - Oral thrush
 - Minor aphthous ulcers
- Questions 7.9 to 7.11 concern the following conditions:
- Constipation
 - Diarrhoea
 - Dyspepsia
 - Haemorrhoids
 - Irritable bowel syndrome

Select, from A to E, which statement best relates to the conditions above:

- 7.9 Is characterized by epigastric pain?
 7.10 Can be treated with antispasmodics?
 7.11 Is associated with left lower quadrant pain?

Questions 7.12 to 7.14 concern the following OTC medications:

- A. Ranitidine
 B. Gaviscon Liquid
 C. Esomeprazole
 D. Milk of Magnesia
 E. Sodium bicarbonate powder

- 7.12 Is most suitable for treating? heartburn, which tends to get worse when lying down
 7.13 Commonly causes constipation
 7.14 Could be used to relieve constipation, as well as indigestion?

Questions 7.15 to 7.17: for each of these questions *one or more* of the responses is (are) correct. Decide which of the responses is (are) correct. Then choose:

- If a, b and c are correct
 If a and b only are correct
 If b and c only are correct
 If a only is correct
 If c only is correct

Directions summarized

A	B	C	D	E
a, b and c	a and b only	b and c only	a only	c only

- 7.15 When questioning a patient seeking advice for gastrointestinal upset, which of the following symptoms would indicate the need for direct referral to the general practitioner?
- a. Feeling of impending vomiting
 b. Loss of appetite over the last 24 hours
 c. Dark-coloured vomit

- 7.16 A common presentation of minor aphthous ulcers is
- a. Pain
 b. Ulcers on the inside of the lip and tongue
 c. Occur in crops of between 1 and 5

- 7.17 Which symptoms in a patient presenting with constipation should be referred?
- a. Melaena
 b. Greater than 7 days duration
 c. Abdominal pain

Questions 7.18 to 7.20: these questions consist of a statement in the left-hand column followed by a statement in the right-hand column. You need to:

- Decide whether the first statement is true or false
- Decide whether the second statement is true or false.

Then choose:

- A. If both statements are true and the second statement is a correct explanation of the first statement
 B. If both statements are true but the second statement is NOT a correct explanation of the first statement
 C. If the first statement is true but the second statement is false
 D. If the first statement is false but the second statement is true
 E. If both statements are false

Directions summarized

	1st statement	2nd statement	
A	True	True	2nd explanation is a correct explanation of the 1st
B	True	True	2nd statement is not a correct explanation of the 1st
C	True	False	
D	False	True	
E	False	False	
	First statement	Second statement	
7.18	IBS is common in people under the age of 40	It can be caused by stress	
7.19	Gingivitis is caused by plaque build up	It is characterized by swollen and red gums	
7.20	Heartburn causes retrosternal pain	In heartburn sphincter competence is compromised	

Answers

7.1 Answer: d

Rationale: The kidneys anatomically are located in the loin area – this means that option d can be eliminated. Pain does radiate but the pain originates anatomically where the kidney is, this means options a, b and e are incorrect. As stated pain does radiate and so option c is also incorrect.

7.2 Answer: d

Rationale: Bulk laxatives (a) take longer to work than 24 hours – usually 48–72 hours, and they can be given all patient groups (b); Lactulose, although a sugar, can still be given to diabetics (c) as the dose used should not pose a problem; and senna (e) does not significantly pass through in to the breast milk to cause a problem.

7.3 Answer: e

Rationale: Antispasmodics (b) could help with cramping but not diarrhoea antibiotics (a) can be used in traveller's diarrhoea but is not an OTC option; options c to e could be used to treat diarrhoea although current recommendations state that fluid replacement is of greatest importance, and should be first-line treatment.

7.4 Answer: e

Rationale: Chelation interactions are well recognized but involve relatively few medicines. From the listed antibiotics, tetracyclines are known to cause this when in combination with di and trivalent cations such as iron, calcium, aluminium, magnesium, bismuth and zinc salts.

7.5 Answer: b

Rationale: Options c to e have no links to precipitating oral thrush; asthma (a) although not a predisposition to thrush the use of inhaled corticosteroids can cause oral thrush.

7.6 Answer: a

Rationale: IBS (b) is most associated with left lower quadrant pain; pancreatitis (c) affects the general abdomen area; pyelonephritis (d) and renal colic (e) are both problems of renal anatomy and associated with loin pain.

7.7 Answer: e

Rationale: Haemorrhoids (d) is often associated with rectal bleeding; bleeding is also seen with anal fissure (a) because of skin tearing; in Crohn's disease and colorectal cancer blood can be observed with the passage of stools.

7.8 Answer: c

Rationale: Herpes simplex ulcers (a) are seen in younger people, as is oral thrush (d). Aphthous ulcers (e) are mostly seen in people under the age of 40, and leukoplakia (b) is associated with older people. Lichen planus is most often seen in middle-aged people and thus the correct answer.

7.9 Answer: C

Rationale: Constipation (A) and diarrhoea (B) can cause abdominal pain but this tends to be generalized. IBS (E) causes lower abdominal pain usually; haemorrhoids (D) cause local anal discomfort.

7.10 Answer: E

Rationale: Mainstay of treatment for constipation (A) are laxatives; diarrhoea (B) is oral rehydration therapy; dyspepsia can be treated with antacids or acid-suppressing medicines; haemorrhoids (D) tend to be treated with local topical preparations.

7.11 Answer: E

Rationale: As per 7.9 IBS causes lower abdominal pain and originates in the left lower quadrant.

7.12 Answer: B

Rationale: Lying down means that stomach contents could flow backwards so a product that can help stop this would be most useful, and in this case an alginate product (B-Gaviscon) would be useful.

7.13 Answer: C

Rationale: The only product that commonly (as per EU definition, that is > 10%) causes constipation is esomeprazole.

7.14 Answer: D

Rationale: Of the listed products, Milk of Magnesia contains magnesium hydroxide, which is a traditional remedy for constipation.

7.15 Answer: E

Rationale: GI disturbances are often associated with symptoms such as nausea and/or vomiting. If infection is suspected then the person may well have symptoms of general malaise, thus options A and B would be common. People describing vomit that is discoloured should be viewed with caution as this suggests possible blood in the vomit.

7.16 Answer: A

Rationale: Ulcers typically cause pain and are often multiple with a typical location toward the front of the mouth.

7.17 Answer: D

Rationale: Constipation can be relatively long standing and often presents with abdominal discomfort/pain. All cases of blood in the stools should be viewed with suspicion.

7.18 Answer: B (True/True – statement 2 not correct explanation of statement 1)

Rationale: Stress is known to precipitate or aggravate IBS but does not explain why it is most often first diagnosed in younger people

7.19 Answer: B (True/True – statement 2 not correct explanation of statement 1)

Rationale: Both statements are correct but the second statement describes the symptoms manifested by plaque build up but not the reasons why this occurs.

7.20 Answer: A (True/True – statement 2 is a correct explanation of statement 1)

Rationale: Because muscle tone of the sphincter is weakened this allows gastric contents to regurgitate backwards and into the oesophagus and thus cause pain.

Case studies

CASE STUDY 7.1

Mrs SJ, a 28-year-old woman asks to speak to the pharmacist because she wants something for her stomach ache. You find out that the pain is located in the lower and upper left quadrant, but mainly the upper quadrant.

a. From which conditions might she be suffering?

A wide range of conditions could present in these locations including reflux, nonulcer dyspepsia, gastritis, primary dysmenorrhoea, endometriosis, irritable bowel syndrome, pancreatitis, renal colic, myocardial infarction (MI) and herpes zoster.

Further questioning reveals Mrs SJ to be suffering with pain she describes as 'an ache'.

b. Name the likely conditions from which she could be suffering?

The use of the word ache means you can rule out conditions that present with severe, stabbing, burning or gnawing pain:

- Pancreatitis, renal colic—severe
- Reflux—burning
- Herpes zoster—severe, lancing

However, it could still be any of these: nonulcer dyspepsia, gastritis, primary dysmenorrhoea, irritable bowel syndrome, endometriosis and MI. But, because the pain is primarily upper quadrant, this makes primary dysmenorrhoea, endometriosis and irritable bowel syndrome less likely. This leaves nonulcer dyspepsia, gastritis and MI as possibilities.

c. Which questions would now allow you to differentiate among these conditions?

MI is the most unlikely of the three conditions, and one would expect the patient to have more severe symptoms. Questions asking about radiation of pain, previous history of similar symptoms and precipitating and relieving factors should be asked.

You reach the differential diagnosis of nonulcer dyspepsia but before you make any recommendations, you find out she takes the following medicines:

- Paracetamol prn: She has taken this for 6 months for knee pain.
- Atorvastatin 40 mg od: She has taken this for the last 3 years for familial hyperlipidaemia.
- Naproxen 500 mg bd prn: She has taken this for 6 months for knee pain.

d. Which of these medications, if any, do you consider are contributing to Mrs SJ's pain? Explain your rationale.

Of the three medicines that Mrs SJ is taking, the one most likely to cause GI irritation is naproxen. However, she has been taking this for the last 6 months, and you would expect that dyspepsia symptoms would have been experienced already if she was going to have a reaction to naproxen. It is then unlikely that naproxen has caused the problem unless the dose has recently been changed. Atorvastatin can also cause GI side effects but has been taken for the last 3 years and is therefore almost certainly not the cause of these symptoms. Paracetamol is not known to cause GI irritation so it can also be ruled out. In conclusion, it is likely that none of the medicines have caused Mrs SJ's symptoms.

Case study

CASE STUDY 7.1

Mr DN, a 45-year-old man, comes into the pharmacy requesting a strong toothpaste. He is concerned because his gums have been bleeding whenever he brushes his teeth.

a. What might be causing the bleeding gums?

Causes could include overzealous toothbrushing, gingivitis and medicine-related factors.

b. What specific questions will help you decide the cause of the bleeding gums?

- *What is your toothbrushing routine and technique?*
 - *Should establish if this technique is good or bad.*
- *Does bleeding occur at times other than toothbrushing?*
 - *Would suggest a cause other than toothbrushing technique.*
- *Has he noticed taste disturbances or halitosis?*
 - *Implies gingivitis or periodontitis.*
- *Are you taking any other medications?*
 - *May establish causality of any medicines known to induce bleeding or aggravate bleeding.*

Mr DN tells you that his dentist recommended that he use a fluoride toothpaste. He (manually) brushes his teeth at least once a day. He has not noticed any bleeding at any other times and has no other symptoms. Mr DN does not take any other medications and has no other medical conditions.

c. What do you think the problem is?

Mr DN's description is suggestive of mild gingivitis that is possibly being worsened by his toothbrushing technique.

d. What would you recommend for Mr DN?

Mr DN should be supplied an appropriate toothpaste and advised to brush his teeth twice a day, preferably with a powered toothbrush; this may overcome any overexuberance in brushing. It may also be useful to suggest a mouthwash containing chlorhexidine in concentrations of 0.1% or 0.2% in the short term. Mr DN should be advised to visit his dentist in 2 to 4 weeks if symptoms do not settle or resolve based on this new regimen.

CASE STUDY 7.2

Mr LR, (~50 years old), presents to the pharmacy at lunchtime asking for something for diarrhoea. The following questions are asked, and responses received.

Information gathering	Data generated
Describe symptoms	Going to the toilet three or four times a day; normal habit is once or twice.
Nature of movements	Very watery
Duration	4 or 5 days
Other symptoms	Generally feels a bit rough Headache and a fever Been getting some cramping pains
Blood noticed	No
Has patient eaten anything different in a day or so before diarrhoea appeared?	No
Additional questions	No foreign travel Does not seem to be worse at any time of day
On examination	General appearance is of a healthy person No obvious signs of dehydration. Pinch test normal

Information gathering	Data generated
Previous history of presenting complaint	Has had the odd bout of diarrhoea before but usually clears up after a couple days
Medicines (OTC, prescription)	Ibuprofen 600 mg tds; aspirin 75 mg od; Dipyridamole 200 mg bd; atenolol 25 mg od No change to medicines for last 6–9 months
Past medical history	RA, HT, mild stroke 2 years ago
Social history, which may include questions relating to smoking, alcohol intake, employment, personal relationships	Of little relevance in this case
Family history	No one in family with similar symptoms

HT, Hypertension; RA, rheumatoid arthritis.

Below summarizes the expected findings for questions when related to the different conditions that can be seen by community pharmacists.

CASE STUDY 7.2 (Continued)

Question	Age group	Acute or chronic	Timing	Periodicity	Weight loss	Blood in stools
Infection	Any	Acute	Any	Acute	No	Unusual
Medicines	Any	Acute or chronic	Any	No	No	No
IBS	<45 years	Acute	Mornings?	Rekurs	No	No
Giardiasis	Any	Acute	Any	Acute	No	No
Faecal impaction	Older adult	Chronic	Any	No	No	No
Ulcerative colitis	Young adult	Acute	AM and PM	Rekurs	No	Yes
Crohn's disease	Young adult	Acute	AM and PM	Rekurs	No	Yes
Coeliac disease	Infant, middle-aged adult	Chronic	Any	No	Yes	No
Carcinoma	>50 years	Chronic	Any	No	Yes	Unusual

IBS, Irritable bowel syndrome.

When this information is compared to that gained from our patient and linking this with known epidemiology

on diarrhoea (see Table 7.13), it should be possible to make a differential diagnosis.

	Age	Acute or chronic	Timing	Periodicity	Blood in stools
Infection	✓	✓	✓	✓	✓
Medicines	✓	✓	✓	✗	✓
IBS	✗	✓	✗?	✓	✓
Giardiasis	✓	✓	✓	✓	✓
Faecal impaction	✗	✗	✓	✗	✓
Ulcerative colitis	✗	✓	✗	✓	✗
Crohn's disease	✗	✓	✗	✓	✗
Coeliac disease	✓	✗	✓	✗	✓
Carcinoma	✓	✗	✓	✗	✓?

We see that her symptoms most closely match an infective cause of diarrhoea (✓ represents symptom match). To differentiate between giardiasis and other infections, asking about recent foreign travel should allow differentiation between the two causes. Safety net:

A conditional referral to the GP in 48–72 hours should be made if symptoms do not improve (with or without any OTC treatment). In which case, it is possible that his medicines may be contributing to his symptoms.

CASE STUDY 7.2

Mrs BA, about 60 years old, comes in wanting to return a product she purchased a week ago. She had bought a constipation remedy (containing docusate sodium, 50 mg) but she says it has not worked.

a. What questions do you need to ask?

- *What were her expectations?*
- *What dose did she take and for how long?*
- *Has she made any dietary changes?*
- *If she takes medicines, has there been any changes?*
 - *It is important to make sure that the patient has taken the product correctly for a sufficient length of time to see an effect. They may have an unrealistic expectation on resolution of symptoms. This is a frequent reason why people stop taking medicines. It is also worth knowing if they have increased dietary fibre and fluid intake as an adjunct to the docusate. Medicines commonly cause constipation, so knowing about what the person takes and recent changes to her or his regimen is important because this may have worsened symptoms and might be a reason for the constipation not to have resolved.*

Mrs BA took two tablets twice a day for 5 days. During a recent visit, her physician had prescribed verapamil because her blood pressure was too high. She started taking verapamil 3 weeks ago. Her medications are as follows:

- Trandolapril, 4 mg daily
- Verapamil, 240 mg daily
- Budesonide, 200 µg/formoterol 6 µg (Symbicort), two inhalations twice daily

Her constipation has been getting progressively worse over the last couple of weeks and she decided last week to try something to treat it.

b. What do you think the problem is?

Verapamil is a calcium channel blocker that has a known common side effect of constipation. Given that this is a recent introduction to her medicine regimen, it is likely this is the cause of symptoms.

c. What would you say to Mrs BA about why docusate did not appear to work?

You should explain that docusate is a mild laxative that really needs to be taken before you get constipation because it needs to be mixed in with the stool to work. As a rule, for most adults, it has a limited role in treating constipation and is best used as a preventative.

d. What is your recommendation?

Mrs BA may consider using an alternative laxative that has a quicker onset of action, such as a stimulant laxative.

CASE STUDY 7.3

Mrs RH, an older patient (~75 years old), picks up her prescription and, at the same time, says she wants something to help get rid of a funny patch on the inside of her cheek. The following questions are asked and responses received.

Information gathering	Data generated
Describe symptoms	White patch about the size of a 10-pence piece
How long has the patient had the symptoms?	Noticed it a couple of weeks ago
Type, severity of pain	Not really painful
Other symptoms	No other obvious symptoms
Additional questions	No systemic symptoms (e.g., fever, chills)
On examination	Discrete white patch; no underlying redness
Previous history of presenting complaint	Had something similar a couple of years ago and the other chemist gave me some cream

Information gathering	Data generated
Medicines (OTC, prescription)	Ibuprofen 600 mg tds; aspirin 75 mg od; Atenolol 25 mg od
Past medical history	Rheumatoid arthritis (8 years), hypertension (~20 years), and stroke 2 years ago
Social history, which may include questions relating to smoking, alcohol intake, employment, personal relationships	Lives on her own and watches TV most of the time; loves quiz shows; nonsmoker now but used to smoke; only occasionally drinks alcohol
Family history	None

Below summarizes the expected findings for questions when related to the different conditions that can be seen by community pharmacists.

CASE STUDY 7.3 (Continued)

Finding	Number	Location	Size and shape	Age	Pain
Thrush	Singular patch	Anywhere	Irregular and variable size	Young and older adults	No (discomfort)
Minor ulcers	Up to about five ulcers	Lips and inside cheeks	<1 cm, round	10–40 years of age most common	Yes
Major ulcers	Numerous	Anywhere	Large (and of variable shape)	All ages	Yes
Herpetiform	Very numerous	Back of the mouth	Pinpoint and round	All ages	Yes
Herpes simplex	Numerous	Anywhere	Small	Children	Yes
Lichen planus	Diffuse	Tongue, cheek, gums	Resembles spider web	Adults	No
Leukoplakia	Singular patch	Tongue or cheek	Irregular and of variable size	Older adult	No
Carcinoma	Singular lesion	Tongue, mouth, lower lip	Irregular and of variable size	Older adult	No, but latter stages, yes

When this information is compared to that gained from our patient and linking this with known epidemiology

on mouth lesions (See Table 7.1), it should be possible to make a differential diagnosis.

Condition	Number	Location	Size and shape	Age	Pain
Thrush	✓	✓	✓	✓	✗
Minor ulcers	✗	✓	✗	✗	✗
Major ulcers	✗	✓	✗	✗?	✗
Herpetiform	✗	✗	✗	✓	✗
Herpes simplex	✗	✓	✗	✗	✗
Lichen planus	✓?	✓	✓	✓	✓?
Leukoplakia	✓	✓	✓	✓	✓
Carcinoma	✗?	✓	✓	✓	✓?

We see that her symptoms most closely match leukoplakia (✓ represents symptom match), even though thrush is more prevalent. The positive smoking history

would make leukoplakia more of a possibility. This person must be referred.

CASE STUDY 7.3 (Continued)

Activity

In cases 7.2 and 7.3, tables have been constructed to summarize the signs and symptoms associated with diarrhoeal and oral lesion presentations. Below is a

blank table for lower abdominal pain. Construct answers for each condition. Answers are shown on *Student Consult*.

Condition	Age affected	Gender affected	Nature of pain	Usual location	Other prominent features
Irritable bowel syndrome (IBS)					
Diverticulitis					
Renal colic					
Appendicitis					
Intestinal obstruction					
Endometriosis					
Salpingitis					

Dermatology

In this chapter

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Background

The skin is the largest organ of the body. It has a complex structure and performs many important functions. These include protecting underlying tissues from external injury and overexposure to ultraviolet light, barring entry to micro-organisms and harmful chemicals, acting as a sensory organ for pressure, touch, temperature, pain and vibration, and for maintaining the homeostatic balance of body temperature.

It has been reported that dermatological disorders account for up to 15% of the workload of UK family doctors, with upwards of 25% of patients attending their general practitioner (GP) about a skin complaint in a given year. Dermatitis, eczema and investigation of suspect skin lesions to exclude skin cancer are the three most common presentations. Statistics for community pharmacy presentations are more difficult to establish but observational studies reveal a similar level of symptom presentation. It is important that community pharmacists can differentiate between common dermatological conditions that can be managed appropriately without referral to a doctor and those that require further investigation or treatment with a prescription-only medicine.

General overview of skin anatomy

Principally, the skin consists of two parts, the outer and thinner layer called the *epidermis* and an inner thicker layer

named the *dermis*. Beneath the dermis lies a subcutaneous layer, known as the *hypodermis* (Fig. 8.1).

The epidermis

The epidermis is the major protective layer of the skin and has four distinct layers when viewed under the microscope. The basal layer actively undergoes cell division, forcing new cells to move up through the epidermis and form the outer keratinized horny layer. This process is continuous and takes approximately 35 days. Pathological changes in the epidermis produce a rash or a lesion with abnormal scale and/or loss of surface integrity. It is also responsible for skin pigmentation because the melanocytes, which produce melanin, are located in the lower epidermis. Pigmentary disorders therefore may result from decreased or increased numbers of melanocytes, such as vitiligo, where melanocytes are absent.

The dermis

Most of the dermis is made of connective tissue: collagen for strength and elastic fibres to allow stretch. It provides support to the epidermis as well as its blood and nerve supply. Located in the dermis are the hair follicle, sebaceous and sweat glands, and arrector pili muscle. Conditions of the dermis usually result in changes in the elevation of the skin (e.g., papules and nodules).

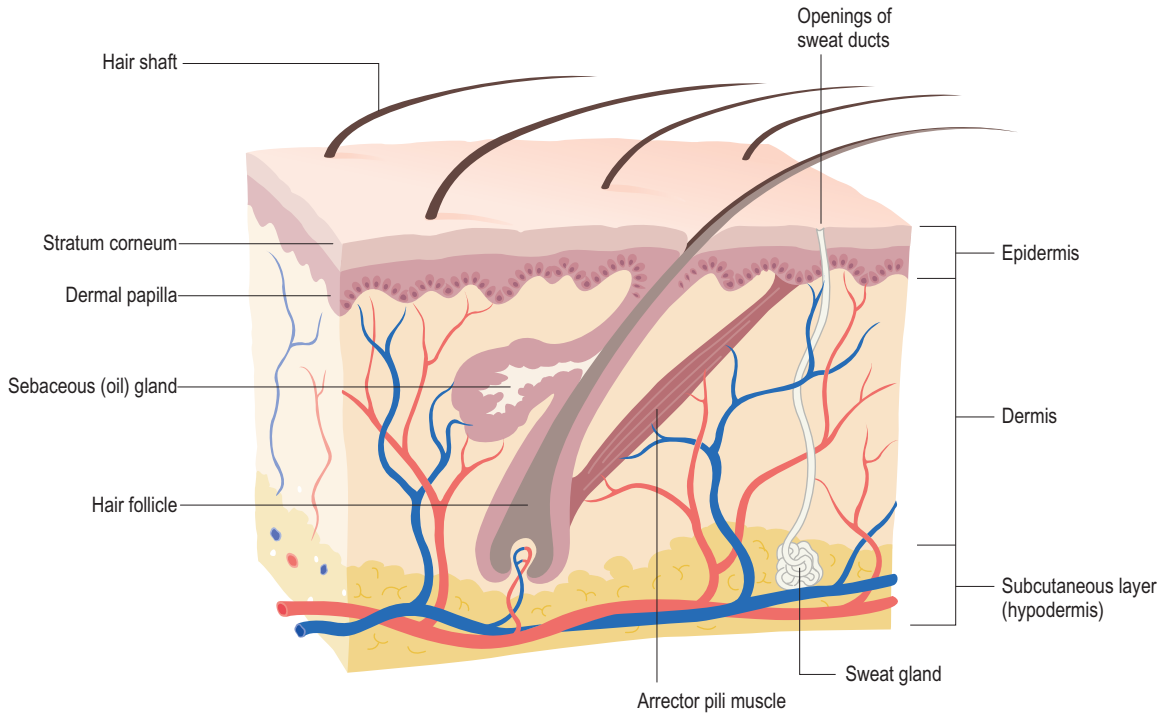


Fig. 8.1 The epidermis, dermis, and associated structures.

The hair

Each hair consists of a shaft, the visible part of the hair, and a root. Surrounding the root is the hair follicle, the base of which is enlarged into a bulb structure. The arrector pili muscle when contracted pulls the hair in to a vertical position to provide thermal protection causing 'goosebumps'. The primary function of hair is protection.

Sebaceous glands

Sebaceous glands are found in large numbers on the face, chest, and upper back. Their primary role is to produce sebum, which keeps hair supple and the skin soft. During puberty, these glands become large and active due to hormonal changes. Frequently, sebum will accumulate in the sebaceous gland and is one of the factors that lead to acne formation.

Sweat glands

These are the most numerous of the skin glands and are classed as apocrine or eccrine. Eccrine glands produce a transparent watery liquid (sweat), are located all over the body, and play a role in the elimination of waste products and maintaining a constant core temperature. Apocrine sweat glands are mainly located in the axilla, begin to function at puberty, and have no known biological function.

History taking

Unlike internal medicine, most dermatological complaints presenting in a community pharmacy can be seen. This affords the community pharmacist an excellent opportunity to base the differential diagnosis not only on questioning but also on the physical examination. General questions that should be considered when dealing with dermatological conditions are listed in [Table 8.1](#). Terminology describing skin lesions can be confusing; the more common terms used to describe their appearance are shown in [Table 8.2](#).

Physical examination

A more accurate differential diagnosis will be made if the pharmacist actually sees the person's athlete's foot or rash on the back. If an examination is performed, clearly explain the procedure you want to perform and gain the person's consent. Examinations should ideally be conducted in consultation rooms. It is worth remembering that many patients will be embarrassed by the appearance of skin conditions, and the pharmacist needs to demonstrate empathy during the consultation. When performing an examination of the skin, a number of things should be sought ([Table 8.3](#)). There

Table 8.1
Questions to consider when taking a dermatological history

Question	Relevance
Where did the problem first appear?	Certain skin problems start in one particular location before spreading to other parts of the body (e.g., chickenpox usually starts on the face before spreading to the trunk and limbs). Patients might need prompting to tell you where the problem started because they are likely to want help for the most obvious or large skin lesion but neglect to tell you about smaller lesions that appeared first.
Are there any other symptoms?	Many skin rashes are associated with itch and/or pain. Mild itch is associated with many skin conditions including psoriasis and medicine eruptions. Severe itch is associated with conditions such as scabies and atopic and contact dermatitis.
Occupational history (relevant to adults only)	This is particularly pertinent for contact dermatitis (e.g., do symptoms improve when away from work?).
General medical history	Many skin signs can be the first marker of internal disease (e.g., diabetes or liver dysfunction can manifest with pruritus; fungal or bacterial infection and thyroid disease can present with hair loss and pruritus).
Travel	More people are taking holidays to non-Western countries and therefore have the potential to contract tropical diseases. Reports are also now being received of people travelling to close Mediterranean countries (e.g., Spain) contracting conditions such as cutaneous leishmaniasis.
Family and household contact history	Infections such as scabies can infect relatives and others with whom the patient is in close contact.
The patient's thoughts on the cause of the problem	Ask for the patient's opinion. This might help with the diagnosis and shed light on anxieties and theories as to the cause of the condition.

is no substitute for experience when recognising skin problems. This is normally gained through seeing multiple similar cases and developing your pattern recognition skills (see Chapter One – making a diagnosis). A free image bank (<http://www.dermnet.com/>) is available from which familiarity can be gained of different presentations of skin conditions.

Hyperproliferative disorders

Background

Hyperproliferative disorders are characterized by a combination of increased cell turnover rate and a shortening of the time it takes for cells to migrate from the basal layer to the outer horny layer. Typically, cell turnover rate is 10 times faster than normal, and cell migration takes 3 or 4 days, rather than 35 days.

Psoriasis

Background

Psoriasis is a chronic, relapsing, inflammatory disorder characterized by a variety of morphological lesions that present in a number of forms. The most common form of psoriasis is plaque psoriasis, accounting for about 80% to 90% of cases (Table 8.4). Depending on the extent and severity of lesions, psoriasis can have a profound effect on the person's work and social life, with increased levels of anxiety and depression.

Prevalence and epidemiology

Psoriasis is a common skin disorder, with an estimated worldwide prevalence between 1% and 3%. In the UK, it has been reported to affect 1% to 2% of the population. However, this is probably an underestimate because some patients with mild psoriasis may not present to their doctor.

Table 8.2
Common terms used to describe skin lesions

Term	Description
Macule	A flat lesion <1 cm in diameter
Patch	A flat lesion >1 cm in diameter
Papule	A raised solid lesion <1 cm in diameter
Nodule	A raised solid lesion >1 cm in diameter
Vesicle	A clear, fluid-filled lesion lasting a few days, <1 cm in diameter
Bulla	A clear, fluid-filled lesion lasting a few days, >1 cm in diameter
Pustule	A pus-filled lesion lasting a few days, <1 cm in diameter
Comedone	A papule plugged with keratin and sebum
Erythema	Redness due to dilated blood vessels that blanch when pressed
Excoriation	Localized damage to the skin due to scratching
Lichenification	Thickening of the epidermis with increased skin markings due to scratching

Psoriasis can present at any time in life, although it appears to be more prevalent in the second and fifth decades. It is rare in infants and uncommon in children. The sexes are equally affected, and is more common in Caucasians.

Aetiology

The exact cause of psoriasis still remains unclear, but it is now recognized as an immune-mediated disorder with a genetic influence. Studies have identified a region on chromosome 6 as a contributor to psoriasis susceptibility (known as *PSORS1*), and this has been associated with at least 50% of psoriasis cases in several populations. However, genetic predisposition to psoriasis does not necessarily mean disease expression. Studies in twins also suggest that environmental factors might be needed for clinical expression of the disease because only 70% of genetically identical twins both develop the condition.

Psoriasis lesions also develop at sites of skin trauma, such as sunburn and cuts (known as the *Koebner phenomenon*), after streptococcal throat infection and during periods of stress.

Table 8.3
Things to consider when performing a dermatological examination

Lesion	Relevance
Temperature	Use the backs of your fingers to make the assessment. This should enable you to identify generalized warmth or coolness of the skin and note the temperature of any red areas (e.g., generalized warmth can indicate infection, whereas localized warmth might indicate inflammation or cellulitis).
Lesions	<p>Distribution – many skin diseases have a typical or classic distribution.</p> <p>Symmetrical, such as acne and psoriasis</p> <p>Asymmetrical, such as contact dermatitis</p> <p>Unilateral, such as shingles</p> <p>Localized, such as nappy rash</p> <p>Arrangement</p> <p>Discrete (with healthy skin in between), such as psoriasis</p> <p>Coalescing (merging together), such as eczema</p> <p>Grouped, such as insect bites</p> <p>Feel of lesions</p> <p>Smooth, such as urticaria</p> <p>Rough, such as actinic keratosis</p>
Recent trauma	Is there any sign that individual lesions have developed on a site of trauma or injury such as a scratch? This is seen in a number of conditions such as psoriasis and warts.

Table 8.4
Causes of psoriasis-like rash and their relative incidence in community pharmacy

Incidence	Cause
Most likely	Plaque psoriasis, scalp psoriasis
Likely	Seborrhoeic dermatitis, medicine-induced/exacerbated psoriasis
Unlikely	Guttate, flexural and localized pustular psoriasis, tinea corporis, lichen planus, pityriasis rosea
Very unlikely	Erythrodermic psoriasis, Tinea capitis

Arriving at a differential diagnosis

Psoriasis can be located on various parts of the body (Fig. 8.2) and presents in a variety of different forms. Plaque and scalp psoriasis are the only forms of the condition that can be managed by the community pharmacist. It is therefore necessary that other forms of psoriasis, and conditions that look like psoriasis, can be recognized and distinguished. Asking symptom-specific questions will help the pharmacist establish a differential diagnosis (Table 8.5).

Clinical features of plaque psoriasis

Plaque psoriasis typically presents with characteristic salmon-pink lesions with silvery-white scales and well-defined boundaries (Fig. 8.3). On darker skin, this characteristic colour is not apparent. Lesions can be single or multiple and vary in size from pinpoint to covering extensive areas. If the scales on the surface of the plaque are gently removed and the lesion then rubbed, it reveals pinpoint bleeding from the superficial dilated capillaries. This is known as the *Auspitz sign* and is diagnostic.

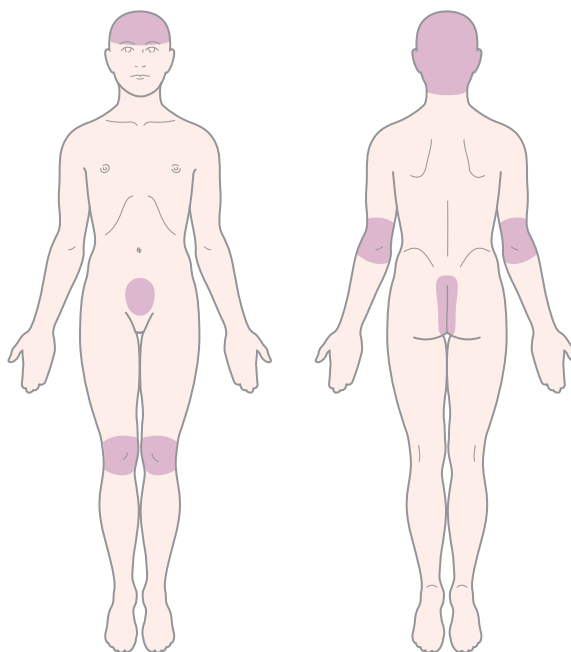


Fig. 8.2 Typical distribution of psoriatic plaques.



Table 8.5
Specific questions to ask the patient: Psoriasis

Question	Relevance
Onset	Psoriasis can develop in patients of any age, although it first occurs most commonly in early adult life. However, in young and older patients, the lesions tend to be atypical, which can make the diagnosis more difficult.
Distribution of rash	Psoriasis often presents in a symmetrical distribution and most commonly involves the scalp and extensor aspects of the elbows and knees. The gluteal cleft and umbilicus can also be affected (see Fig. 8.2). Conditions that resemble psoriasis, such as lichen planus (often inside of the wrists) and pityriasis rosea (thighs and trunk), have a different distribution than psoriasis.
Other symptoms	Itch is not normally the predominant feature of psoriasis, unlike other conditions such as dermatitis and fungal infections Nail involvement in the form of pitting (see Fig. 8.16) and onycholysis (separation of the nail plate from the nail bed) is often seen and can involve one or more of the nails. This is normally observed in patients with long-standing psoriasis.
Look of rash	Scalp and plaque psoriasis usually show scaling as an obvious feature. This is not seen with other common skin conditions (e.g., dermatitis) or other forms of psoriasis. When scalp involvement is mild, psoriasis can be impossible to distinguish from seborrhoeic dermatitis.
Previous history of lesions	Psoriasis is a chronic relapsing and remitting disease, and it is likely that the patient will have had lesions in the past. Other skin diseases, such as fungal infections, are acute, and patients do not normally have a history of the problem.

Clinical features of scalp psoriasis

Scalp psoriasis affects upwards of 90% of people with psoriasis. It can be mild, exhibiting slight redness of the scalp, to severe, with total head involvement, marked inflammation and thick scaling (Fig. 8.4). The redness often extends beyond the hair margin and is commonly seen behind the ears.

Conditions to eliminate

Likely causes

Seborrhoeic dermatitis

Mild scalp psoriasis can be very difficult to distinguish from seborrhoeic dermatitis. However, in practice, this is rarely



Fig. 8.3 Typical psoriatic plaques. From Gawkrödger, D. J. (2007). *Dermatology: An illustrated colour text* (4th ed.). Churchill Livingstone.

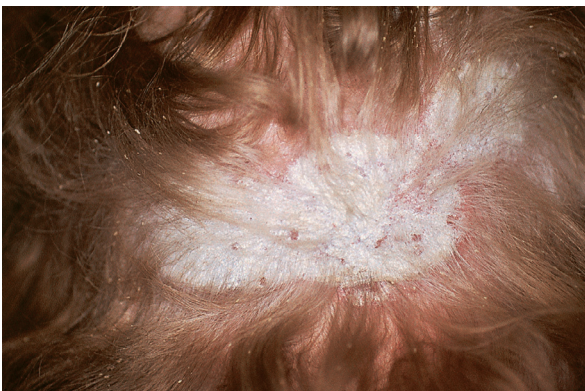


Fig. 8.4 Scaly plaques of psoriasis in the scalp, with localized hair loss. From Gawkrödger, D. J. (2007). *Dermatology: An illustrated colour text* (4th ed.). Churchill Livingstone.

a problem because treatment for both conditions is often the same.

Medication-exacerbated psoriasis

A number of medicines can precipitate, worsen or aggravate existing psoriasis. Medicines most commonly associated are lithium, antimalarials, beta blockers, angiotensin-converting-enzyme inhibitors (ACE inhibitors) and nonsteroidal antiinflammatory drugs (NSAIDs). Other medicines with a reported association with psoriasis include digoxin, clonidine, amiodarone, gold, tumour necrosis factor alpha (TNF α) inhibitors, fluoxetine, cimetidine, antibacterials (tetracycline and penicillin) and gemfibrozil (Kim & Del Rosso, 2010). Sudden withdrawal of corticosteroids can also precipitate psoriasis.

Unlikely causes

Guttate psoriasis (also known as raindrop psoriasis)

Guttate psoriasis is characterized by crops of scattered small lesions (<1 cm) covered with light flaky scales that often affects the trunk and proximal part of the limbs (Fig. 8.5). This form of psoriasis usually occurs in adolescents and often



Fig. 8.5 Guttate psoriasis. From Wilkinson, J., Shaw, S., & Orton, D. (2004). *Dermatology in focus*. Churchill Livingstone.

follows a streptococcal throat infection or in people genetically predisposed to psoriasis. The condition is usually self-limiting.

Flexural psoriasis

Flexural psoriasis refers to lesions that resemble plaque psoriasis but lack scaling and have atypical distribution; namely, in the body folds, especially the groins and axillae. Itching affects over 50% of people.

Tinea corporis

Tinea corporis can superficially look like plaque psoriasis. For further information on tinea infection, refer to the fungal infection section later in the chapter.

Lichen planus

Lichen planus is an uncommon condition and is reported to only account for 0.2% to 0.8% of dermatological outpatient consultations. The lesions are similar in appearance to plaque psoriasis but are itchy and normally located on the inner surfaces of the wrists and on the shins, an atypical distribution for psoriasis. Additionally, oral mucous membranes can be affected (~20% of patients) with white, slightly raised lesions that look a little like a spider's web. The person will not have a family history of psoriasis.

Pityriasis rosea

The condition is characterized by multiple discrete circular or oval lesions that show erythematous scaling mainly on the trunk, but also on the thighs and upper arms, and exhibits symmetry. The colour of the rash tends to be a lighter pink than psoriasis and can be mildly itchy. A target disc lesion (herald patch) normally appears on the trunk a few days before the generalized rash. It most commonly affects young adults. The condition usually remits spontaneously after 4 to 8 weeks. An accurate history will normally eliminate pityriasis rosea from psoriasis because the condition is acute in onset and the patient can often identify the initial target lesion.

Localized pustular psoriasis

In this form of psoriasis, sterile pustules are an obvious clinical feature. The pustules tend to be located on the advancing edge of the lesions and typically occur on the palms of the hands and soles of the feet (Fig. 8.6). It is more common in women than in men.

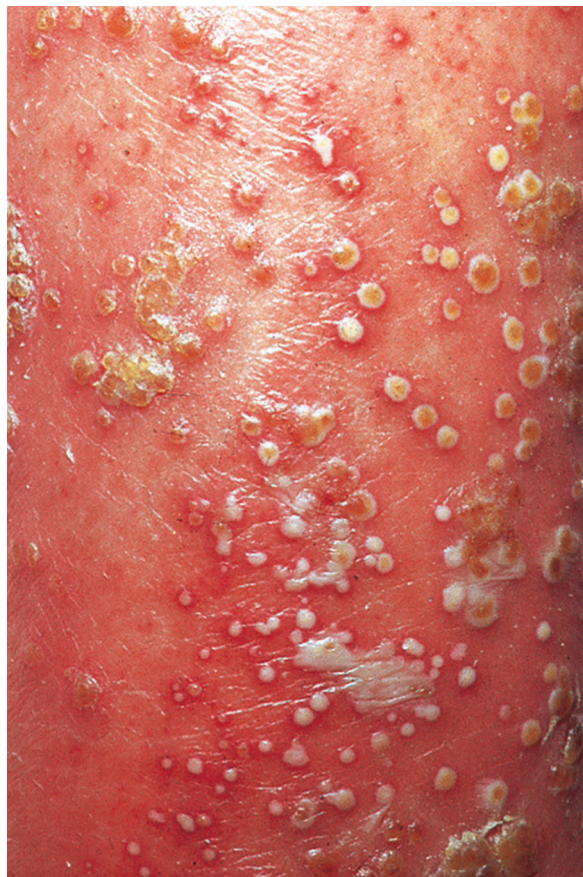


Fig. 8.6 Pustular psoriasis. From Wilkinson, J., Shaw, S., & Orton, D. (2004). *Dermatology in focus*. Churchill Livingstone.

Very unlikely causes

Erythrodermic psoriasis

Erythrodermic psoriasis presents as an extensive erythema and shows very few typical lesions. It is therefore difficult to diagnose. Systemic symptoms can be severe and include fever, joint pain, and diarrhoea. The condition is serious and can even be life-threatening. Patients are extremely unlikely to present at a community pharmacy.

Tinea capitis (fungal infection of the scalp)

Tinea capitis is the most common infection in children worldwide but in Western nations it is rare. Symptoms are characterized by scaling and itch of the scalp, broken hairs and patches of alopecia. The scalp may show a black dot appearance caused by broken-off hair stubs and a degree of erythema.

Fig. 8.7 will aid in the differentiation of plaque psoriasis.

! TRIGGER POINTS indicative of referral: Psoriasis

Symptoms/signs	Possible danger/ reason for referral	Urgency of referral
Lesions that are extensive, follow recent infection, have atypical psoriasis lesions, or cause moderate to severe itching	Suggest more severe forms of psoriasis or other conditions such as fungal infection	As soon as practicable
Precipitation or aggravation of lesions while taking medicines	If the medicine is suspected as the causative agent, re-assessment of therapy is required	

Evidence base for over-the-counter medication

Over-the-counter (OTC) remedies are effective in treating mild to moderate plaque and scalp psoriasis. However, before treatment is offered, it would be prudent to assess the impact the rash is having on the person. This can be done by using validated tools as described in Hints and Tips [Box 8.1](#). Any treatment recommended should also be in conjunction with reassurance about its benign, noncontagious nature, but emphasize that the condition is chronic and long-term and has periods of remission and relapse. Signposting to additional information provided by charities such as the Psoriasis Association (<http://www.psoriasis-association.org.uk/>)

should be considered. Treatment is limited to the use of emollients, keratolytics, coal tar, or dithranol (see below regarding its use), despite limited published literature supporting the efficacy of these treatments. Calcipotriol received a UK reclassification licence from the Medicines and Healthcare products Regulatory Agency (MHRA) in August 2017, but the product has not been brought to market by the manufacturer.

Emollients

No published literature appears to have addressed emollient efficacy or whether one emollient is superior to another in treating psoriasis. Subjective evidence over a long period of time has shown that emollients are useful and an important aspect of psoriasis treatment. Emollients are used to help soften scaling and soothe the skin to reduce irritation, cracking and dryness. Patients might have to try several emollients before finding one that is most effective for their skin.

Keratolytics

Keratolytics, such as salicylic and lactic acid, have been incorporated into emollients to aid the clearance of skin scaling. Although there appears to be no published evidence for their efficacy, clinical practice suggests that they have a role to play in the removal of scale (National Institute for Health and Care Excellence [NICE], 2017; section 1.3.3.3).

Coal tar

Coal tar remained the mainstay of treatment until the introduction of dithranol, corticosteroids and, more recently, vitamin A and D analogues. A number of clinical studies have confirmed the beneficial effect of coal tar on psoriasis, although a major drawback in assessing the effectiveness of

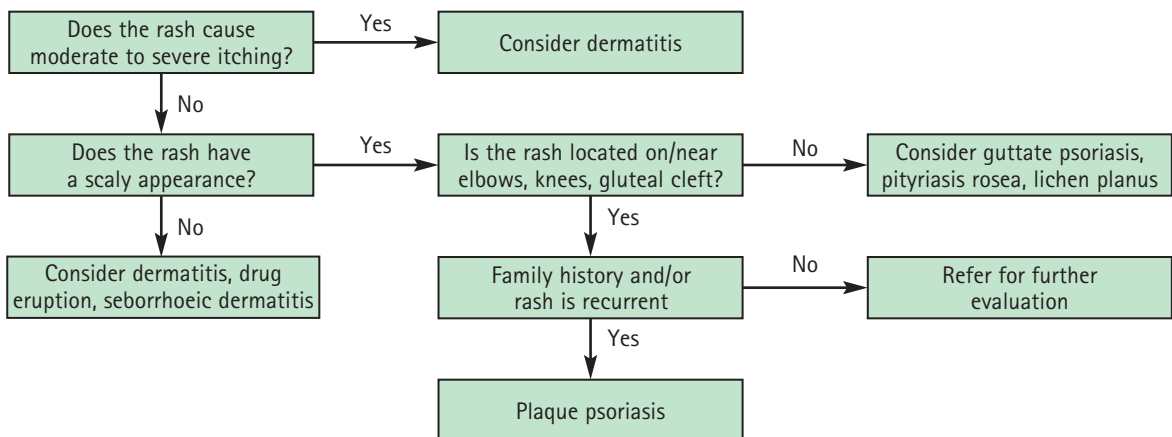


Fig. 8.7 Primer for differential diagnosis of plaque psoriasis.

HINTS AND TIPS BOX 8.1: PSORIASIS

Assessing the severity of psoriasis	Two validated tools can be used to assess how psoriasis affects the patient: DLQI (Dermatology Life Quality Index – a score that measures the impact of psoriasis on daily activities) and PASI (Psoriatic Arthritis Severity Index – a score that measures the severity of joint symptoms in psoriasis)
Problems with tar and dithranol products	Coal tar and dithranol share common problems of patient adherence. Both are messy to use, have a strong odour (which some find unpleasant); they can also stain skin and clothing.
UV light	90% of patients see an improvement in their psoriasis when exposed to sunlight, and most patients notice an improvement when they go on holiday.
Emollient use	Remind patients that these should be used regularly and liberally.
Emollient bath additives	Some bath additives (e.g., Oilatum) will make the bath slippery, and patients should be warned to be careful when getting out of the bath.

coal tar preparations is the variability in their composition, making meaningful comparisons between studies difficult. Comparisons between coal tar and other treatment regimens have been conducted. Tham et al. (1994) compared the effectiveness of calcipotriol, 50 µg twice daily, versus 15% coal tar solution each day. Both treatments were shown to be effective, although calcipotriol was significantly better than the coal tar solution. Harrington (1989) compared two commercially available OTC products at that time, Psorin and Alphosyl. Findings showed that both helped in the treatment of psoriasis but Psorin, (which includes 0.11% dithranol) was significantly more effective. NICE guidance from 2017 endorses the use of coal tar but it is generally used as a second- or third-line treatment.

Dithranol

A systematic review conducted by Mason et al. (2013) identified three placebo-controlled trials with dithranol, with all demonstrating a statistically significant improvement over placebo. There appears to be no definitive answer about which strength is most appropriate; however, current practice dictates starting on the lowest possible concentration and gradually increasing it until improvement is noticed. Its place in practice is now generally limited to psoriasis affecting the limbs or trunk in which other treatments have been ineffective and should not be initiated by community pharmacists.

Practical prescribing and product selection

Prescribing information relating to the medicines used to treat psoriasis is summarized in [Table 8.6](#); useful tips relating

to patients presenting with psoriasis are given in 'Hints and Tips' in [Box 8.1](#).

Emollients

All emollients should be regularly and liberally applied, with no upper limit on how often they can be used. All are chemically inert and can therefore be safely used from birth onwards by all patients. They do not have any interactions with other medicines. For more information on emollients, see later in this chapter and the National Eczema Factsheet (<http://www.eczema.org/emollients>).

Tar-based products

All patient groups can safely use these products on the skin or scalp. They can cause local skin or scalp irritation and stain skin and clothes. There has been concern over topical tar products' association with an increased risk of skin cancer, although this appears to be unfounded (Roelofzen et al., 2010).

Dithranol

Dithranol (Dithrocream) should not be routinely recommended due to the high likelihood of skin irritation and/or burning, as well as skin and cloth staining. If used, the lowest strength should always be tried initially for at least 1 week and then increased to higher concentrations if needed. The aim should be to build up gradually over approximately 4 weeks to the highest tolerated strength that results in the best therapeutic effect.



Table 8.6
Practical prescribing: Summary of tar-based products

Product	Scalp, skin or both	Salicylic acid	Sulphur	Other ingredients	Children	Application
Alphosyl 2-in-1 Shampoo	Scalp	No	No	No	All ages	Once or twice weekly
Capasal	Scalp	Yes	No	Coconut oil 1%	All ages	Daily
Cocois	Scalp	Yes	Yes	No	>6 years	Weekly
Exorex	Both	No	No	No	All ages	Two or three times a day
Polytar, Polytar Plus	Scalp	No	No	No	All ages	Once or twice weekly
Psoriderm	Both	No	No	No	All ages	Once or twice a day
SebCo	Scalp	Yes	Yes	No	>6 years	Daily when needed
T/Gel	Scalp	No	No	No	All ages	Two or three times a week

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- Psoriasis Association: <https://www.psoriasis-association.org.uk/>

Dandruff (pityriasis capitis)

Background

Dandruff is a chronic, relapsing, noninflammatory hyperproliferative skin condition often seen as socially unsightly and a source of embarrassment. It is a straightforward diagnosis. (Table 8.7).

Table 8.7
Causes of scalp flaking and their relative incidence in a community pharmacy

Incidence	Cause
Most likely	Dandruff
Unlikely	Contact and seborrhoeic dermatitis
Very unlikely	Tinea capitis

Prevalence and epidemiology

Dandruff is very common and affects both genders and all age groups, although it is unusual in prepubescent children. It has been estimated to affect 1% to 3% of the population (Gupta et al., 2004).

Aetiology

Increased cell turnover rate is responsible for dandruff, but why cell turnover increases is unknown. Increasingly, research has focused on the role of microorganisms on the pathogenesis of dandruff, and in particular the yeast *Malassezia* (previously known as *Pityrosporum ovale*), although the evidence is inconclusive as to whether *Malassezia* is the primary cause of dandruff or a contributory factor. It has been shown that *Malassezia* makes up more of the scalp flora of dandruff sufferers, which might explain why dandruff improves in the summer months (fungal organisms thrive in warm and moist environments that exist on the scalp due to wearing hats and caps). Further evidence to support a role of *Malassezia* in the cause of dandruff is the positive effect of antifungal therapy on clearing dandruff.

Arriving at a differential diagnosis

Most patients will diagnose and treat dandruff without seeking medical help. However, for those patients that do ask for help and advice, it is important to differentiate dandruff from other scalp conditions. Asking symptom-specific questions will help the pharmacist determine whether referral is needed (Table 8.8).

Clinical features of dandruff

The scalp will be dry, itchy and flaky. Flakes of dead skin are usually visible in the hair close to the scalp and are visible on the shoulders and collars of clothing.



Table 8.8
Specific questions to ask the patient: Dandruff

Question	Relevance
Presence of erythema	Dandruff is not associated with scalp redness unless the person has been scratching. Redness is characteristic of psoriasis and is common in adult seborrhoeic dermatitis.
Itch	Dandruff tends to cause itching of the scalp, unlike psoriasis and seborrhoeic dermatitis.
Presence of other skin lesions	An adult with only scalp involvement is likely to have dandruff, especially in the absence of erythema. Many patients who have scalp psoriasis also have plaque psoriasis affecting the arms, legs and back.

Conditions to eliminate

Unlikely causes

Seborrhoeic dermatitis

Typically, seborrhoeic dermatitis will affect areas other than the scalp. In adults, the trunk is commonly involved, as are the eyebrows, eyelashes and external ears. If only scalp involvement is present, the patient might complain of severe and persistent dandruff, and the skin of the scalp will be red.

Contact dermatitis

Ask about the use of new hair products such as dyes and perms. These can cause skin irritation and scaling. Avoidance of the irritant should see an improvement in the condition. If no improvement is seen after avoiding the suspected irritant after 1 to 2 weeks, then a reassessment of the symptoms is needed.

Very unlikely causes

Tinea capitis

If the problem is persistent and associated with hair loss, fungal infection of the scalp should be considered. Symptoms are characterized by scaling and itch of the scalp, broken hairs and patches of alopecia. The scalp may show a black dot appearance caused by broken-off hair stubs and a degree of erythema.

Fig. 8.8 will aid the differentiation of dandruff from other scalp disorders.

! TRIGGER POINTS indicative of referral: Dandruff

Symptoms/signs	Possible danger/ reason for referral	Urgency of referral
OTC treatment failure with a medicated shampoo	Suggests alternative diagnosis such as dermatitis or fungal infection	Nonurgent; as soon as practicable

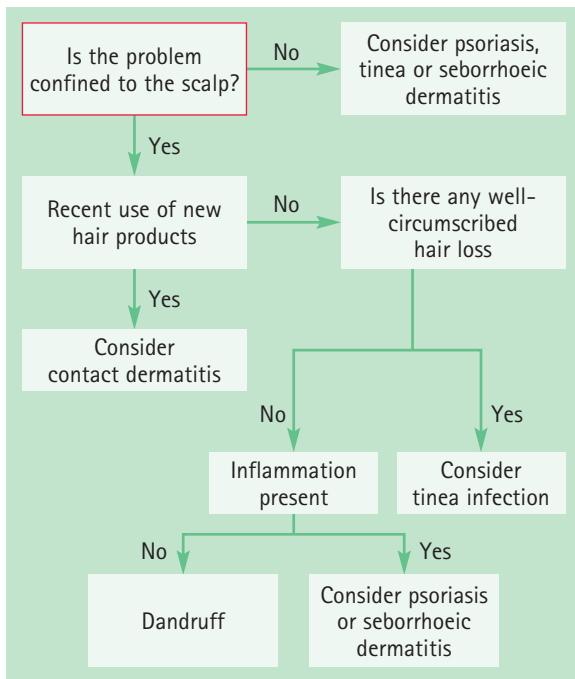


Fig. 8.8 Primer for differential diagnosis of dandruff.

Evidence base for over-the-counter medication

The use of a hypoallergenic shampoo on a daily basis will usually control mild symptoms. In more persistent and severe cases, a medicated shampoo can be used to control the symptoms. Treatment options include coal tar, selenium sulphide, zinc pyrithione and ketoconazole.

Coal tar

The mechanism of action for crude coal tar in the management of dandruff is unclear, although it appears that tars affect DNA synthesis and have an antimetabolic effect. There

are virtually no published studies in the literature to assess the efficacy of coal tars in the treatment of dandruff. One study comparing coal tar to placebo (Manriquez & Uribe, 2007), involving 111 people with seborrhoeic dermatitis or dandruff, found that coal tar reduced dandruff scores and redness compared with placebo at 29 days. Despite the lack of evidence, tar derivatives are found in a plethora of nonprescription medicated shampoos and have been granted Food and Drug Administration (FDA) approval in the US as an antidandruff agent.

Selenium sulphide

Selenium is thought to work by its antifungal action. It is accepted that selenium is effective as an antidandruff agent, and studies have shown it to be significantly better than placebo and nonmedicated shampoos (Manriquez & Uribe, 2007; Rapaport, 1981).

Zinc pyrithione

Zinc pyrithione, like selenium, exhibits antifungal properties but also reduces cell turnover rates. It is believed that one or both of these properties confers its effectiveness in treating dandruff. Few trials have been conducted with zinc pyrithione, although they have shown significant improvement in dandruff severity scores.

Ketoconazole

Ketoconazole inhibits *Malassezia* replication by interfering with cell membrane formation. It helps in controlling the itching and flaking associated with dandruff. Studies have shown it to be an effective treatment; it has been shown to be significantly better than zinc pyrithione and has similar efficacy to selenium (Sanfilippo & English, 2006). Ketoconazole has also been shown to act as a prophylactic agent in preventing relapse.

In addition, salicylic acid is included in some products (e.g., Capasal) for its keratolytic properties, although trials are lacking to substantiate its effect.

Practical prescribing and product selection

Prescribing information relating to the specific products used to treat dandruff is discussed and summarized in Table 8.9; useful tips relating to dandruff shampoo are given in 'Hints and Tips' in Box 8.2.

All antidandruff shampoos can cause local scalp irritation. If this is severe, the product should be discontinued. Any patient group can use them, although some manufacturers state that these products should be avoided during pregnancy. However, there appear to be no data to substantiate this precaution.



Table 8.9
Practical prescribing: Summary of medicines for dandruff

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
Coal tar products	All ages	Local irritation and dermatitis reported but rare	None	None	OK
Selenium	>5 years				Manufacturers state to avoid in pregnancy and while breastfeeding due to lack of safety data. However, safety data show it to be OK when used on small areas over a limited time; no evidence to say it would be absorbed into breast milk.
Zinc pyrithione	All ages				OK
Ketoconazole	All ages				

HINTS AND TIPS BOX 8.2: DANDRUFF

Selsun shampoo Gold, silver, and other metallic jewellery should be removed before use because they can be discoloured. It also has an odour that some may find unpleasant.

Coal tar products

Products containing coal tar are discussed under practical prescribing for psoriasis. Information on coal tar products, is provided under the psoriasis section.

Selenium sulphide (e.g., Selsun)

Adults and children over the age of 5 should use the product twice a week for the first 2 weeks and then once a week for the next 2 weeks. The hair should be thoroughly wet before applying the shampoo and left in contact with the scalp for 2 to 3 minutes before rinsing out. Selenium should be avoided if the patient has inflamed or broken skin because irritation can occur. Selenium can discolour hair but this can be minimised by thoroughly washing the product out.

Zinc pyrithione (e.g., Head & Shoulders)

Zinc-based products should be used on a daily basis until dandruff clears. Dermatitis has been reported with zinc pyrithione and should be borne in mind when treating patients with pre-existing dermatitis.

Ketoconazole (Nizoral Dandruff and Nizoral Anti-Dandruff Shampoo)

This can be used to treat acute flare-ups of dandruff or as prophylaxis. To treat acute cases, adults and children should wash the hair thoroughly, leaving the shampoo on for 3 to 5 minutes before rinsing it off. This should be repeated every 3 or 4 days (twice a week) for between 2 and 4 weeks. If used for prophylaxis, the shampoo should be used once every 1 to 2 weeks. It can cause local itching or a burning sensation on application and may rarely discolour hair.

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Seborrheic dermatitis

Background

There are two distinct types of seborrheic dermatitis, an infantile form, often referred to as *cradle cap*, and an adult form. Seborrheic dermatitis can present with varying degrees of severity, ranging from mild dandruff to a severe and explosive form in acquired immunodeficiency syndrome (AIDS) patients.

Prevalence and epidemiology

Estimates of the prevalence of clinically significant seborrheic dermatitis range from 1% to 5% of the population. Cradle cap is more prevalent than the adult form (Naldi & Rebora, 2009). Cradle cap usually starts in infancy, before the age of 6 months and is usually self-limiting; the adult form tends to be chronic and persistent. The adult form is more common in men than in women and also more common

in people with an underlying neurological illness; for example, Parkinson disease (Johnson & Nunley, 2000).

Aetiology

Despite its name, there appears to be no changes in sebum secretion. Like psoriasis and dandruff, seborrheic dermatitis is characterized by an increased cell turnover rate. The precise cause of seborrheic dermatitis remains unknown; several theories have been put forward, ranging from immunological, hormonal and nutritional mechanisms. Like dandruff, *Malassezia* plays an important role in the development of seborrheic dermatitis; however, it has not yet been established whether it has a primary or secondary role in the clinical expression of seborrheic dermatitis.

Arriving at a differential diagnosis

The infantile form is relatively easy to recognize but can sometimes be confused with atopic dermatitis. Arriving at a differential diagnosis of the adult form is more problematic because the condition can affect various areas and present with different degrees of severity. In mild cases, it needs to be differentiated from dandruff and, in more severe forms, from allergic contact dermatitis, psoriasis and pityriasis versicolor (Table 8.10). Asking symptom-specific questions will help the pharmacist establish a differential diagnosis (Table 8.11).

Clinical features of seborrheic dermatitis

Cradle cap appears as large, yellow, greasy scales and crusts on the scalp. This can become thick and cover the whole scalp (Fig. 8.10). Other areas can be involved, such as the face and napkin area.

The adult form is characterized by a history of intermittent skin problems. The distribution of rash is synonymous with skin areas with high numbers of sebaceous glands, typically the central part of the face, scalp, eyebrows, eyelids, ears, nasolabial folds and midchest (Fig. 8.11). The rash is red, with greasy-looking scales, and is mildly itchy. Blepharitis and otitis externa are also common secondary complications.

Table 8.10
Causes of seborrheic dermatitis-like rash and their relative incidence in community pharmacy

Incidence	Cause
Likely	Scalp psoriasis
Unlikely	Rosacea, atopic dermatitis, contact dermatitis
Very unlikely	Medicines, pityriasis versicolor



Table 8.11
Specific questions to ask the patient: Seborrhoeic dermatitis

Question	Relevance
Itching	In cradle cap, the rash does not itch. This is useful in differentiating cradle cap from atopic dermatitis because there is often overlap in the age at which they present.
Location	Infantile and adult forms of seborrhoeic dermatitis present in different locations (Fig. 8.9). Additionally, the distribution in the adult form varies from other similar skin conditions (e.g., psoriasis, typically involves knees, elbows and sacral area).
Positive family history	Patients tend not to have a family history in seborrhoeic dermatitis. This is in contrast to patients with psoriasis or atopic dermatitis.
Other symptoms	Ear and eyelid problems are associated with seborrhoeic dermatitis. The general health of a child with seborrhoeic dermatitis will be unaffected. In contrast, a child who is fractious and miserable is more likely to have atopic dermatitis. Seborrhoeic dermatitis presents as usually a yellow greasy scaliness to the skin, unlike psoriasis, which presents as a silvery scaliness to the skin.
Physical signs	If you run your fingers through the hair of someone with seborrhoeic dermatitis, little is felt. In psoriasis, accumulation of scales gives the scalp an uneven, lumpy feel.

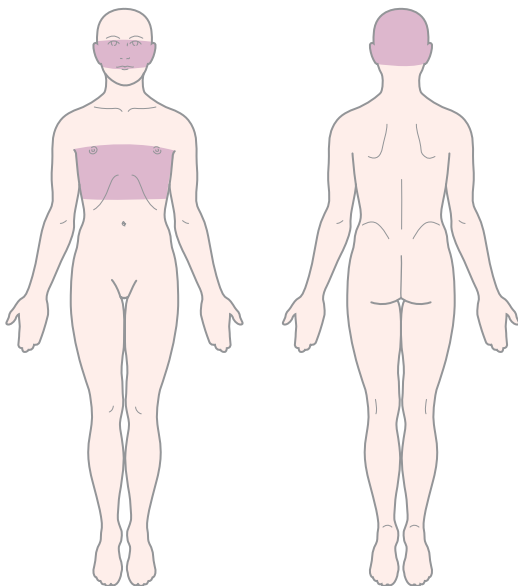


Fig. 8.9 Typical distribution of seborrhoeic dermatitis.

Conditions to eliminate

Likely causes

Psoriasis

Adults with scalp psoriasis can be confused with patients who present with severe and persistent dandruff caused by



Fig. 8.10 Infantile seborrhoeic dermatitis. Kliegman, R., Behrman, R. E., Emerson Nelson, W., & Jenson, H. B. (2007). *Nelson textbook of paediatrics*. Saunders Elsevier.

seborrhoeic dermatitis. However, in scalp psoriasis, the plaques tend to be crusty and extend away from the hairline.

Unlikely causes

Rosacea

Rosacea predominately affects adults between 30 and 50 years, typically involving the central face, an area also affected in adult seborrhoeic dermatitis. For more information on rosacea, refer to the acne section.



Fig. 8.11 Seborrhoeic dermatitis affecting the face. From Gawkrödger, D. J. (2007). *Dermatology: An illustrated colour text* (4th ed.). Churchill Livingstone.

Atopic dermatitis

In infants, atopic dermatitis usually presents as itchy lesions on the cheeks and forehead. Scalp involvement is less common, and the nappy area is usually spared. A positive personal or family history of the atopic triad of dermatitis, asthma or hay fever is common. For further information on differentiating atopic dermatitis from other conditions, see chapter 10.

Very unlikely causes

Pityriasis versicolor

Pityriasis versicolor (meaning branlike scaly rash of various colours), a yeast infection (90% of cases are caused by to *Malassezia* spp.), can be mistaken for adult seborrhoeic dermatitis. The lesions exhibit fine superficial scale and are located on the upper trunk. The macular lesions, which vary in colour, are usually small (<1 cm) but can join together to form larger plaques. The condition is associated more with warm climates, and most people will have acquired the infection when on holiday. The rash does not itch significantly, and the face is usually spared. It is most commonly seen in young adults. It can be treated with antifungal lotions and shampoos or imidazole creams for small numbers of lesions. If extensive areas are involved, antifungal shampoos, such as ketoconazole, are applied for 10 minutes

and then washed off; this is repeated daily for 5 days. For small areas, imidazole creams can be applied twice a day for 2 weeks.

Medications that can trigger or aggravate seborrhoeic dermatitis

A number of medicines are associated with triggering or aggravating existing seborrhoeic dermatitis. These include buspirone, cimetidine, gold, griseofulvin, haloperidol, interferon alfa, lithium, methyl dopa and phenothiazines.



TRIGGER POINTS indicative of referral: Seborrhoeic dermatitis

Symptoms/signs	Possible danger/reason for referral	Urgency of referral
Treatment failure with OTC medicines	Suggests misdiagnosis or severity of seborrhoeic dermatitis is unresponsive to OTC treatment	Nonurgent
Lesions that appear after holiday to warm climates	May indicate pityriasis versicolor	As soon as practicable

Evidence base for over-the-counter medication

Treatment options for seborrhoeic dermatitis are the same as dandruff. Ketoconazole, in a 2015 Cochrane review (Okokon et al., 2015), was shown to be effective compared with placebo.

For infants, simple measures, such as the daily use of a baby shampoo followed by gentle hair brushing, are usually only required to improve the condition. If this fails, the scales can be removed by applying olive oil to the scalp overnight, followed by using a baby shampoo the next morning. If symptoms persist, a medicated shampoo could be tried. If this fails, the child should be referred to the doctor. In adults, zinc pyrithione can be tried for mild cases of scalp involvement. Selenium and ketoconazole should be used for resistant or more moderate disease. For involvement on the face and torso, antifungals and corticosteroids are effective, but OTC product licenses currently preclude their use.

Practical prescribing and product selection

Prescribing information relating to specific products used to treat seborrhoeic dermatitis is discussed under Dandruff in this chapter. In addition, at least one product (Dentinox Cradle Cap Shampoo) is marketed specifically for cradle cap. This contains sodium lauryl ether sulfosuccinate, 6%, and sodium lauryl ether sulphate, 2.7%. The shampoo should be applied twice during each bath time until the scalp clears, after which it can be used when needed.

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Fungal skin infections

Background

Two main groups of fungi infect people, *Candida* yeasts and dermatophytes. However, in this section, only dermatophyte infections are discussed. Dermatophyte skin infections are classed by anatomical location – for example, athlete's foot (tinea pedis), groin infection (tinea cruris or *jock itch*), ringworm of the skin (tinea corporis), and scalp ringworm (tinea capitis).

Prevalence and epidemiology

Globally, dermatophytic fungi are more prevalent in tropical and subtropical areas because fungal organisms prefer high

temperatures and high humidity. Having said this, dermatophyte infections (*Trichophyton* spp.) are commonly seen in more temperate Western countries. Tinea pedis (athlete's foot) is the most common fungal infection, although prevalence rates vary, depending on the population studied and whether the diagnosis is made by clinical symptoms or culture confirmation. Athlete's foot is said to affect about 15% of the UK population and is common in people of all ages.

Other tinea infections such as tinea corporis and tinea cruris do present in the community pharmacy but are uncommon.

Aetiology

Dermatophyte infections are contagious and transmitted directly from one host to another. They invade the stratum corneum of the skin, hair and nails but do not generally infiltrate living tissues. The fungus then begins to grow and proliferate in the nonliving cornified layer of keratinized tissue of the epidermis. Transmission of athlete's foot is thought to be commonly acquired from communal rooms (e.g., changing rooms), whereas infection of the groin can be acquired from contaminated towels and bed sheets or by autoinoculation from an existing foot infection.

Arriving at a differential diagnosis

Depending on the area affected, the infection will manifest itself in a variety of clinical presentations. Recognition of symptoms for each site affected (Fig. 8.12) will facilitate

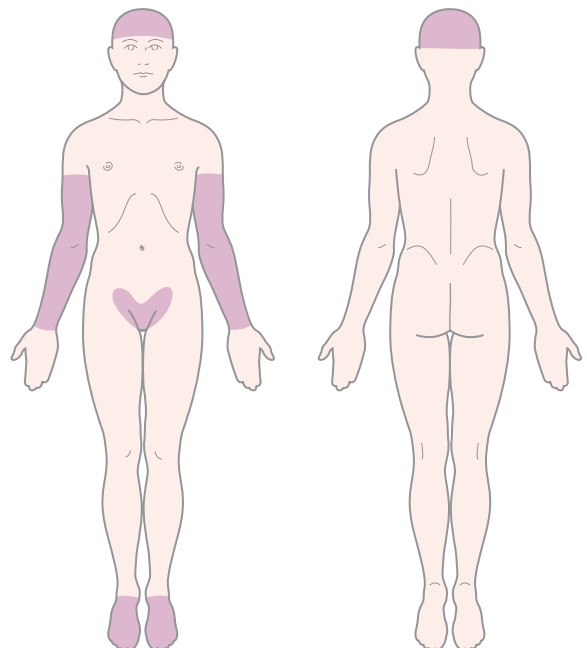


Fig. 8.12 Distribution of fungal infections.

Table 8.12
Causes of fungal-like rash and their relative incidence in community pharmacy

Incidence	Cause
Most likely	Athlete's foot, tinea corporis, psoriasis
Likely	Dermatitis, discoid eczema
Unlikely	Tinea cruris, pityriasis versicolor
Very unlikely	Pityriasis rosea, tinea faciei, tinea manuum

an accurate diagnosis. All forms of tinea infection, perhaps with the exception of isolated lesions on the body, should be relatively easy to recognize (Table 8.12).

Patients with athlete's foot will often self-diagnose the condition accurately. However, the pharmacist should still confirm this self-diagnosis through a combination of questions (Table 8.13) and inspection of the feet. This is important because it also provides an opportunity to check for fungal nail involvement.

Clinical features of tinea infections

Athlete's foot

Athlete's foot is characterized by itching, flaking and fissuring of the skin, which can also appear white and soggy due to maceration of the skin (Fig. 8.13). The usual site of infection



Fig. 8.13 Athlete's foot. From Fleischer, A. B., Feldman, S., Clayton, E., Katz, A. (2000). *20 common problems*. McGraw-Hill.

is in the toe webs, especially the fourth web space (web space next to the little toe). The feet often smell.

Once acquired, the infection can spread to other sites, including the sole and instep of the foot. Over time, this can infect the nails (see discussion of fungal nail infection later in this chapter). Cases of tinea infection where the plantar surface has become involved may be persistent and difficult to treat.

Tinea corporis

Tinea corporis is defined as an infection of the major skin surfaces that do not involve the face, hands, feet, groin or scalp. Fungal infection of the body is usually seen in children and young adults. The usual clinical presentation is of itchy



Table 8.13
Specific questions to ask the patient: Fungal infections

Question	Relevance
Age and sex of patient	Athlete's foot is most prevalent in adolescents and young adults, especially in males. Nail involvement usually occurs in older adults. Infection in the groin is much more common in men than in women.
Presence of itch	Fungal infections usually cause itch, irritation or burning sensations. This usually eliminates conditions such as psoriasis but not dermatitis and eczema.
Associated symptoms	Fungal lesions tend to be dry and scaly (except athlete's foot) and have a sharp margin between infected and noninfected skin.
Previous and family history	Fungal infections are usually acute in onset with no previous episodes, although athlete's foot may become recurrent. For lesions that do not show a classic textbook description, a positive family history of dermatitis or psoriasis should influence your differential diagnosis.



Fig. 8.14 Tinea corporis. From Buttaravoli, P. (2007). *Minor emergencies* (2nd ed.). Mosby.

pink or red, scaly, slightly raised annular patches with a well-defined inflamed border (Fig. 8.14). Over time, the lesions often show central clearing because the central area is relatively resistant to colonization. This appearance led to the term *ringworm*. Lesions can occur singly, be numerous, and rarely overlap to produce a single large lesion and appear polycyclic (several overlapping circular lesions).

Conditions to eliminate

Most likely cause

Plaque psoriasis

Isolated fungal body lesions can be difficult to distinguish from plaque psoriasis. However, if the patient has psoriasis, there will normally be a personal or family history of psoriasis. Lesions tend to be less itchy, exhibit more scaling and do not show central clearing.

Likely causes

Dermatitis – allergic and contact forms

Both fungal infections and dermatitis present as red itchy lesions and therefore can be difficult to distinguish from one another. Patients with dermatitis will often have a personal history of dermatitis or be able to describe an event that triggered the onset of the rash. For further information on dermatitis, refer to that section later in this chapter.

Misdiagnosis of a fungal infection for dermatitis, and subsequent treatment with a steroid-based cream, will diminish the itch, redness and scaling, but the infecting organism will proliferate. On withdrawal of the steroid cream, the visible signs of the infection will return and be worse than before, often in a papular form (*tinea incognita*).

Discoïd dermatitis

This presents as round, raised, coin-shaped itchy lesions that particularly affect the arms and legs and often occur symmetrically. It occurs mainly in middle-aged people.

Unlikely causes

Tinea cruris

The rash is usually isolated to the groin and inner thighs, but can spread to the buttocks. It is often bilateral and is normally intensely itchy, reddish brown, with a well-defined edge and does not exhibit central clearing.

Pityriasis versicolor

Pityriasis versicolor presents with patchy, sharply demarcated macules with fine scale. The rash tends not to itch and shows less inflammation than in tinea corporis. It is most commonly seen in young adults. For further information see page 244.

Very unlikely causes

Tinea faciei

Fungal infections on the face are rare and are consequently often mistaken for other facial skin conditions. The lesions are similar in appearance to tinea corporis in that they will normally have a sharp, well-defined border, show scaling and be itchy. Conditions such as acne, rosacea and lupus need to be considered in its differential diagnosis.

Tinea manuum

Tinea manuum is often misdiagnosed as eczema or psoriasis due to its atypical tinea appearance. The patient usually suffers from chronic diffuse scaling of one palm. Often, athlete's foot will be present because the infection has spread to the hands from the feet due to the patient scratching their feet. If no foot involvement is implicated, the diagnosis strongly points to dermatitis.

Pityriasis rosea

Initially, a target disc lesion (herald patch) appears a few days before the eruption of an extensive erythematous scaly rash, which mainly affects the trunk but also the thighs and upper arms. The herald patch is often misdiagnosed as tinea corporis.


**TRIGGER POINTS indicative of referral:
Tinea infections**

Symptoms/ signs	Possible danger/ reason for referral	Urgency of referral
Involvement of large areas of the trunk OTC treatment failure	Possible oral treatment needed	Nonurgent
Suspected facial or hand involvement	Confirmation of diagnosis required – both are rare causes of fungal infection	

Evidence base for over-the-counter medication

Superficial dermatophyte infections can be treated effectively with topical OTC preparations. Six classes of medicines are available, with varying levels of proven efficacy.

Allylamines

Terbinafine inhibits the biosynthesis of ergosterol, an essential component of fungal cell membranes. Studies have shown terbinafine to have high cure rates, significantly better than placebo and slightly better than imidazoles (Crawford & Hollis, 2007).

Imidazoles

Imidazoles, like allylamines, act by inhibiting ergosterol production but at a later stage in the ergosterol biosynthesis pathway. They have largely replaced older agents (e.g., benzoic acid, undecenoates, tolnaftate) because they have greater efficacy and an excellent safety record (Crawford & Hollis, 2007). There appear to be no clinically significant differences in cure rates among the different imidazoles, and the treatment choice will probably be driven by patient acceptability and cost.

Benzoic acid

Benzoic acid acts by lowering intracellular pH of dermatophytes; it is combined with salicylic acid (Whitfield's ointment). Although Whitfield's ointment has been on the market for nearly a century, there is insufficient evidence to determine its efficacy (El-Gohary et al., 2014). Newer products, with higher cure rates, quicker resolution and more cosmetically acceptable formulations, have replaced its widespread use.

Griseofulvin

Griseofulvin (as a 1% spray) works by inhibiting cellular mitosis. It has proven effectiveness when taken orally but has only limited trial data as a topical formulation. One trial reported an 80% mycological cure rate after 4 weeks with once-daily application (Aly et al., 1994).

Undecenoates

The exact mechanism of action for undecenoates is not understood. They have been used to treat athlete's foot for over 30 years and is featured in the most recent *US Pharmacopoeia*. In a Cochrane review, undecanoic acid was said to be efficacious in treating fungal infections for skin and nail infections of the foot (Crawford & Hollis, 2007).

Tolnaftate

Tolnaftate is thought to work by distorting fungal hyphae. It appears to have the least amount of trial data supporting its use. Low patient numbers involved in the studies further compounds the difficulty in assessing its efficacy.

Summary

On current evidence, an imidazole or terbinafine would be first-line treatment. Both have similar mycological and symptom cure rates, although terbinafine might be preferred because it clears symptoms in a shorter time, although it is more expensive.

Practical prescribing and product selection

Prescribing information relating to specific products used to treat fungal infections is summarized in [Table 8.14](#), and available products are summarized in [Table 8.15](#); useful tips relating to patients presenting with fungal infections are given in 'Hints and Tips' in [Box 8.3](#).

Imidazoles

All topical imidazoles have excellent safety records and can be used by all patient groups. Side effects experienced are irritation on application. To prevent reinfection, imidazoles should be used after the lesions have cleared, although the length of time varies from product to product. Full symptom resolution can take up to 1 month, depending on pathogen, location and severity of infection.

Clotrimazole (e.g., Canesten range)

Clotrimazole-containing products can be used for all dermatophyte and candidal infections. All Canesten



Table 8.14
Practical prescribing: Summary of medicines for tinea infections

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
<i>Imidazoles</i>					
Bifonazole	All ages	Mild burning or itching	None	None	OK
Clotrimazole					
Miconazole					
Ketoconazole					
Imidazole/steroid combination	>10 years				
<i>Tolnaftate</i>					
Scholl Advance Athlete's Foot range	No lower age stated	None	None	None	OK
<i>Undecenoates</i>					
Mycota	No lower age stated	None	None	None	OK
<i>Benzoic acid</i>					
Whitfield's ointment	No lower age stated	None	None	None	OK
<i>Terbinafine</i>					
Lamisil range	>16 years (>18 years for Lamisil Once)	Redness, itching	None	None	OK
Griseofulvin (Grisol AF)	No lower age stated	Stinging	None	None	OK

Table 8.15
Summary of antifungal products and formulations

Active ingredient	Brand	Formulations
Bifonazole	Canesten Bifonazole Once Daily	Cream
Clotrimazole 1%	Canesten AF Dual Action	Cream
	Canesten	Cream, spray, solution
	Care	Cream
Clotrimazole 1% and hydrocortisone 1%	Canesten Hydrocortisone	Cream
Miconazole 2%	Daktarin Activ	Cream, spray, powder
	Daktarin	Cream and powder
Miconazole 2% and hydrocortisone 1%	Daktacort Hydrocortisone	Cream
Ketoconazole	Daktarin Gold	Cream
Terbinafine	Lamisil AT	Spray, cream, gel
	Lamisil Once	Solution
	Scholl Advance Athlete's Foot Cream	Cream
Tolnaftate	Scholl Athlete's Foot	Spray, powder
Undecanoic acid	Mycota	Cream, powder

HINTS AND TIPS BOX 8.3: FUNGAL INFECTION

Reinfection and transmission	It is not known if improving foot hygiene or changing footwear can help cure athlete's foot but measures to reduce transmission include the following: <ol style="list-style-type: none"> 1. Dry the skin thoroughly after showering or having a bath. Keep a personal towel and do not share it to prevent the infection spreading from person to person. 2. Wear cotton socks and change at least once a day. 3. Avoid the use of occlusive nonbreathable shoes. 4. Dust shoes and socks with antifungal powder. 5. Avoid scratching infected skin. 6. Use flip-flops (or equivalent) when using communal changing rooms.
Steroid-containing products	The license states that the maximum period of treatment is 7 days. This limits their usefulness because many fungal infections will take longer to clear than 7 days, especially because products need to be used after the lesions have cleared to prevent reinfection. Therefore, they are probably best used to control initial symptoms of redness and itch before switching to an imidazole-only product after the initial 7 days of treatment.

products should be applied two or three times a day with the exception of Canesten hydrocortisone, which can only be used twice a day.

Bifonazole (Canesten Bifonazole Once Daily 1% w/w Cream)

Bifonazole is licensed for athlete's foot. For all patients, the cream should be applied once daily.

Ketoconazole (Daktarin Gold, Daktarin Intensiv)

Ketoconazole has a license for athlete's foot, groin infection, and candidal intertrigo. For athlete's foot, the cream should be applied twice daily for 1 week. For groin infections and candidal intertrigo, the cream should be applied once or twice daily. If no improvement in symptoms is experienced after 4 weeks, the patient should be referred to the doctor. For all conditions, treatment should be continued for 2 to 3 days after all signs of infection have disappeared to prevent relapse.

Miconazole (e.g., Daktarin, Daktarin Aktiv, Daktacort Hydrocortisone)

Products containing miconazole are suitable for all patients and should be applied twice a day. Treatment should continue for 10 days after all lesions have disappeared to prevent relapse. Daktacort hydrocortisone is suitable for children over 10 years of age and is licensed for candidal intertrigo and athlete's foot.

Tolnaftate (e.g., Scholl Athlete's Foot range)

They can be used for athlete's foot and infections of the groin and should be used twice a day, with treatment continuing for at least 1 week after the infection has cleared up.

Undecenoates (e.g., Mycota)

They are licensed for athlete's foot, and should be used twice a day, with treatment continued for at least 1 week after the infection has cleared up. Local irritation has been reported.

Benzoic acid (e.g., Whitfield's ointment)

Benzoic acid (in combination with salicylic acid) is now rarely used. However, it is a safe medicine and can be used by all patients.

Terbinafine (e.g., Lamisil range)

Terbinafine can be used to treat athlete's foot, groin infection, and tinea corporis and is applied once daily. All products are licensed for those older than 16 years, except Lamisil Once, which is for use in people older than 18 years.

Griseofulvin (Grisol AF spray)

Licensed for athlete's foot, Grisol should be applied to the area once daily. One spray (delivering 400 µg of griseofulvin) should be applied to the affected area once daily for mild infections, which can be increased to a maximum of three sprays in 24 hours for more extensive or severe infection.

The spray should be used for 10 days after the lesions clear to prevent reinfection. It has few reported side effects and can be used by all patients.

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Fungal nail infection (onychomycosis)

Background

The deregulation of amorolfine in the UK and other Western countries (e.g., Australia) now makes it possible for community pharmacists to treat infection affecting the toenails. Onychomycosis is defined as a chronic fungal infection of the fingernails or toenails, although only infection of the toenail is covered here. The infection is common but probably underreported because of patient embarrassment or ignorance that they have an infection. If left untreated, it can lead to pain and discomfort, which can make wearing shoes difficult. The nails, over time, will disfigure and crumble away.

Prevalence and epidemiology

It is estimated that 5% to 10% of the general population suffers from onychomycosis (Thomas et al., 2010). The incidence of infection increases with increasing age and is particularly common in people older than 70 years (estimated at up to 50%).

Aetiology

Over 90% of cases are caused by dermatophytes (*Trichophyton rubrum* and *Trichophyton interdigitale*), with the remainder caused by yeasts and moulds. In most cases, predisposing

factors can be determined in the development of nail infection; for example, an initial skin infection (tinea pedis), in immunocompromised patients, or poor peripheral circulation and neuropathies (e.g., diabetes).

Arriving at a differential diagnosis

There are a number of different types of onychomycosis, and it is important to be able to differentiate between them because amorolfine is only licensed for the treatment of distal lateral subungual onychomycosis. Taking a history of the presenting symptom will be helpful, but a visual inspection of the toenails is strongly advocated.

Clinical features of distal lateral subungual onychomycosis

Distal lateral subungual onychomycosis (DLSO) is usually asymptomatic, and people often seek medical help because of concerns about the appearance of the nail. The nail takes on a dull opaque and yellow appearance. Over time, the nail thickens and distorts and, as infection spreads and worsens, the nail becomes brittle and crumbles away or falls off (Fig. 8.15). The key clinical symptoms that differentiate DLSO from other types of onychomycosis are summarized in Table 8.16.

Other conditions to eliminate

Psoriasis, eczema and trauma can affect the nail and need to be considered. With psoriasis, nail pitting is visible



Fig. 8.15 Tinea unguium. From Buttaravoli, P. (2007). *Minor emergencies* (2nd ed.). Elsevier Mosby.

Table 8.16

Main types of onychomycosis

Type	Key characteristics	Spread of infection
Distal lateral subungual onychomycosis (DLSO)	Mainly big toe	Yellowing starts at distal part of toe or side of nail
Proximal subungual onychomycosis (PCO)	Immunocompromised patients	White or yellow spots appear at the base of the nail (i.e., in the half-moon area of the nail)
Superficial white onychomycosis	Often occurs in previously damaged nails Chalky-white in appearance and can be scraped off the nail surface	Located on the surface of the nail

(Fig. 8.16); for trauma, there should be an identifiable event that affected the nail; and, in eczema and psoriasis, the skin should be affected, near and around the feet (eczema) or remotely (psoriasis plaques on areas such as knees and elbows).


TRIGGER POINTS indicative of referral: Distal lateral subungual onychomycosis (DLSO)

Symptoms/signs	Possible danger/ reason for referral	Urgency of referral
Fungal infection other than DLSO	Requires medical confirmation and possible oral treatment	Nonurgent, as soon as practicable
OTC treatment failure or suspected poor compliance	Suggests misdiagnosis or the need for oral treatment	

Evidence base for over-the-counter medication

Amorolfine is a broad-spectrum antifungal agent that works by inhibiting ergosterol synthesis. An open-labelled, nonrandomized trial has shown it to be effective, producing clinical cure in 37% of toenail infections (Zaug & Bergstraesser, 1992). However, the study suffered from large dropout rates (nearly 30%), and there were no comparisons with other available topical antifungal treatments. A further trial comparing once- versus twice-weekly application of amorolfine reported similar cure rates (46%) with weekly application (Reinel, 1992). A Cochrane review found limited evidence for the efficacy of any topical treatments for nail infections, but suggested that

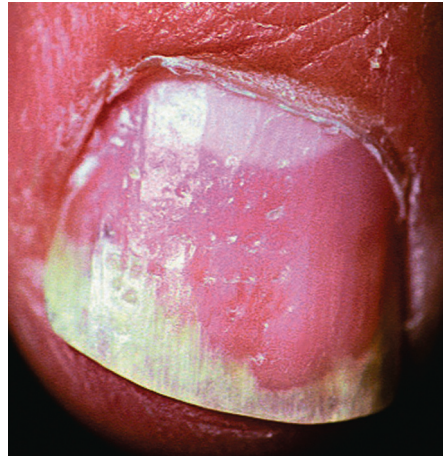


Fig. 8.16 Nail pitting seen in psoriasis.

cure rates may be better with amorolfine, although this was based on small trials (Crawford & Hollis, 2007).

Practical prescribing and product selection

Prescribing information relating to amorolfine is summarized in Table 8.17; useful tips relating to patients presenting with fungal nail infection are given in 'Hints and Tips' in Box 8.4.

Amorolfine

Amorolfine (e.g., Loceryl Curanail, Care antifungal nail lacquer, Schollmed once-weekly fungal nail treatment) is available as a 5% nail lacquer. It is used weekly, and treatment continues until the affected nail(s) have regrown and are clear of infection. This takes approximately 9 to 12 months for toenails. Each pack provides treatment for 3 months, which affords the pharmacist an opportunity to review treatment before further medication is given. The product licenses



Table 8.17
Practical prescribing: Summary of medicines for fungal nail infections

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
Amorolfine	>18 years	None	None	None	Manufacturers state to avoid, although evidence suggests it is safe to use.

HINTS AND TIPS BOX 8.4: CURANAIL

Why only two nails?	This is in line with UK guidance because more severe infections require systemic treatment (e.g., terbinafine).
Hygiene measures	<ul style="list-style-type: none"> ● Keep the area clean. ● Change socks regularly. ● Keep nails trimmed short and filed down. ● Avoid trauma to the nails. ● Avoid sharing towels.

restrict use to no more than two nails in people older than 18 years and who have no underlying medical conditions that predispose them to fungal infection (e.g., immunocompromised individuals and diabetics). To apply amorolfine, the nail must first be filed and cleaned. Files and cleaning pads are provided in the treatment pack and are not reusable. The lacquer should then be evenly applied and left to dry. Amorolfine is unlikely to cause side effects, but skin irritation has been reported. Manufacturers recommend it should not be used in pregnant or breastfeeding women.

References

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Website

For more images of fungal nail infection visit: <https://www.dermnetz.org/topics/fungal-nail-infections>.

Hair loss (androgenetic alopecia)

Background

Each hair consists of a shaft made up of dead keratinized cells and a root (see Fig. 8.1), and is found on most skin surfaces (palms of hands, soles of feet and lips being notable exceptions). Each hair follicle goes through a growth cycle, which consists of a long growing phase (anagen), followed by a short resting phase (telogen). At the end of the resting phase, the hair falls out (catagen), and a new hair starts growing in the follicle, beginning the cycle again. The hair cycle occurs randomly for each follicle so that normal hair loss from the adult scalp is approximately 100 hairs/day; when the rate is greater than this, clinical signs of hair loss can be observed. Hair loss affects both men and women and is associated with strong emotional and psychological consequences. Hair loss can have a number of causes; however, this section concentrates on androgenetic alopecia because it is the most common cause of hair loss. Androgenetic alopecia describes a distinctive pattern of hair loss that may occur in genetically predisposed people and is thought to be androgen dependent.

Prevalence and epidemiology

Men are more susceptible than women to androgenetic alopecia and usually experience more severe hair loss. Men tend to be affected from the second decade onwards (30% of men by 30 years old will be affected to some degree), and the prevalence of male pattern baldness in Caucasians

who reach old age approaches 100%. Asian and black men are less prone to hair loss. In women, the condition becomes more pronounced after menopause.

Patients usually have a positive family history. The nature and extent of hair loss will follow identical patterns to those seen in the patient's immediate parents and grandparents, which can be used as a predictor to the patient's potential hair loss pattern.

Aetiology

Hair is classified as terminal or vellus hair. Terminal hair is longer and thicker and is found on the scalp and eyebrows. Vellus hair covers the remainder of the body and is shorter and downy. In androgenetic alopecia, terminal hair follicles transform into more vellus-like hair follicles as a result of preferential binding by dihydrotestosterone (produced from the conversion of androgen by 5 α -reductase) to hair follicle receptors. Eventually, the follicle ceases activity completely, with resulting hair loss. Complete hair loss can take between 15 and 25 years.

Arriving at a differential diagnosis

Hair loss is obviously easy to notice. Empathy and understanding towards the patient need to be shown. Although androgenetic alopecia is the most common form of hair loss, other causes need to be eliminated (Table 8.18 and Fig. 8.17). Asking symptom-specific questions will help the pharmacist determine whether referral is needed (Table 8.19).

Clinical features of androgenetic alopecia

Men initially notice a thinning of the hair and a bitemporal receding hairline that might or might not be accompanied by hair loss at the crown. In women, the frontal hairline is maintained with diffuse hair loss that is somewhat accentuated at the crown.

Table 8.18

Causes of hair loss and their relative incidence in community pharmacy

Incidence	Cause
Most likely	Androgenetic alopecia
Likely	Postpartum, stress, nutritional deficiency states, medicines
Unlikely	Alopecia areata, endocrine disorder
Very unlikely	Tinea capitis, traction alopecia, trichotillomania

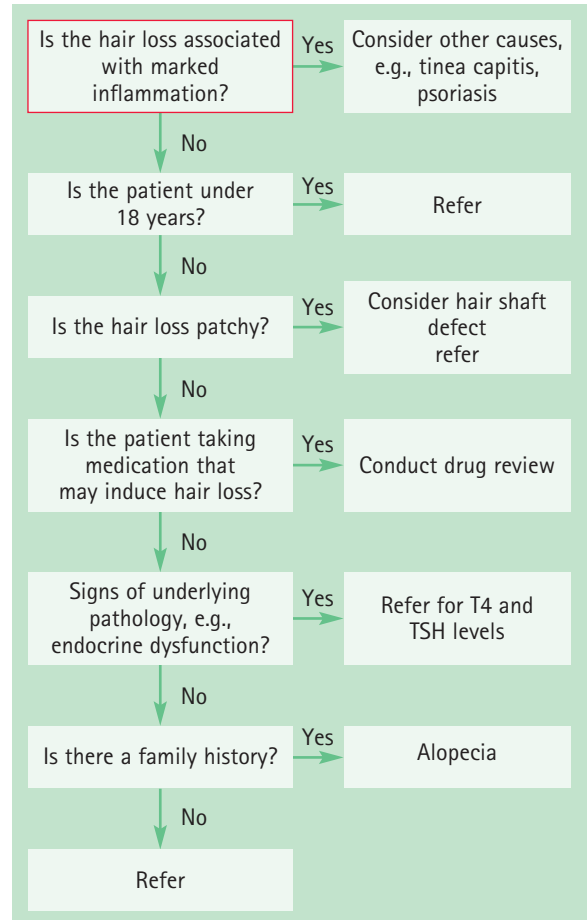


Fig. 8.17 Primer for differential diagnosis of hair loss.

Conditions to eliminate

Likely causes

Postpartum

During pregnancy, circulating levels of oestrogen increase, with a resulting rise in the number of follicles in anagen (growth phase); the hair therefore thickens. However, after delivery, the hair follicles return to the resting phase, and the hair is shed. Women might believe that they are experiencing hair loss when in reality the hair is returning to the normal prepregnancy state. Reassurance should be given that this is a temporary and self-limiting problem.

Stress

Stress is known to induce hair loss. The reason behind this is poorly understood. Enquiry to ascertain lifestyle factors that might have caused recent stress and anxiety to the patient should be explored.



Table 8.19
Specific questions to ask the patient: Hair loss

Question	Relevance
Hair loss accompanied with other symptoms	Androgenetic alopecia is not associated with other symptoms. Itch and/or erythema are indicators of another cause; (e.g., fungal scalp infection, psoriasis or seborrhoeic dermatitis).
Pattern of hair loss	In men, hair loss begins at the front of the head and recedes backwards or at the crown. In women, hair loss tends to be generalized and diffuse. Presentations that differ from this or are sudden in onset suggest another cause of hair loss.
Medical and drug histories	There is now strong evidence that iron deficiency in women can cause hair loss. A number of endocrine conditions can cause hair loss, most notably thyroid disorders. A number of medicines can cause hair loss (see Table 8.20).
Hair loss triggered by a specific event	Hair loss can be caused by a stressful event or following surgery or after childbirth.

Nutritional factors

Iron deficiency is associated with female hair loss. If iron deficiency is the cause, a 2-month course of iron supplementation should result in a thickening of the hair. If the patient fails to respond to treatment, the patient should be reassessed.

Medicine-induced causes

Many medicines can interfere with the hair cycle and cause transient hair loss, with cytotoxic medicines being one of the most obvious examples. However, many medicines have been associated with hair loss. Table 8.20 lists some of the more commonly implicated medicines. If medicines other than cytotoxics are suspected of causing hair loss, the prescriber should be contacted to discuss other possible treatment options.

Unlikely causes

Alopecia areata

Refers to hair loss of unknown origin, although there is often an association with atopy and autoimmune disease, and a positive family history is found in up to 25% of patients. It is relatively uncommon, affecting 0.1% to 0.2% of the UK population. Unlike androgenetic alopecia, the hair loss mainly affects children and adolescents (60% will have had their first episode before the age of 20). It is most commonly observed as patchy hair loss of sudden onset, although the whole scalp can be affected. The condition is usually self-limiting, and regrowth of hair is often observed, but repeated episodes are not unusual.

Underlying endocrine disorder

Hypothyroidism (and other endocrine disorders such as diabetes) can result in poor hair growth. In hypothyroidism, the hair is thin and brittle, and the patient might be lethargic and



Table 8.20
Medicines known to cause hair loss

Medicine or medicine class	Incidence of hair loss
Antineoplastics	Almost 100% (to varying degrees)
Anticoagulants	Telogen effluvium ^a in approximately 50%
Lithium carbonate	Telogen effluvium in approximately 10%
Interferons	Telogen effluvium in 20% – 30%
Oral contraceptives	Seen 2–3 months after stopping
Retinoids	Approximately 20% of patients
Colchicine, carbimazole	Rare

^aTelogen effluvium: shift of more hairs into resting phase (telogen) of the hair cycle, which results in shedding of hair.

have a history of recent weight gain. If suspected, referral to the doctor for blood tests is required.

Very unlikely causes

Fungal scalp infection (*tinea capitis*)

The first sign of infection is the appearance of a well-circumscribed round patch of alopecia that is associated with itch and scaling. Common areas of involvement include the occipital, parietal, and crown regions. Inspection of the area

might reveal erythema and black dots on the scalp as a result of broken-off hair stubs.

Traction alopecia

Most commonly seen in women, traction alopecia refers to hair loss due to excess and sustained tension on the hair, usually as a result of styling hair with rollers or a particular type of hairstyle. It is reversible if the tension on the hair is removed.

Trichotillomania

Trichotillomania is a psychiatric disorder that refers to patients who have an impulsive desire to twist and pull scalp hair, but often deny it. Hair loss is asymmetrical and an unusual shape. It is more commonly seen in women.

! TRIGGER POINTS indicative of referral: Hair loss

Symptoms/signs	Possible danger/ reason for referral	Urgency of referral
Patients <18 years old Sudden onset Suspected iron deficiency anaemia or hypothyroidism	Unlikely to be androgenetic alopecia Medical referral for blood test	Nonurgent referral
Trichotillomania Fungal infection of the scalp Possible endocrine cause	All require further assessment and medical confirmation	As soon as practicable

Evidence base for over-the-counter medication

Currently, minoxidil is the only product marketed for androgenetic alopecia. It is available in 2% and 5% concentrations.

A number of clinical trials have investigated the efficacy and safety of minoxidil at both concentrations. Most of these have been conducted on precisely the population that would respond the best to treatment: men between 18 and 50 years of age, with mild to moderate thinning of the hair at the vertex. Despite this, trial results are not totally convincing. Minoxidil is superior to placebo (although placebo does promote a large initial response), promotes a small increase in regrowth of vellus hair, and increases the diameter of the hair shaft. In a randomized 48-week trial of 2% and 5% minoxidil, both preparations produced a statistically significant increase in hair count and investigator-rated benefit from treatment (Olsen et al., 2002). However, the average investigator-rated benefit from treatment using a scale of 0 to 100 (with 0 no benefit 50 moderate

benefit and 100 great benefit) was only 33.7 for the 5% solution, 30.2 for the 2% solution and 12.6 for placebo. In another randomized controlled trial, minoxidil increased hair growth moderately after 16 weeks in 7.8% of men using the product compared with 0.6% in those on placebo (Olsen et al., 2007). However, longitudinal studies show that less than half of patients treated experience moderate to marked hair growth. Hair counts appear to be greatest after 12 months of treatment, but by 30 months hair counts have decreased (albeit still above baseline), and the bald area increases back in size to its initial diameter (Koperski et al., 1987).

Minoxidil, therefore, appears to delay and slow down hair loss in less than half of its target patient population. Furthermore, if treatment is stopped, any hair growth achieved is lost within 6 to 12 months on discontinuation of therapy, and baldness returns to pretreatment levels.

The situation in women is not too dissimilar, although the 5% solution offers no advantage over the 2% solution and has therefore not been granted a product license at that strength.

A 2015 meta-analysis by Gupta and Charette confirmed these findings, concluding that despite significant clinical efficacy, cosmetically acceptable results are present in only a subset of patients.

Summary

Minoxidil will not significantly help most balding individuals. It will promote moderate or marked hair growth in approximately one-third of minimally balding young men, one third will have minimal regrowth, and one-third will remain unchanged. In other words, the use of minoxidil is useful for specific patients who want to 'buy' themselves time from the inevitable balding process.

Oral finasteride (1 mg/day) (on private prescription in the UK) can be used to treat androgenic alopecia in men, but currently there is no good-quality evidence that it is superior to minoxidil.

Practical prescribing and product selection

Prescribing information relating to minoxidil is discussed and summarized in [Table 8.21](#); useful tips relating to the treatment of patients with minoxidil are given in 'Hints and Tips' in [Box 8.5](#).

Minoxidil (e.g., Regaine range as either solution or foam)

The dose for minoxidil is 1 mL of solution (or 1 g of foam, equivalent to half a capful) applied to dry hair on the total affected areas of the scalp twice daily. If fingertips are used to facilitate drug application, the hands should be washed



Table 8.21
Practical prescribing: Summary of medicines for hair loss

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
Minoxidil (Regaine)	Not applicable	Skin irritation, headache	None	Avoid in patients with cardiovascular disease	Avoid

HINTS AND TIPS BOX 8.5: HAIR LOSS

Changes to hair colour and texture	Some patients have experienced changes in hair colour and/or texture with minoxidil use. The patient should be warned of this possible problem before using the product.
How long should the patient use Regaine?	It can take 4 months or more before evidence of hair growth can be expected. Users should discontinue treatment if there is no improvement after 1 year.

afterwards. Although minoxidil is applied topically, absorption into the systemic circulation can occur and commonly gives rise to chest pain and, uncommonly, rapid heartbeat, faintness, or dizziness. If these occur, the patient should stop using the product immediately. Other common but less important adverse effects associated with topical minoxidil are local irritation, redness and itching, but these appear to be related to the vehicle, propylene glycol, rather than minoxidil. Changes in blood pressure should not occur because the serum level of minoxidil after topical application is below the amount needed to cause changes to blood pressure; however, as a precaution, minoxidil should be avoided in hypertensive patients if possible. Some patients also report a temporary increase in hair shedding 2 to 6 weeks after beginning treatment. This subsides and is most likely due to the action of minoxidil, shifting hairs from the resting telogen phase to the growing anagen phase.

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Warts and verrucas

Background

Warts and verrucas are benign growths of the skin caused by the human papilloma virus (HPV). Certain types of HPV have an affinity for certain body locations; for example, the hands, face, anogenital region, and feet. Spontaneous resolution is seen in 30% of people within 6 months and two-thirds of cases within 2 years. Despite their self-limiting nature, they are cosmetically unacceptable to many patients and, with nearly 60% of people trying an OTC treatment before visiting a doctor, the pharmacist has a major role to play in their management.

Prevalence and epidemiology

The prevalence of warts has not been accurately documented, and published prevalence data vary widely. Children are most affected, with 2% to 20% experiencing symptoms before the age of 16. Warts are uncommon in infants and in older adults, and caution should be exercised if an older patient presents to the pharmacy with a self-diagnosed wart.

Aetiology

HPV gains entry to the host by epithelial defects in the epidermis. It is transmitted by direct skin to skin contact, although contact with an infected person's shed skin can also transmit the virus. Infection via the environment is more likely to occur if the skin is macerated and in contact with roughened surfaces; for example, in swimming pools and communal washing areas. Once established in the epithelial cells, the virus stimulates basal cell division to produce the characteristic lesion.

Patients, especially children, should be warned not to pick, bite, or scratch warts because this can allow viral particle shedding to penetrate skin breaks. This process is known as *autoinoculation* and is responsible for multiple lesions becoming established and transferred to other parts of the body.

Table 8.22
Causes of wartlike lesions and their relative incidence in community pharmacy

Incidence	Cause
Most likely	Common warts and verrucas
Likely	Corns, molluscum contagiosum
Unlikely	Plane warts, seborrhoeic keratosis
Very unlikely	Basal cell carcinoma

Arriving at a differential diagnosis

Warts and verrucas are not difficult to diagnose. However, pharmacists must be able to recognize other similar conditions that superficially look like warts and verrucas (Table 8.22). Asking symptom-specific questions will help the pharmacist establish a differential diagnosis (Table 8.23). HPV infections involving the anogenital area are outside the remit of community pharmacists and must be referred.

Clinical features of warts and verrucas

Warts

Warts most often occur on the backs of the hands, fingers and knees, either singly or in crops. When examined, the wart appears as a raised hyperkeratotic papule with thrombosed black vessels often visible as black dots within the wart. They tend to be rough textured and skin coloured and are usually less than 1 cm in diameter (Fig. 8.18).

Verrucas

Verrucas are found on the soles of the feet, usually in weight-bearing areas; for example, on the metatarsal heads or heel. Owing to constant pressure imparted on the sole of the foot, the normal outward expansion of the wart is thwarted and instead grows inward. Pressure on nerves can then cause considerable pain, and patients often complain of pain when walking. Inspection of the lesion will normally reveal tiny black dots (thrombosed capillaries) on the surface (Fig. 8.19). Owing to keratin buildup, this characteristic sign might not be visible unless the hardened skin is first shaved away. Verrucas, like warts, are rarely larger than 1 cm in diameter and can occur singly or in crops. A number of closely located plantar warts can coalesce to form a large single plaque termed a *mosaic wart*.



Table 8.23
Specific questions to ask the patient: Human papilloma virus

Question	Relevance
Age of patient	Warts are unusual in very young children, such as infants. Young children and adolescents are most likely to get warts but this is also the age group in which molluscum contagiosum is most prevalent. The likelihood that nodular lesions are caused by seborrhoeic warts or carcinoma increases with increasing age.
Location	Warts are common on the hands and knees; verrucas are usually on the weight-bearing parts of the sole. Warts can occur on the face but so too can plane warts and carcinoma. Referral is always needed because all OTC treatments can cause scarring.
Associated symptoms	Itching and bleeding is not associated with warts and verrucas and must be viewed with suspicion, especially in older patients. Pain on walking is often associated with verrucas.
Colour, appearance	Typically, warts have a cauliflower appearance and are raised and pale. Warts with a reddish hue or that change colour should be referred. Lesions that are raised, smooth and have a central dimple suggest molluscum contagiosum.



Fig. 8.18 Common wart. From Wilkinson, J., Shaw, S., & Orton, D. (2004). *Dermatology in focus*. Churchill Livingstone.

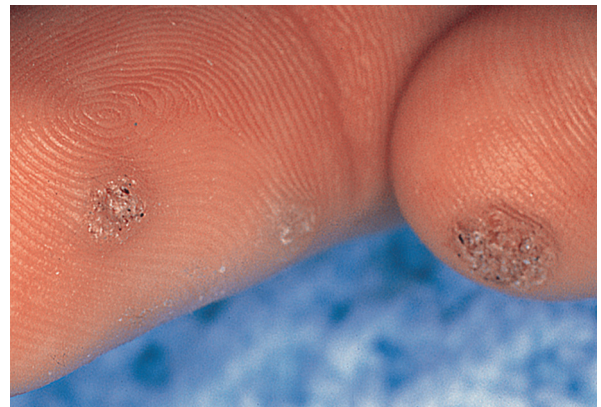


Fig. 8.19 Verruca. From Gawkrödger, D. J. (2007). *Dermatology: An illustrated colour text* (4th ed.). Churchill Livingstone.

Conditions to eliminate

Likely causes

Molluscum contagiosum

Molluscum contagiosum is caused by a poxvirus and primarily affects children under 5 years old. It presents with multiple lesions, usually on the face and neck, although the trunk can be involved. The lesions resemble common warts but each raised papule tends to be smooth and have a central dimple; the latter is a useful diagnostic point (see Fig. 10.6). Lesions tend to be between 1 and 5 mm in diameter. The condition is self-limiting and will resolve without medical intervention.

Patients should be told this but, if they believe treatment is necessary, referral to the doctor is advisable.

Corns

Corns and plantar warts can be confused. The reader is referred to the section on corns and calluses for information on differentiating corns from verrucas.

Unlikely causes

Plane warts (flat warts or *verruca plana*)

These most frequently occur in groups on the face and the back of the hands. They are small in size (1–5 mm in diameter), slightly raised, and can take on the skin colour of the patient (Fig. 8.20). Because drug treatment is destructive in nature, plane warts located on the face should be referred to avoid the risk of scarring.

Seborrhoeic keratosis

Seborrhoeic keratosis (also known as *seborrhoeic warts* or *basal cell papillomas*) are benign growths that are increasingly common with increasing age. They usually occur on the trunk and present as raised, often multiple lesions that have a superficial 'stuck-on' or waxy appearance (Fig. 8.21). Lesions are usually brown but can range in colour from pink to black.

Very unlikely causes

Basal cell carcinoma

Basal cell carcinoma is the most common form of skin cancer, and its incidence is related to sunlight exposure. It typically occurs in older people, especially when there is a history of prolonged skin exposure. Men are twice as likely to be affected. The usual site where lesions develop is the face.



Fig. 8.20 Plane warts. From Gawkrödger, D. J. (2007). *Dermatology: An illustrated colour text* (4th ed.). Churchill Livingstone.



Fig. 8.21 Seborrhoeic keratosis. From Gawkrödger, D. J. (2007). *Dermatology: An illustrated colour text* (4th ed.). Churchill Livingstone.

Any wartlike lesion that is itchy, has an irregular outline, is prone to bleeding, and exhibits colour change should be referred to eliminate serious pathology. For more information on skin cancers, see later in this chapter under sun exposure.



TRIGGER POINTS indicative of referral: Warts and verrucae

Symptoms/signs	Possible danger/reason for referral	Urgency of referral
Anogenital warts Multiple and widespread warts	Outside scope of OTC treatment	As soon as practicable
Diabetic patients Lesions on the face	Treatment options can cause skin damage	Nonurgent
Patients >50 years presenting with a first-time wart Warts that itch or bleed without provocation Warts that have grown and changed colour	Potential sinister pathology	Immediate to GP

Evidence base for over-the-counter medication

A number of ingredients are used to treat warts and verrucas, although salicylic acid is the most commonly used agent and can be found in many OTC treatments.

A Cochrane review (Kwok et al., 2012) investigated topical treatments for treating nongenital warts. This review identified 85 trials that included a range of different treatments. Overall, the quality of the trials was low due to poor methodology and reporting. Salicylic acid was found to significantly increase the chance of cure by just over 50% compared with placebo. In addition, there is some evidence to show that common warts are more responsive to keratolytic therapy than plantar warts, and resolution can be enhanced by soaking the wart prior to application and/or occlusion of the site.

Salicylic acid is often combined with other ingredients, in particular lactic acid. However, there is no evidence to support greater efficacy when lactic acid (or another ingredient) is added.

Other agents commercially available include glutaraldehyde and silver nitrate pencils. Information regarding their effectiveness stems from small-scale or poorly designed studies, and they should not be routinely recommended.

Adherence with treatment has been identified as a limiting factor in the cure rate for warts and verrucas. One study that investigated occlusal (salicylic acid 50%) reported an 80% cure rate after only 2 weeks of therapy (Parish et al., 1988). This might be an alternative option for patients whose adherence could be questioned. However, the study suffered from poor design and had only a small number of patients, so the results must be viewed with caution.

Cryotherapy, using liquid nitrogen, has been used for many years as a treatment of recalcitrant or widespread warts. Trials comparing cryotherapy with salicylic acid show that cryotherapy is beneficial for hand warts but not verrucas (Kwok et al., 2012). It should be noted that this review did not consider OTC freezing treatments that contain dimethyl ether and propane (e.g., Wartner products). It has been reported elsewhere that these are not as effective as liquid nitrogen because they only achieve temperatures of around -57°C compared with -196°C (Lynch et al., 2014).

Summary

Any salicylic acid-based product should have modest success rates in clearing warts and verrucas after a 12-week treatment period, providing that patient adherence is good. If treatment has been unsuccessful with salicylic acid, a second-line agent such as glutaraldehyde could be tried.

Cryotherapy should be performed through the doctor and OTC freezing products avoided due to the potential for adverse side effects associated with their use.

Practical prescribing and product selection

Prescribing information relating to specific products used to treat warts and is summarized in [Table 8.24](#); useful tips relating to patients presenting with warts and verrucas are given in 'Hints and Tips' in [Box 8.6](#).

Because most warts and verrucas will spontaneously resolve, treatment is not necessarily needed. Pharmacists should determine from the patient how much the wart or verruca affects daily life and also what social impact the lesions have on the patient. It is also worth assessing patient motivation to comply with medication regimens because treatment is over a period of months, not days or weeks.

Salicylic acid products (e.g., Bazuka Extra Strength (26%), Occlusal (26%), Verrugon (50%)) and Salicylic acid/lactic acid combinations (Bazuka, Cuplex, Duofilm, Salactol, Salactac)

Before using a salicylic acid-based product, the affected area should be soaked in warm water and towelled dry. The surface of the wart or verruca should be rubbed with a pumice stone or emery board to remove any hard skin. A few drops of the product should be applied to the lesion, taking care to localise the application to the affected area. The procedure should be repeated daily. Salicylic acid can be recommended to most patients, although diabetics are a notable exception. Salicylic acid does not interact with any medicines. It can cause local skin irritation and, because of its destructive action should be kept away from unaffected skin.

Glutaraldehyde (Glutarol)

The application of glutaraldehyde is the same as for salicylic acid but it should be used twice a day. It can cause skin irritation and stains the outer layer of the skin brown.

Silver nitrate

To use silver nitrate pencils (e.g., Avoca) the tip must first be moistened and then applied to the wart or verruca for 1 to 2 minutes. This should be repeated after 24 hours. It is



Table 8.24
Practical prescribing: Summary of medicines for warts and verrucas

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
<i>Salicylic acid</i>					
Compound W	>6 years	Local skin irritation	None	Avoid in diabetic patients	OK
Bazuka Extra Strength	>2 years				
Occlusal	No lower age stated				
Verrugon					
Wartex					
<i>Salicylic acid and lactic acid</i>					
Bazuka	>2 years	Local skin irritation	None	Avoid in diabetic patients	OK
Cuplex	No lower age stated				
Duofilm	>2 years				
Salactol	No lower age stated				
Salatac					
<i>Glutaraldehyde</i>					
Glutarol	No lower age stated	Local skin irritation; skin will be stained brown	None	Avoid in diabetic patients	OK
Silver nitrate	No lower age stated	Local skin irritation	None	Avoid in diabetic patients	OK

HINTS AND TIPS BOX 8.6: VERUCCAS AND WARTS

Is it a verruca or a corn?	If diagnosis is uncertain, then removal of the top layer of skin from the lesion can be performed. If black spots are not visible, this implies that the lesion is a corn and not a verruca.
Length of treatment	Patients should be told that it is a slow process. Treatment commonly lasts 3 months. If OTC medication has been unsuccessful after this time, then the patient could be referred to the GP.
Cure rates	There is some evidence that resolution might be enhanced by soaking the wart or verruca before application and/or occlusion of the site (by use of plasters or collodion-like vehicle) to aid penetration.
Bazuka and Bazuka Extra Strength	Do not be fooled into thinking that the extra strength formulation has better cure rates. It has a higher concentration of salicylic acid (26% as opposed to 12%), but this does not necessarily equate to a more efficacious product.
Salatac gel	The gel forms an elastic film after application. This has to be removed each time before the gel can be reapplied.

recommended that three applications be used for warts and six applications for verrucas. Like other treatments, the process is destructive, and the surrounding skin should be protected.

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Website

British Association of Dermatologists – information on cutaneous warts: http://www.bad.org.uk/library-media%5Cdocuments%5CWarts_2014.pdf

Corns (helomas) and calluses

Background

Foot disorders can be broadly subdivided into those that result from opportunistic infection or those that result from incorrect distribution of pressure. This section discusses the latter.

Prevalence and epidemiology

The exact prevalence of corns and calluses is not known. Surveys have indicated that up to 18% of working people complain of corns and calluses (Springett et al., 2003).

Corns and calluses tend to more often be seen in older patients and women.

Aetiology

Corns form due to a combination of friction and intermittent pressure against one of the bony prominences of the feet (e.g., heel and metatarsal heads). Inappropriate footwear is frequently the cause. Continued pressure and friction results in hyperkeratoses (excessive skin growth of the keratinized layer), leaving even less space between the shoe and the foot, and therefore the corn is pressed even more firmly against the underlying soft tissues and bone.

Callus formation is also caused by constant friction and pressure. Calluses can be beneficial, providing a natural barrier to objects and protecting underlying tissues; however, when such a thickened mass of skin occurs in abnormal places (e.g., border of the big toe), pain is experienced.

Arriving at a differential diagnosis

Diagnosis of corns and calluses is best done by appearance. Pharmacists should therefore ask to inspect the person's feet. Differential diagnosis should be straightforward and is usually between corns, calluses and verruca. Most patients will self-diagnose and seek advice and help to remedy the situation. The pharmacist's role will be to confirm the self-diagnosis and give advice and/or treatment where appropriate. Asking symptom-specific questions will help the pharmacist determine the best course of action (Table 8.25).

Clinical features of corns

Corns have been classified into a number of types, although only soft and hard corns are commonly seen in practice. Hard corns (heloma durum) are generally located on the top of the toes. Corns exhibit a central core of hard grey skin surrounded by a painful, raised, yellow ring of inflammatory skin. Any of the toes can be affected but a corn is most common on the second toe. Soft corns (heloma molle) form between the toes rather than on the tops of toes and are due to pressure exerted by one toe against another. They have a whitened appearance and remain soft due to moisture being present between the toes, causing maceration of the corn. Soft corns are most common in the fourth web space.



Table 8.25
Specific questions to ask the patient: Corn and callus

Question	Relevance
Location	Lesions on the tops or between the toes suggest a corn compared with verrucas, which are on the plantar surface of the foot.
Aggravating or relieving factors	Pain experienced with corns is a result of pressure between footwear and the toes. If footwear is taken off, then the pain is relieved. Pain associated with verrucas will be felt whether or not footwear is worn.
Appearance	Corns and calluses appear as white or yellow hyperkeratinized areas of skin, unlike verrucas, which show black thrombosed capillaries seen as black dots on the surface of the verruca.
Previous history	Patients with corns will often have a previous history of foot problems. The cause is usually due to poorly fitting shoes, such as high heels. Prolonged wear of such footwear can lead to calluses and permanent deformity of bunions.

Clinical features of calluses

Calluses, depending on the cause and site involved, can range in size from a few millimetres to centimetres. They appear as flattened, yellow-white, thickened skin. In women, the balls of the feet are a common site. Other sites that can be affected are the heel and lower border of the big toe. Patients frequently complain of a burning sensation, resulting from fissuring of the callus.

Conditions to eliminate

Verrucas

Verrucas can be mistaken for a corn or callus, although verrucas tend to have a spongy texture, with the central area showing tiny black spots. They are also rarely located on or between the toes and commonly occur in younger patients more than corns and calluses. For further information, see earlier in this chapter.

Bunions

Bunions are 10 times more common in women than in men and are directly related to wearing tight shoes. Initially, irritation of skin by ill-fitting shoes causes bursitis of the big toe. Over time, the inflamed area begins to harden and subsequently bursal fluid solidifies into a gelatinous mass. The result will be a bunion joint (the first metatarsal phalangeal joint). Patients often complain of pain and have difficulty walking whilst wearing normal shoes. Referral to a podiatrist is recommended.



TRIGGER POINTS indicative of referral: Corns and calluses

Symptoms/signs	Possible danger/ reason for referral	Urgency of referral
Discomfort, pain causing difficulty in walking Soft corns are present Treatment failure	Better assessed and managed by a podiatrist	Nonurgent
Impaired peripheral circulation (e.g., with diabetes)	Needs assessment by podiatrist or doctor	As soon as practicable

Evidence base for over-the-counter medication

Corns and calluses are due to friction and pressure. Removal of the precipitating factors will result in resolution of the problem. Therefore, preventive measures should form the mainstay of treatment. Correctly fitting shoes are essential to help prevent corn and callus formation. (see Hints and Tips Box 8.7) If pressure and friction still persist when correctly fitted shoes are worn, patients can obtain relief by shielding or padding. Moleskin or thin podiatry felt placed around the corn allows pressure to be transferred from the corn to the padding. Specific proprietary products are available for such purposes. In callus formation, a shock-absorbing insert such

HINTS AND TIPS BOX 8.7: CORNS

Shoes to relieve pressure Patients should be encouraged to wear open shoes such as sandals or flip-flops.

as a metatarsal pad is useful to relieve weight off the callus and thus reduce stress on the plantar skin.

Treatment should be avoided, if possible, but if deemed appropriate, keratolytics can be used, although there is no evidence to suggest that they are effective.

Practical prescribing and product selection

Products used to treat corns and calluses are exactly the same as those used for warts and verrucas. Prescribing information relating to specific products used to treat corns and calluses is therefore discussed in the section on OTC medication for warts and verrucas. However, a number of proprietary products are marketed for sufferers with corns and calluses; for example, products in the Carnation and Scholl range. These products contain high concentrations of salicylic acid (usually 40%) that are surrounded by a nonmedicated, self-adhesive ring.

Reference

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Scabies**Background**

Scabies can be defined as an intensely pruritic skin condition caused by the mite *Sarcoptes scabiei*. The diagnostic burrows are small, and scratching often makes them difficult to see.

Prevalence and epidemiology

The incidence of scabies in the UK is low (0.1% of the population) but epidemics can occur on a cyclic basis

approximately every 15 to 20 years. Outbreaks in schools and care homes are not uncommon. In temperate climates (e.g., the UK), it appears to be more prevalent in urban areas and in the winter months.

Aetiology

The mite is transmitted by direct physical contact (e.g., holding hands, hugging or sexual contact), although transmission through casual contact such as shaking hands is unlikely. Mating occurs on the skin surface, after which the female mite burrows into the stratum corneum to lay eggs. The faecal pellets left in the burrow cause a local hypersensitivity reaction and is assumed to cause the release of inflammatory mediators that trigger an allergic reaction invoking intense itching. This normally takes 15 to 20 days in a primary infestation but can take up to 6 weeks to develop. In subsequent infestations, this hypersensitivity reaction develops much more quickly. During the asymptomatic period, the mite can be passed onto others unknowingly. The eggs hatch and mature in 14 days, after which the cycle can begin again.

Arriving at a differential diagnosis

A definitive diagnosis of scabies is confirmed by extraction of the mite from its burrow, although in primary care this is rarely performed, and a differential diagnosis is made on clinical appearance, patient history and symptoms reported by close family. Confusion can arise from mistaking scabies for other pruritic skin disorders (Table 8.26). Asking symptom-specific questions will help the pharmacist establish a differential diagnosis (Table 8.27).

Clinical features of scabies

Severe pruritus, especially at night, is the hallmark symptom of scabies. Besides the classic location of lesions, in men the

Table 8.26
Causes of scabies-like rash and their relative incidence in community pharmacy

Incidence	Cause
Most likely	Insect bites, allergic contact dermatitis
Likely	Scabies
Unlikely	Pompholyx
Very unlikely	Dermatitis herpetiformis

and in the winter months.



Table 8.27
Specific questions to ask the patient: Scabies

Question	Relevance
Visible signs of the mite	Burrows, which are up to 1 cm long and blue-grey in colour, might be visible, although in practice they are often not present. For the pharmacist who will only see a limited number of cases, it is best to concentrate on other clinical signs rather than attempt to look for signs of burrows.
Location of rash	Scabies typically affects the finger webs, the sides of the fingers, and wrists.
History of presenting complaint	If contact dermatitis is suspected, questioning should reveal a past history of similar skin lesions. Often, people with scabies will be care workers looking after institutionalized people. A positive history in other family members increases the likelihood that the patient has scabies.

penile and scrotal skin and in women beneath the breasts and nipples can be affected. Infants who are not yet walking may have marked sole involvement. The rash is usually made up of small red papules seen in the interdigital web spaces and sides of the fingers.

Conditions to eliminate

Insect bites

A host of insects, fleas and mites can inflict a bite or sting. This usually results in itchy papules that can become firm and last several days. Bites often tend to be in groups and are asymmetrical. Occasionally, these blister normally as a result of scratching, and secondary bacterial infection can then occur. See Chapter 11 and Fig. 11.2 for further information.

Allergic contact dermatitis

The condition presents as an area of inflamed itchy skin with papules or vesicles being present. However, enquiry into the patient's history should reveal a past history of similar lesions in allergic contact dermatitis. Information on dermatitis is discussed later in this chapter.

Unlikely cause

Dyshidrotic eczema (pompholyx)

Pompholyx simply means *bubble* and refers to the presence of crops of intensely itchy, small vesicles or blisters on the palms of the hands (and, occasionally on the soles of the feet). Stress and heat are known to precipitate the condition.

Very unlikely cause

Dermatitis herpetiformis

Dermatitis herpetiformis is a condition characterized by intense itchy clusters of papules and vesicles. It is more often seen in middle-aged people, especially in men. It commonly involves the buttocks, elbows, knees and sacral region, with hand involvement being rare. The lesions usually exhibit a symmetrical distribution. On investigation, up to 90% of patients are found to have a gluten enteropathy.



TRIGGER POINTS indicative of referral: Scabies

Symptoms and signs	Possible danger and reason for referral	Urgency of referral
Secondary infection of the skin	May require antibiotics	As soon as practicable
Severe and extensive symptoms	Outside scope of community pharmacy	Urgent, ideally same day referral, to GP
Institutional outbreaks		
Suspected dermatitis herpetiformis		

Evidence base for over-the-counter medication

The efficacy and safety of scabicide agents are difficult to determine due to limited trial data. Benzyl benzoate, crothamiton, permethrin, and malathion have all been used. A Cochrane review (Strong & Johnstone, 2007) found permethrin to have high cure rates and to be more effective than other scabicide agents.

The efficacy of malathion is questionable because no randomized controlled trials appear to have been conducted. However, case reports have suggested that malathion is effective in curing scabies, with a cure rate of approximately 80%.

Benzyl benzoate has been used to treat scabies for many years. However, its efficacy has not been demonstrated in

randomized controlled trials. In uncontrolled trials, benzyl benzoate has been shown to provide cure rates of approximately 50%.

Practical prescribing and product selection

Prescribing information relating to specific products used to treat scabies is discussed and summarized in [Table 8.28](#); useful tips relating to patients presenting with scabies are given in 'Hints and Tips' in [Box 8.8](#).

It is important that all people in the same household and in close contact with the affected individual be treated at the same time to prevent reinfection, even though they might be asymptomatic (latent period before itch develops). *Permethrin* is the drug of choice, although all products used to treat scabies can be given to all patient groups and have no drug interactions.

Permethrin (Lyclear Dermal Cream)

General guidance for application is that adults and children over 12 should use up to a full tube as a single application. Some adults might need to use more than one tube to ensure total body coverage, but a maximum of two tubes (60 g in

total) is recommended for a single application. For children under 12 the manufacturers suggest the following: ¼ tube for those 2 months to 5 years of age and ½ tube for those between 6 and 12 years of age. The whole body should be washed thoroughly 8 to 12 hours after treatment. Treatment should be repeated after 7 days.

Malathion (Derbac M)

The liquid can be used on adults and children over 6 months old and is left on for 24 hours. If hands or any other parts of the body are washed during this period, the treatment must be reapplied to those areas immediately. Treatment should be repeated after 7 days.

Benzyl benzoate

Benzyl benzoate should not be routinely recommended but, if used, it is for adult use only. Dosing (as per *British National Formulary* [BNF] 78) is that it should be applied to the whole body and repeated the following day. A third application may be required in some cases. It causes skin irritation and a transient burning sensation in approximately 25% of patients. This is usually mild but can occasionally be severe in sensitive individuals. In the event of a severe skin reaction,



Table 8.28
Practical prescribing: Summary of medicines for scabies

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
Permethrin	>2 months	Burning, stinging or tingling	None	None	OK
Benzyl benzoate	>12 years	Burning, irritation			
Malathion	>6 months	Skin irritation but rare			

HINTS AND TIPS BOX 8.8: SCABIES

Application	UK guidelines state that treatment should be applied to the whole body including the scalp, neck, face and ears.
Itching after treatment	Pruritus can persist for 2–3 weeks after treatment, and the patient might benefit from crotamiton. Antihistamines appear to have a limited role in relieving itch but their sedative effect (e.g., chlorphenamine) might be useful for temporary help in aiding sleep.
Hygiene measures	Clothes, towels, and bed linen should be machine washed (at 50°C or above) at the time of the first application of treatment to prevent reinfestation and transmission to others.
Bathing	Treatment should not be applied after a hot bath because this increases systemic absorption and removes the drug from its treatment site.

the preparation should be washed off using soap and warm water. It is also irritating to the eyes, which should be protected when applied to the scalp.

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Acne vulgaris

Background

Acne can be defined as an inflammatory disease of the pilosebaceous follicles, causing comedones, papules and pustules on the face (99% of cases), chest (60%) and upper back (15%). It affects approximately 80% to 95% of adolescents. Diagnosis is usually straightforward, and most patients presenting in the community pharmacy will generally be seeking appropriate advice on correct product selection rather than wanting someone to put a name to their rash. Most cases seen in the pharmacy setting will be mild and can be managed appropriately without referral to the doctor. However, more persistent and severe cases need referral for more potent topical or systemic treatment. Acne often causes significant psychological impact, such as lack of confidence, low self-esteem and depression.

Prevalence and epidemiology

Acne lesions develop at the onset of puberty. Girls therefore tend to develop acne at an earlier age than boys. The peak

incidence for girls is between the ages of 14 and 17 years compared with 15 and 19 years for boys. Evidence has shown that the average age when acne develops has decreased by 1 year over the last 30 or 40 years, from 15.8 years old in 1979 to 15 in 2007 (Goldberg et al., 2011). Although acne is closely associated with adolescence, up to 12% of women and 3% of men aged 25 to 40 years continue to get facial acne or develop acne (late-onset acne) after adolescence. Acne persists in a very small proportion of patients (5% of women and 1% of men) into their 40s. There might be a familial tendency to acne, and it is slightly more common in boys, who also experience more severe involvement. In addition, white patients are more likely to experience moderate to severe acne than black patients, although black skin is prone to worse scarring.

Aetiology

At the onset of puberty, a cascade of events takes place, resulting in the formation of noninflammatory and inflammatory lesions. In response to increased testosterone levels, the pilosebaceous gland begins to produce sebum – if the sebaceous glands become oversensitive to testosterone, they produce excess oil and the skin becomes greasy; a hallmark of acne. At the same time, epithelial cells lining the follicle undergo change. Before puberty, dead cells are shed smoothly out of the ductal opening but, at puberty, this process is disrupted, and in patients with acne, these cells develop abnormal cohesion, partially blocking the opening and effectively reducing sebum outflow. Over time, the opening of the duct becomes blocked, trapping oil in the hair follicle. Bacteria, particularly *Propionibacterium acnes*, proliferate in the stagnant oil, stimulating cytokine production, which in turn produces local inflammation, leading to the appearance of a spot. In response to the proliferation of bacteria, white blood cells infiltrate the area to kill the bacteria and, in turn, die, leading to pus formation. The pustule eventually bursts on the skin surface, carrying the plug away. The whole process can then start again.

Arriving at a differential diagnosis

Only about 30% of people with acne consult their doctor; the pharmacist, therefore, plays an important role in the management of patients with acne. The first step in the management of acne is to assess severity because this will shape management decisions. Several rating scales have been developed with the aim of trying to grade the severity of an individual's condition. None have gained universal acceptance, although most dermatology texts simply grade the severity of acne into mild, moderate or severe. [Table 8.29](#) describes mild, moderate, and severe acne presentations.

Table 8.29
Grading of acne

Mild acne consists mainly of noninflammatory comedones, with few inflammatory (papulopustular) lesions, mainly confined to the face.
Moderate acne can be described as having many inflammatory lesions that are not confined to the face. Lesions are sometimes painful and there is a possibility of mild scarring.
Severe acne has all the characteristics of moderate acne plus the development of nodules and cysts. Lesions are often widespread, involving the upper back and chest. Scarring will usually result. Acne of any severity causing psychological upset should be classified as severe.

OTC treatment should be limited to patients with mild to moderate acne.

Clinical features of mild acne vulgaris

Patients suffering from mild acne characteristically have predominantly open and closed comedones, with a small number of active lesions normally confined to the face (Fig. 8.22). Acne can sometimes consist predominately of blackheads and whiteheads, with very few inflammatory lesions. This is termed *comedonal acne* and occurs most commonly in Asian and Afro-Caribbean patients. Seborrhoea is commonly present. Certain jobs can predispose patients to acne-like lesions and are commonly associated with long-term contact with oils.

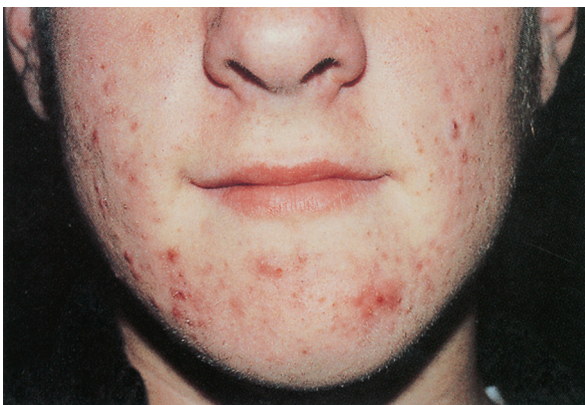


Fig. 8.22 Mild acne. From Fleischer, A. B., Feldman, S., Clayton, E., & Katz, A. (2000). *20 common problems*. McGraw-Hill.

Conditions to eliminate

Rosacea

Rosacea is an inflammatory disease of the skin follicles. It is uncertain what causes rosacea, although successful treatment with antibiotics suggests that bacterial pathogens play a significant role in the disease. It is normally seen in patients between 30 and 50 years of age and is more common in women than in men. It is typically characterized by recurrent flushing and blushing of the central face, especially the nose and medial cheeks. Crops of inflammatory papules and pustules are also a common feature, although comedones are not present (Fig. 8.23). Eye irritation and blepharitis are present in about 20% of patients.

Medicines causing acne-like skin eruptions

A number of medicines can produce acne-like lesions. Steroids (oral or topical) are commonly implicated. Other medicines associated include lithium, oral contraceptives (especially those with high progestogen levels), phenytoin, azathioprine and rifampicin.

Perioral dermatitis

Perioral dermatitis tends to affect young women between 25 and 40 years of age and exhibits an acne-like rash, generally around the mouth and nasolabial folds (Fig. 8.24). Itching and burning can also be present, and the rash can take on a dermatitis-like quality.



Fig. 8.23 Rosacea. From Wilkinson, J., Shaw, S., & Orton, D. (2004). *Dermatology in focus*. Churchill Livingstone.



Fig. 8.24 Perioral dermatitis. From Wilkinson, J., Shaw, S., & Orton, D. (2004). *Dermatology in focus*. Churchill Livingstone.

Polycystic ovary syndrome

A clinical manifestation of this condition can be acne vulgaris. Any woman who has menstrual irregularity (infrequent or no periods) and also exhibits hirsutism and/or is overweight must be referred for further investigation.

! TRIGGER POINTS indicative of referral: Acne		
Symptoms/signs	Possible danger/reason for referral	Urgency of referral
Moderate or severe acne OTC treatment failure Suspected rosacea	Generally require antibiotic therapy	As soon as practicable
Prepubertal or older people	Acne is uncommon in these age groups	

Evidence base for over-the-counter medication

The aim of treatment must be to clear the lesions and prevent scarring. Mild or moderate acne can be managed OTC. It is important to show understanding and empathy when advising patients, given that acne is predominantly a condition that affects adolescents, a time when appearance is all-important. It is worth taking a few minutes to counsel patients about their condition, allay fears, and make sure that their expectations of treatment are realistic.

OTC acne treatments contain benzoyl peroxide, salicylic acid, sulphur, nicotinamide or an antibacterial.

Benzoyl peroxide

Benzoyl peroxide exerts its main effect by reducing the concentration of *P. acnes* by releasing oxygen into the anaerobic microenvironment. Bacteria cannot develop resistance to this mode of action. Many studies have investigated the efficacy of benzoyl peroxide. It has been proven to be effective, especially in mild to moderate acne. However, there is no evidence to suggest that 10% benzoyl peroxide is more effective than lower strengths.

A variety of other agents have been compared against or in combination with benzoyl peroxide. None of these products have shown to be significantly better than benzoyl peroxide alone; for example, the addition of miconazole 2% (Acnidazol [now discontinued in the UK]) or hydrocortisone (Quinoderm HC).

Evidence of efficacy for salicylic acid and sulphur is poor. Both agents have been used for many years on the basis of their keratolytic action, but according to current evidence, they are best avoided. Nicotinamide is a more recent addition to the OTC market. Data suggest that it is as effective as clindamycin 1% gel; however, no randomized controlled trials seem to have been conducted to support this finding (Shalita et al., 1995).

Complementary treatments

Evidence is lacking to support the use of complementary treatments. A 2015 Cochrane review (Cao et al., 2015) found some low-quality evidence for reduction in acne lesions using bee venom or tee tree oil and in those following a low glycaemic load diet. However, these data were drawn from single trials of varying methodological quality.

Summary

First-line treatment of acne should be benzoyl peroxide, 2.5% or 5%. Patients should see an improvement in their symptoms after 6 weeks. If the patient's symptoms fail to improve in this time, referral to a doctor would be appropriate. However, if beneficial, treatment should be continued for at least 4 to 6 months.

Practical prescribing and product selection

Prescribing information is discussed and summarised in [Table 8.30](#); useful tips relating to patients presenting with acne are given in 'Hints and Tips' in [Box 8.9](#).

Benzoyl peroxide (e.g., Acnecide)

Benzoyl peroxide is licensed for use in adults and children. Benzoyl peroxide is usually applied once or twice daily,



Table 8.30
Practical prescribing: Summary of medicines for acne

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
Benzoyl peroxide	Not appropriate	Skin irritation, burning or peeling	None	None	OK
Nicotinamide	Not appropriate	Dry skin, pruritus, erythema, burning, irritation	None	None	OK

HINTS AND TIPS BOX 8.9: ACNE

Myths surrounding acne	Sunshine helps reduce acne. There is no convincing evidence that this is the case, Chocolate causes spots. There is no proof that any food causes acne. Stress causes acne. Stress cannot cause acne although it can make it worse.
Applying benzoyl peroxide	Benzoyl peroxide has a potent bleaching effect. It has the ability to bleach clothing and bed linens permanently. Patients should be advised to always wash their hands after applying the product.

depending on the patient's response, although once-daily application is often sufficient. It should be applied to all areas of the skin where acne occurs and not just to the active lesions. It can cause drying, burning and peeling on initial application. If this occurs, the patient should be told to stop using the product for 1 or 2 days before starting again. Patients should therefore start on the lowest strength commercially available, especially if the patient suffers from sensitive skin or has fair skin colour. Occasionally, patients will experience contact dermatitis, although it has been reported to affect less than 1% of patients.

Nicotinamide (Frederm, Nicam)

Nicotinamide should be applied to the affected area twice daily after the skin has been washed using enough gel to cover the affected area. Like benzoyl peroxide, drying of the skin is the main side effect. If this occurs, the dose should be reduced to once daily.

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Cold sores (herpes simplex labialis)

Background

A cold sore is an infection caused by the herpes simplex virus (HSV). There are two main subtypes of the virus, HSV1 and HSV2. Cold sores are caused by HSV1, whereas HSV2 is most commonly implicated in genital lesions.

Prevalence and epidemiology

Herpes simplex virus infection is one of the most commonly encountered human viral infections. It is estimated that more than 90% of adults worldwide show serologic evidence of having been infected by HSV1, with 20% to 40% of people experiencing a cold sore at some time during their lifetime. Most people with recurrent cold sores will have approximately two episodes per year, but 5% to 10% of affected people can have six or more recurrences per year.

Aetiology

Infection is spread by viral shedding into saliva and results from direct mucous membrane contact (e.g., kissing) at sites of abraded skin between an infected and uninfected individual. The virus then infects epidermal and dermal cells, causing skin vesicles. After primary infection, the virus travels to the sensory ganglia, where it lies dormant in the dorsal root ganglia of the trigeminal nerve until reactivation. Once reactivated (often triggered by some known stimulus, [Table 8.31](#)), the virus migrates from these sensory ganglia to the outer layer of the skin of lips and forms cold sore lesions again.

Arriving at a differential diagnosis

Cold sores should not be too difficult to diagnose, although conditions such as impetigo can look similar. Asking symptom-specific questions will help the pharmacist establish a differential diagnosis ([Table 8.32](#)).

Clinical features of cold sores

Patients typically experience prodromal symptoms of itching, burning, pain or tingling symptoms 6 to 48 hours before skin eruption. The lesions appear as blisters and vesicles with associated redness on the outer lip ([Fig. 8.25](#)). These crust over, usually within 24 hours, tend to be itchy and painful, and might bleed. Lesions spontaneously resolve in 7 to 10 days; therefore, most outbreaks last 14 days from the recognition of prodromal symptoms to the resolution of lesions.

Many patients can identify a cause of their cold sore, with sunlight (ultraviolet [UV] light) reported to induce cold sores in 20% of sufferers. Recurrence is common, and lesions tend to occur in the same location. Immunocompromised patients or patients taking immunosuppressive medicines can experience severe symptoms and should be referred.

Conditions to eliminate

Impetigo

Impetigo usually starts as a small, red, itchy patch of inflamed skin that quickly develops into vesicles that rupture and weep. The exudate dries to a brownish-yellow sticky crust. The area around the mouth and nose is usually affected, rather than the lip itself (see [Fig. 10.7](#)). Currently, referral is needed for topical (e.g., fusidic acid) or systemic (flucloxacillin) therapy.



Table 8.31
Practical prescribing: Summary of medicines for cold sores

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
Aciclovir (Virasorb, Zovirax, Cymex Ultra)	All state can be used in children but no lower age limit stated	Stinging	None	OK	OK
Ammonia and phenol (Blistex Relief Cream)	Yes, but no lower age stated	None	None	None	OK
Zinc and lidocaine (Lypsyl Cold Sore Gel)	>12 years	Stinging	None	None	OK
Urea (Cymex)	Yes, but no lower age stated	None	None	None	OK



Table 8.32
Specific questions to ask the patient: Cold sores

Question	Relevance
Appearance	Patients with cold sores will often experience prodromal symptoms before the skin eruption, whereas no warning signs are present with impetigo or angular cheilitis.
Location	Cold sores typically occur around the mouth and for this reason are known as herpes simplex labialis. They can also occur around and inside the nose, but this is less common. Impetigo also occurs in the same areas but is more prone to spread to other areas of the face or move to other parts of the body; for example, the arms. Angular cheilitis occurs at the corners of the mouth and can be mistaken for cold sores due to their similar locations.
Trigger factors	Stress, ill health, sunlight, viral infection (e.g., the common cold), and menstruation are all implicated in triggering cold sore attacks. These triggers are not associated with other similar conditions and the patient should be asked if they can identify what brought on the lesions.



Fig. 8.25 Cold sore. From White, G. (2004). *Color atlas of dermatology* (3rd ed.). Churchill Livingstone.

Angular cheilitis

Angular cheilitis can occur at any age. It is more common in patients who wear dentures. The corners of the mouth become cracked, fissured and red. The lesions can become boggy and macerated and are slow to heal because movement of the mouth hinders healing of the lesions (Fig. 8.26). It is painful but generally does not itch or crust over, as is typical with cold sores.

Aphthous ulcers

These can occur on the lip but tend to be on the inside rather than the outer part of the lip. For further information about ulcers, see [chapter 7](#).



Fig. 8.26 Angular cheilitis. From Cawson, R., et al., (2002). *Essentials of oral pathology and oral medicine*. Churchill Livingstone.



TRIGGER POINTS indicative of referral: Cold sores

Symptoms/signs	Possible danger/reason for referral	Urgency of referral
Duration > 14 days	Unlikely to be cold sores	As soon as practicable
Cold sores located in the mouth Severe and widespread lesions	Outside scope of community pharmacy	
Lesions that spread away from the lips and onto the face	Impetigo more likely	

HINTS AND TIPS BOX 8.10: COLD SORES

Sun-induced cold sores	For patients in whom the sun triggers cold sores, a sun block would be the most effective prophylactic measure.
Applying products	Patients should be encouraged to use a separate towel and wash their hands after applying products because viral particles are shed from the cold sore and can be transferred to others.
Decrease transmission	Risk of transmission is highest during the first 1–4 days of symptoms, and people should be advised not to kiss others.

Evidence base for over-the-counter medication

A number of products are marketed for the relief and treatment of cold sores. None have shown conclusively to be effective for its prevention and treatment. Products containing ammonia, zinc and phenol appear to have no evidence of efficacy. However, they might be useful in drying lesions and preventing secondary bacterial infections. Local anaesthetics (e.g., lidocaine) might be useful for mildly painful lesions.

Only the antiviral aciclovir which works by inhibiting the herpes virus DNA polymerase, has demonstrated clinical effectiveness against the herpes virus. Orally, antivirals such as aciclovir are highly effective, but the evidence for topical administration is less conclusive. Trial data have shown topical antivirals not to have a preventive effect (Chi et al., 2015). With regard to speeding up the resolution of established cold sores (when using aciclovir), if applied in the prodromal stage, the total healing time of subsequent lesions is reduced by half to 1 day.

A hydrocolloid patch is available for the treatment of cold sores (Compeed Cold Sore Patch). Hydrocolloid dressings are available for wounds and enhance healing by providing a moist environment. A study comparing Compeed patch with aciclovir 5% cream found similar efficacy in terms of self-reported global assessment of efficacy and time until healing (7.57 days for Compeed vs 7.03 days for aciclovir; $P = .37$; Karlsmark et al., 2008). However, the study was not blinded for the primary outcome (self-reported global assessment), casting some doubts on the findings. Furthermore, the study was not set up as an equivalence study; therefore, the lack of difference in the outcomes could be due to too small a sample size.

Summary

Aciclovir is the first-line therapy for the treatment of cold sores. However, it should be used as soon as the patient experiences symptoms for them to have any effect. (Note that penciclovir was available in the UK but was withdrawn, although it is still available in other countries).

Practical prescribing and product selection

Prescribing information relating to antivirals is discussed and summarized in Table 8.32. For completeness, the table also contains some of the other commonly used cold sore products; useful tips relating to patients presenting with cold sores are given in Box 8.10.

Aciclovir (e.g., Cymex Ultra, Virasorb, Zovirax)

Aciclovir can be used topically by all patient groups, including pregnant and breastfeeding women, although manufacturers advise caution because of limited data regarding the exposure of aciclovir in these patient groups. It has no drug interactions and causes only transient stinging after first application in the minority of patients. Aciclovir should be applied five times daily at approximately 4-hour intervals, and treatment should be continued for 5 days.

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Eczema and dermatitis

Background

The terms *eczema* and *dermatitis* are often used interchangeably. Dermatitis simply means inflammation of the skin, whereas eczema has no universally agreed definition but, in some countries, indicates a more acute condition. Many authorities subdivide eczema and dermatitis into exogenous (due to an obvious external cause) or endogenous (assumed to be of a genetic cause); however, the distinction is not clear. The condition is also referred to as acute, a single exposure to an irritant; or chronic, repeated exposure. In this section, for consistency, the term *dermatitis* will be used.

Dermatitis is characterized by sore, red, itching skin. In primary care, the two most common forms of dermatitis are irritant and allergic dermatitis.

Prevalence and epidemiology

The exact prevalence of irritant contact dermatitis and allergic contact dermatitis (ICD and ACD) is unclear, although ICD is much more common than ACD and has been reported to account for 80% of all occupational skin disorders. ACD is said to affect 1% to 2% of the population with certain patient groups, such as patients with leg ulcers, at a higher risk of developing ACD.

Aetiology

Different physiological mechanisms are responsible for ICD and ACD. In ICD, an agent must penetrate the outer layer of skin, the stratum corneum, to provoke a physiological response. The type of irritant, the concentration, quantity involved and length of exposure will affect the severity of reaction. This can occur with a single exposure, or more commonly, with frequent exposures when the irritant accumulates in the stratum corneum. For example, strong acids and alkaline substances can produce ulceration on a single exposure, whereas other agents (e.g., zinc oxide tape) potentially require multiple exposures and tend to provoke a weaker reaction and cause a prickly heat type of dermatitis.

ACD first requires sensitization to occur. This leads to specific cell-mediated sensitization. Once the skin has become sensitized to an allergen, reexposure to the allergen triggers memory T cells to initiate an inflammatory response 24 to 48 hours after reexposure. Because these T cells are distributed throughout the body, the reaction is not limited to the site of exposure and explains why lesions are seen away from the site of exposure. The risk of sensitization can depend on the individual's susceptibility as well as the particular

allergen's concentration and quantity. Reexposure can occur days and sometimes years after initial exposure. Common irritants and allergens are listed in [Table 8.33](#).

Arriving at a differential diagnosis

Many causes of dermatitis are related to certain occupations, including beauticians, construction workers, hairdressers and mechanics. Questions about exposure to irritants and allergens at work can often identify the cause of symptoms.

Determining an accurate diagnosis can be difficult because clinical features of similar conditions overlap ([Table 8.34](#)). Asking symptom-specific questions will help the pharmacist establish a differential diagnosis ([Table 8.35](#)).

Table 8.33
Irritants and allergens known to precipitate dermatitis

Irritants that can precipitate irritant contact dermatitis	Allergens that can precipitate allergic contact dermatitis
Detergents and soaps	Nickel (especially in jewellery) Chromate in cement
Solvents and abrasives	Topical corticosteroids (5% of patients)
Oils	Cosmetics, particularly fragrances, hair dyes, preservatives and nail varnish resin
Acids and alkalis, including cement	Rubber, including latex
Reducing agents and oxidising agents	Dyes, formaldehyde and epoxy resins

Table 8.34
Causes of dermatitis-like rash and their relative incidence in community pharmacy

Incidence	Cause
Most likely	Irritant contact dermatitis
Likely	Urticaria, allergic contact dermatitis, psoriasis, atopic dermatitis
Unlikely	Fungal infection, discoid dermatitis, scabies
Very unlikely	Pompholyx



Table 8.35
Specific questions to ask the patient:
Dermatitis

Question	Relevance
Location	The distribution of rash for contact dermatitis is closely associated with clothing and jewellery (Fig. 8.27).
Exposure	A history of when the rash occurs gives a useful indication as to the cause; for example, a construction worker might complain of sore hands while at work but when on holiday, the condition improves, only for it to worsen when he or she goes back to work.

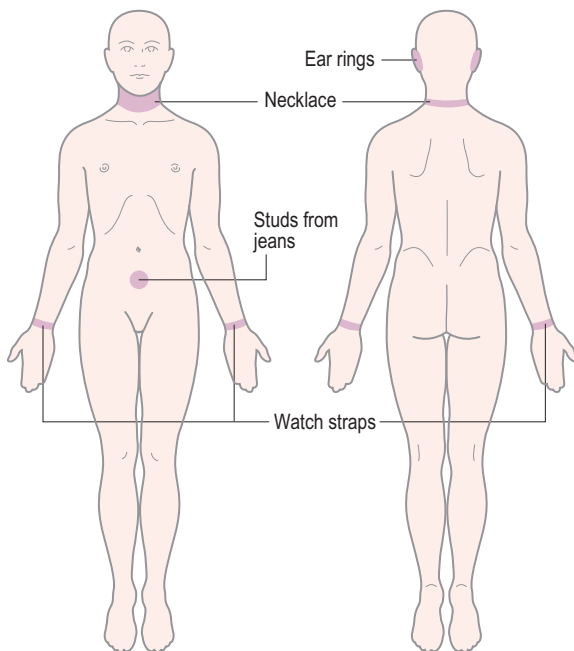


Fig. 8.27 Distribution of contact dermatitis.

Clinical features of irritant contact dermatitis and allergic contact dermatitis

All forms of dermatitis cause redness, drying of the skin, and irritation and pruritus to varying degrees and might show papules and vesicles. Itching is a prominent feature and often causes the patient to scratch, which results in broken skin with subsequent weeping. In chronic exposure, the skin becomes dry and scaly and can crack and fissure (Fig. 8.28). In both cases, rash develops at the site of exposure. In the acute phase, lesions appear rapidly, within 6 to 12 hours of



Fig. 8.28 Irritant dermatitis. From White, G. (2004). *Color atlas of dermatology* (3rd ed.). Churchill Livingstone.

contact, although this can be up to 72 hours in ACD. The rash in ICD tends to be well demarcated. In ACD, the rash tends to be less well defined; milder involvement away from the site of exposure is seen on repeated exposure and can reactivate at previously exposed sites. It is estimated that 75% of all cases of contact dermatitis and 80% to 90% of occupational dermatitis involve the hands.

Conditions to eliminate

Likely causes

Urticaria

Urticarial rashes can have many causes, most notably food allergies, food additives (Table 8.36) and medicines. Like dermatitis, the rash is itchy and red but resembles the rash seen when stung by a stinging nettle (Fig. 8.29). Weals can be red or white, itch and be surrounded by an area of redness. The rash appears suddenly and tends to fade and disappear after 24 hours. In addition, the skin can be oedematous and blanches when pressed. Urticarial reactions often respond well to systemic antihistamines.

Psoriasis

Isolated lesions of psoriasis can be superficially similar to dermatitis; they appear red and scaly, although a key difference is the lack of prominent itch in psoriasis. The distribution of lesions is also usually different, and psoriasis is not precipitated by exposure to certain irritants or allergens. Further information on psoriasis can be found earlier in this chapter.

Unlikely causes

Fungal infections

Fungal infections exhibit the typical dermatitis-type symptoms of itchy red rash and can therefore be easily confused. Very clear lesion demarcation, along with differing location and central clearing, all point towards fungal infection. Further information on psoriasis can be found earlier in this chapter.

Table 8.36
Food additives known to cause allergic reaction

Additive	Uses
Sulphites (E220–E227)	Sulphites are used to preserve smoked and processed meats, dried fruit (apricots), and salads. They are commonly found in liquid form in cold drinks and fruit juice concentrates and wine and sprayed onto foods to keep them fresh and prevent discolouration or browning.
Benzoic acid and parabens (E210–E219)	Benzoates and parabens have antibacterial and antifungal properties for prevention of food spoilage. These agents are added to pharmaceutical and food products and occur naturally in prunes, cinnamon, tea and berries.
Antioxidants (E320–E321)	Fat and oils in food turn rancid when exposed to air. Synthetic phenolic antioxidants, butylated hydroxyanisole, and butylated hydroxytoluene prevent this spoilage from happening but can trigger asthma, rhinitis and urticaria.
Flavour enhancers (E620–E635)	These are used to enhance food palatability, most notably aspartame, which can trigger urticaria and swelling, and monosodium glutamate (E620), which can trigger the so-called Chinese restaurant syndrome of headache and burning plus tightness in the chest, neck and face.
Colourings (E100–E180)	Colourings are used to make food visually more attractive; the azo dyes (Tartrazine, E102, Sunset Yellow, E110) and nonazo dyes (erythrosine) have been associated with triggering urticaria, asthma and generalized allergic reactions.



Fig. 8.29 Urticarial reaction to grass.

Discoid dermatitis

This differs from other forms of eczema because the lesions have clearly demarcated edges and are circular or oval. Lesions tend to affect the arms and legs and are often distributed symmetrically. It is more common in middle-aged people.

Scabies

Scabies presents with itch affecting the hands and therefore can present very much like dermatitis. For further information on scabies, see earlier in this chapter.

Very unlikely causes

Dyshidrotic eczema (*pompholyx*)

Pompholyx simply means *bubble* and refers to the presence of intensely itchy vesicles or blisters on the palms of the hands and occasionally on the soles of the feet. Stress and heat are known to precipitate the condition.

Fig. 8.30 will aid the differentiation of dermatitis.



TRIGGER POINTS indicative of referral: Dermatitis

Symptoms/signs	Possible danger/ reason for referral	Urgency of referral
Children <10 years in need of corticosteroids Lesions on the face, unresponsive to emollients	Steroid use outside current OTC product licenses	As soon as practicable
Widespread or severe dermatitis OTC treatment failure	Need for medical intervention	

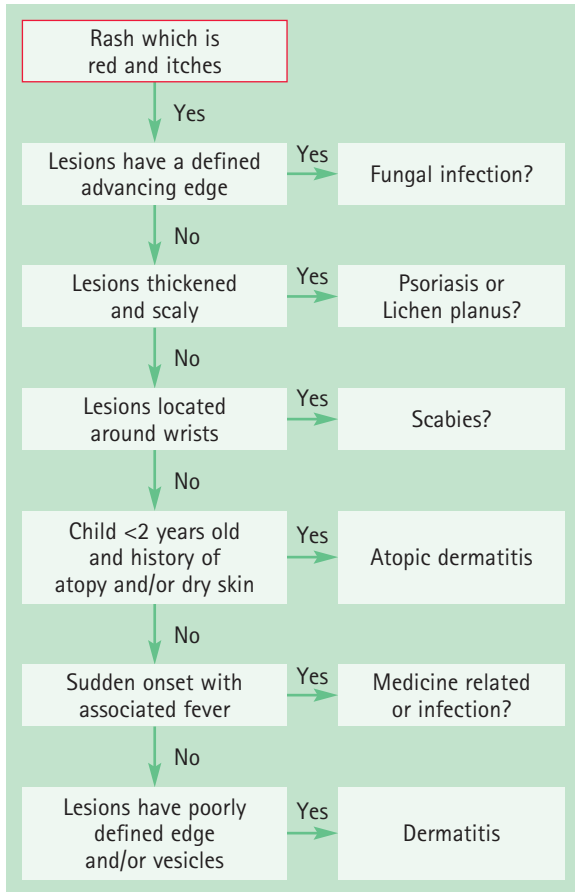


Fig. 8.30 Primer for differential diagnosis of dermatitis.

Evidence base for over-the-counter medication

Treatment should include three steps: avoiding irritants, managing the itch and maintaining skin integrity. Nonpharmacological interventions include avoidance of the causative agent; however, determining the cause is often difficult, and avoidance is sometimes impractical. Sweating intensifies the itching, so strategies to keep the person cool will help; cotton and loose-fitting clothing can be worn.

Pharmacological treatment of dermatitis should be managed with a combination of emollients and steroid-based products.

Emollients

Emollients should be used on a regular basis to keep the condition under control, and flare-ups can then be treated with corticosteroids. Choosing the most efficacious emollient for an individual is difficult due to the lack of comparative trial data between products and the variable nature of patients' responses. In general, patients respond to a thicker emollient rather than an elegant cosmetic brand because these allow

greater retention of water: for example, 50% liquid paraffin and 50% white soft paraffin. However, patient acceptability of such products needs to be considered. Cream formulations rather than ointments tend to be more readily accepted by patients because they are easier and less messy to use. In general, skin that is moderately dry to very dry will respond best to an ointment, and skin that is mildly dry will respond best to a cream. If the skin is broken or weeping, a water-soluble cream can be useful. To avoid the drying effects of soap, a soap substitute should be used.

Steroids

In the UK, hydrocortisone (classified as mild potency) and clobetasone (moderately potent) are available. Both have proven efficacy in treating dermatitis and should be considered first-line treatment for acute dermatitis. The choice between hydrocortisone and clobetasone is based on the severity of the dermatitis and the site of the dermatitis, with hydrocortisone being best for areas that have thin skin (e.g., flexures) and clobetasone possibly better for other areas (e.g., hands and palms) or where hydrocortisone has failed to control symptoms.

Practical prescribing and product selection

Prescribing information relating to specific products used to treat dermatitis is summarized in Table 8.37; useful tips relating to using products to treat dermatitis are given in 'Hints and Tips' in Box 8.11.

Emollients

There are a large number of emollients on the market. They come in a range of formulations to suit all skin types and patient preference (Table 8.38). Patients should be instructed to apply emollients liberally and whenever needed. They are pharmacologically inactive and so can be used by all patients, regardless of age or medical status. A number of ingredients incorporated into emollients do have the potential to sensitize skin, and patients should be advised to carry out a patch test with the product on the back of the hand before starting to use it routinely.

Corticosteroids

Although corticosteroids can be sold to patients OTC, there are a number of restrictions to their sale. In the UK, these are as follows:

- The patient must be older than 10 years for hydrocortisone (>2 years of age in Australia) and older than 12 years of age for clobetasone.
- Duration of treatment is limited to a maximum of 1 week.
- A maximum of 15 g can be sold at any one time.
- They cannot be used on facial skin, the anogenital region, or broken or infected skin.



Table 8.37
Practical prescribing: Summary of medicines for dermatitis

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
Emollients	From birth onwards	None	None	None	OK
<i>Corticosteroids</i>					
Hydrocortisone	>10 years	None	None	None	OK
Clobetasone	>12 years				

HINTS AND TIPS BOX 8.11: DERMATITIS

Patch testing for allergies	If the rash persists despite avoiding likely irritants and allergens, patch testing could be tried.
How much to apply?	<p>Patients should be instructed to use a fingertip unit. This is the distance from the tip of the adult index finger to the first crease. This unit measurement is especially useful for application of steroids.</p> <p>The amount of cream that should be used varies with the body part:</p> <ul style="list-style-type: none"> ● One hand: Apply one fingertip unit. ● One arm: Apply three fingertip units. ● One foot: Apply two fingertip units.
Quantity required?	<p>The BNF gives the following guidance for 1 week's use:</p> <p>Both hands, 15–30 g Both arms, 30–60 g Both legs or trunk, 100 g</p>
When to apply emollients and corticosteroids?	After using a corticosteroid, an emollient can be applied to the same area 30 minutes later.

Table 8.38
Summary of proprietary emollient products

Product name	Formulation	Ingredients other than emollient	Contains potential sensitizing agents
Adex	Gel		Yes
Aveeno	Cream, bath oil, wash, lotion		Yes
AproDerm	Cream, gel, ointment		No
Aquamax	Cream, wash		Yes
Aquadrate	Cream	Urea	No
Aquamol	Cream		Yes
Aripro	Mousse		Yes

Continued

Table 8.38
Summary of proprietary emollient products—cont'd

Product name	Formulation	Ingredients other than emollient	Contains potential sensitizing agents
Balneum	Bath oil, cream	Urea (cream)	Yes
Balneun Plus	Bath oil, cream	Urea (cream)	Yes
Calmurid	Cream	Urea, lactic acid	No
Cetaben	Cream, cleansing cream, lotion, ointment, bath additive		Yes
Cuderm	Cream, lotion, wash		Yes
Dermamist	Spray		No
Dermalo	Bath additive		No
Dermol 200	Shower emollient	Antimicrobials	Yes
Dermol 500	Lotion	Antimicrobials	Yes
Dermol 600	Bath emollient	Antimicrobials	Yes
Dermol	Cream, wash	Antimicrobials	Yes
Dexeryl	Cream		Yes
Diprobase	Cream, ointment, lotion		Yes (cream)
Doublebase	Dayleve, gel, emollient shower gel, wash gel and bath additive		No, apart from bath additive
Eczmol	Cream	Antimicrobials	Yes
E45	Cream, lotion, bath oil		Yes (cream and lotion)
E45 Emollient	Wash cream	Zinc oxide	No
E45 Itch relief	Cream	Urea	Yes
Emcrem	Cream		Yes
Emelpin	Ointment		Yes
Emollin	Spray		No
Emulsiderm	Bath emulsion	Antimicrobials	Yes
Enopen	Cream		Yes
Epaderm	Cream, ointment		Yes
Epimax	Cream, oatmeal cream, ointment, paraffin-free ointment		Yes
Eucerin	Cream, lotion ^a	Urea	Yes
ExCetra	Cream		Yes
Exmaben	Cream		Yes
Exmabase	Gel		No

Continued

Table 8.38
Summary of proprietary emollient products—cont'd

Product name	Formulation	Ingredients other than emollient	Contains potential sensitizing agents
ExmaQS	Cream		Yes
Fifty:50	Ointment		Yes
Flexitol	Cream	Urea	Yes
Hydromol Intensive	Cream	Urea	No
Hydromol	Cream, ointment, bath and shower emollient		Yes (cream and ointment)
HypoBase	Gel		No
imuDERM			Yes
Isomol	Gel		No
Kreamoint	Ointment		Yes
Lipobase	Cream		Yes
LPL 63.4	Bath oil		Yes
Myribase	Gel		No
Nutraplus	Cream	Urea	Yes
Oilatum	Cream, emollient, gel, junior bath additive, junior cream, shower gel		Yes
Oilatum Plus	Bath additive	Antimicrobials	Yes
QV	Cream, ointment, lotion, bath oil, gentle wash		Yes (except oil)
Soffen	Cream		Yes
Ultrabase	Cream		Yes
Unguentum M	Cream		Yes
ZeroAQS	Cream		Yes
Zerobase	Cream		Yes
Zerocream	Cream		Yes
Zeroderm	Ointment		Yes
Zerodouble	Gel		No
Zeroguent	Cream		Yes
Zerolatum	Bath additive		No
Zeroneum	Bath additive		Yes
Zeroveen	Cream		Yes

^aMultiple formulations listed under similar names.

Hydrocortisone

Hydrocortisone can be bought alone (e.g., Hc45) or in combination with other ingredients (e.g., Eurax Hc, Canesten Hydrocortisone). It is prudent to use products solely containing hydrocortisone for dermatitis, applying them twice daily. If secondary infection is suspected; for example, with a fungal infection – products such as Canesten Hydrocortisone can be used.

Clobetasone

Like hydrocortisone, clobetasone (Eumovate eczema and dermatitis cream) should be applied twice a day.

Further reading

Bellingham, C. (2001). Proper use of topical corticosteroids. *The Pharmaceutical Journal*, 267, 377.

Clark, C., & Hoare, C. (2001). Making the most of emollients. *The Pharmaceutical Journal*, 266, 277–279.

Websites

National Eczema Society: <http://www.eczema.org/>
<http://www.eczema.org/emollients>

National Eczema Association: <http://www.nationaleczema.org/>

Sun exposure and melanoma risk

Background

It is now well recognized that excessive or prolonged exposure to the sun's rays and inadequate skin protection can result in precancerous and cancerous neoplasms. There are many types of skin cancer, but three types are associated with sun exposure – squamous cell carcinoma (SCC), basal cell carcinoma (BCC) and malignant melanoma (MM) – and are responsible for more than 95% of all skin cancers. SCC and BCC result from chronic long-term exposure to sunlight, whereas MM is associated with acute, intense and intermittent blistering sunburns. BCC and SCC are often grouped together as nonmelanoma skin cancer (NMSC).

Prevalence and epidemiology

The incidence of cancers related to skin damage has dramatically increased since the 1980s, and is highest in Caucasian people living in equatorial regions. Approximately 16 000 cases of melanoma are currently diagnosed each year in the UK. MMs are slightly more common in women, although the incidence in both sexes has been steadily increasing.

Affluent women appear to be at highest risk of developing MM, whereas men from lower socioeconomic groups are at greatest risk of developing NMSC.

Aetiology

The body's response to the effects of UVA and UVB light is protective. On exposure to UV light, melanocytes increase the production of melanin, thus causing a darkening of the skin (the all-important suntan). Melanin absorbs both UVA and UVB and effectively protects the skin from damage; however, melanin synthesis is slow, and skin damage might well have already occurred, manifesting as sunburn. Sunburn is an inflammatory response to excessive exposure to UV light whereby an increase in inflammatory mediators results in capillary vasodilation and increased capillary permeability. In addition to melanin production, epidermal hyperplasia occurs, causing the skin to thicken, providing further protection.

Arriving at a differential diagnosis

Pharmacists have a major role to play in dealing with patients who have been exposed to excessive amounts of sunlight. They can promote sun safety messages, both passively and actively (when dealing with requests regarding sunburn), and make appropriate referrals with regard to suspicious lesions. Pharmacists must be able to recognize suspicious lesions, especially those resembling MM, because it has the highest mortality of skin cancers but, if detected early, has very high (90%) 10-year survival rates.

Clinical features of malignant melanoma

MM is one of the few cancers that is associated with young adults, although it is most common in people older than 75. There are four common subtypes – superficial spreading melanoma, nodular melanoma, lentigo maligna melanoma and acral lentiginous melanoma – although the latter subtype is rare. It can appear on all body sites, yet distribution between men and women does differ (Fig. 8.31). In the UK population, the most common site is the lower leg in women and on the back in men. Risk factors include early childhood sun exposure, people with multiple moles, and those with susceptible sunburn skin types. The first sign of melanoma is often a change in the size, shape or colour of a mole, although melanoma can also appear on the body as a new mole (Fig. 8.32). Early identification is essential; two commonly used checklists are used to aid diagnosis: the Seven-Point checklist and the ABCDE list, although NICE advocates the use of the seven-point checklist.

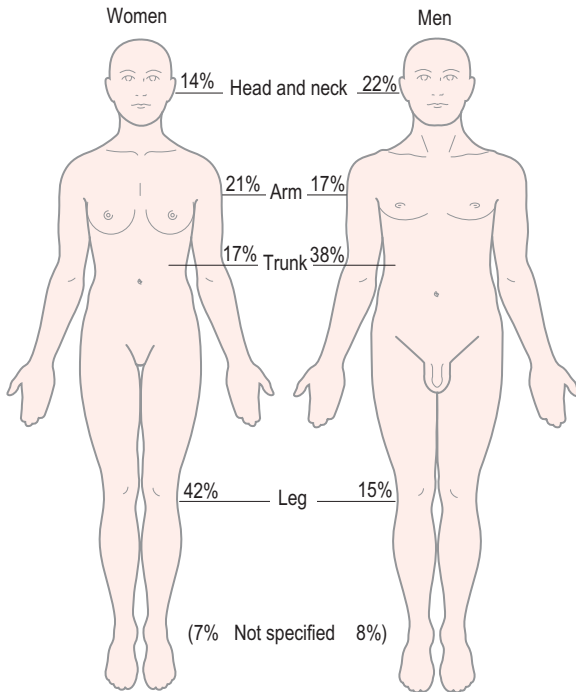


Fig. 8.31 Distribution of malignant melanoma.

The seven-point checklist

This checklist consists of three major and four minor points:

Major (scores 2)

1. Change in shape
2. Change in size
3. Change in colour

Minor (scores 1)

1. Largest diameter 7 mm or more
2. Inflammation
3. Oozing
4. Change in sensation (e.g., itch or irritation)

Any lesion should be suspected as MM with a score of 3 or more.

The ABCDE rule

This checklist consists of five points:

- **Asymmetry.** Ordinary moles are usually symmetrical in shape. Melanomas are likely to be irregular or asymmetrical.
- **Border.** Moles usually have a well-defined, regular border. Melanomas are more likely to have an irregular border with jagged edges.
- **Colour.** Moles are usually a uniform brown. Melanomas tend to have more than one colour. They may be



Fig. 8.32 Superficial spreading melanoma, irregular in colour and shape. From Wilkinson, J., Shaw, S., & Orton, D. (2004). *Dermatology in focus*. Churchill Livingstone.

varying shades of brown mixed with black, red, pink, white or a bluish tint.

- **Diameter.** Moles are normally no bigger than the blunt end of a pencil (~6 mm across). Melanomas are usually more than 7 mm in diameter.
- **Evolution.** The symmetry, border, colour or diameter of a mole has changed over time.

It is essential that these people be given information, ideally both orally and written, regarding the changes that might subsequently suggest MM and be instructed to seek medical help as soon as they notice changes.

Nonmelanoma skin cancers

NMSCs are the most common cancers in the UK. They are associated with older people, with the average age of

diagnosis in the early 70s. The cancers are rarely fatal but can cause substantial morbidity. Both cancers commonly occur on skin surfaces that are exposed to a lifetime accumulation of UV radiation, such as the hands, face and scalp. They are more common in people who have worked outdoors, in fair-skinned people, and those living in tropical and subtropical climates. BCC and SCC vary in their appearance. SCC initially presents as raised lesions that exhibit a horny or scaly appearance that later become nonhealing lesions often larger than 1 cm, which can ulcerate; BCC starts as a small translucent papule with a rolled edge and obvious telangiectasia over the surface. Over time (growth can be very slow), the size of the papule increases and can ulcerate and crust over.

Conditions to eliminate

There are several other types of pigmented lesions that can sometimes be difficult to differentiate from melanomas.

Actinic keratosis

Actinic keratosis is the most common premalignant skin condition, with approximately 1 in 1000 cases progressing to SCC. Lesions occur on parts of the body that are exposed to long-term sun exposure (e.g., head, forearms, hands). They begin as small rough spots. Roughness is a key feature, often referred to as feeling like rubbing sandpaper. They are generally flat and brown and have well demarcated edges. Symptoms of actinic keratosis include tenderness, itchiness and burning. Over a period of years, they enlarge and often become red and scaly.

Seborrhoeic keratosis

Seborrhoeic keratoses (also known as *seborrhoeic warts* or *basal cell papillomas*) are benign flat, or raised lesions that vary in colour. Initially, they take on the colour of the person's skin but gradually darken. They range in colour from light brown to jet black and have a stuck-on appearance (see Fig. 8.20). They are more usual on the trunk and increase in incidence from 40 years onwards. Over time, they can become wartlike. Occasionally, they can become inflamed, itchy or bleed, but this is normally because they have been caught on clothing.

Atypical moles

These are usually flat and more than 5 mm in diameter and can show an irregular shape, indistinct borders, and variable colours. A number of types have been described: a *halo naevus* is surrounded by a depigmented halo of normal skin and is common in older children and young teenagers; a *Spitz*

naevus is a firm, round, pink, red or reddish-brown nodule less than 2 cm in diameter that usually occurs on the face or legs; a *blue naevus* is a raised smooth lesion that is blue or blue-black in colour. It is usually found on the extremities.

Age spots

Age spots (also known as *lentigines* or *liver spots*) vary in size but most are less than 5 mm in diameter and appear as flat brown-black, sometimes irregularly shaped lesions. They are caused by chronic sun exposure and normally occur from middle age onward.



TRIGGER POINTS indicative of referral: Sunburn/damage

Symptoms/signs	Possible danger/reason for referral	Urgency of referral
Facial lesions, especially in people >60	Suggests actinic keratosis or SCC or BCC	As soon as practicable
Lesions that have become itchy, irritated or are prone to bleeding	Suggests potential melanoma	Immediate same-day referral to GP
Moles that have changed in size, shape, or colour		

Evidence base for over-the-counter medication

Avoidance measures

The most effective strategy for preventing skin damage and sunburn and reducing the chance of developing cancers is avoidance of UV light. Cancer research UK has promoted a SunSmart campaign that highlights the key sun avoidance measures that should be promoted to the public:

S Spend time in the shade between 11 AM and 3 PM.

M Make sure you never burn.

A Aim to cover up with a T-shirt, hat and sunglasses.

R Remember to take extra care with children.

T Then use factor 15+ sunscreen and four stars.

The SunSmart programme (www.sunsmart.com.au) also has public guidance (free App download) on how to avoid sun damage called *Slip! Slap! Slap! Seek! Slide!*

1. Slip on sun-protective clothing that covers as much of your body as possible.
2. Slop on an SPF 30+ broad-spectrum sunscreen liberally to dry skin at least 20 minutes before sun exposure. Reapply every 2 hours when outdoors.
3. Slap on a broad-brimmed hat that shades your face, neck and ears.
4. Seek shade, particularly between the hours of 10 AM and 2 PM (and 11 AM and 3 PM during daylight saving time).
5. Slide on sunglasses.

Sunscreens

Although sunscreens play an important role in sunburn protection, they should never replace minimizing sun exposure. Sunscreens use the sun protection factor (SPF) system to indicate the level of protection against UV radiation. It is a measure of the protection from UVB radiation. This has been calculated under experimental conditions using four times the amount of sunscreen usually applied by consumers. It is important that patients and consumers do not assume a linear increase in protection as the SPF increases. For example, a sunscreen with an SPF of 15 blocks 93% of UVB, whereas a doubling to SPF 30 only increases protection by 4% to 97%.

In the UK, a star rating also exists to indicate the level of protection offered against UVA relative to protection against UVB. A five-star rating indicates that the product has a balanced amount of UVA and UVB protection. The lower the star rating, the greater the protection offered against UVB compared with UVA. Ideally, a product should have a minimum four-star rating.

Practical prescribing and product selection

Prescribing information relating to sunscreen products is discussed and summarized in Table 8.39; useful tips relating to patients asking for advice about protection from the sun are given in 'Hints and Tips' in Box 8.12.

All products should be applied 20 to 30 minutes before exposure to the sun, reapplied after 30 minutes and then every 2 hours. Standard practice until recently was to match skin type with the level of SPF protection the person required. However, this approach, although preventing sunburn, does not prevent long-term skin damage. Rather than selecting a specific sunscreen for skin type, it is advocated that all white-skinned people should use a sunscreen with an SPF of at least 15 but preferably SPF 20 to 30, given that most people do not adequately supply sunscreen.

Chemical sunscreens

Chemical sunscreens work by absorbing UV energy and give protection against UVA or UVB, although they tend to be more effective against UVB radiation. Most marketed products contain a combination of agents, including benzophenones, cinnamates, dibenzoylmethanes and *para*-aminobenzoic acid. The latter is now infrequently used because *para*-aminobenzoic acid was frequently associated with contact sensitivity.

Physical sunscreens

Physical sunscreens are opaque reflective agents and offer protection against UVA and UVB radiation. Examples of physical sunscreens include zinc and titanium oxide.



Table 8.39
Practical prescribing: Summary of sun protection products

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
Chemical sunscreens	Infant upwards but some manufacturers do have lower age limits	Allergic reactions, but may be linked to the vehicle and not the active ingredients	None	None	OK
Physical sunscreens		None, but may be cosmetically unacceptable			

HINTS AND TIPS BOX 8.12: SUN DAMAGE

Water-resistant sunscreens	These are claimed to be effective after immersion in water. However, studies have shown that sunscreen effectiveness decreases after water exposure. It would be prudent therefore, to reapply sunscreens after swimming.
Eye protection	Prolonged (over years) sun exposure can contribute to age-related macular degeneration. Therefore, wraparound sunglasses and lenses that effectively filter UV light should be worn.
Treatment of sunburn?	Mild sunburn can be managed with a combination of topical cooling preparations, such as calamine, moisturizers and systemic analgesia.
Medicine-induced photosensitivity	NSAIDs, tetracyclines, chlorpromazine, phenothiazines and amiodarone can cause pruritus and skin rash when the skin is exposed to natural sunlight, primarily due to UVA radiation. Patients on photosensitive drugs should use a broad-spectrum sunscreen because these filter both UVA and UVB radiation. https://www.dermnetnz.org/topics/drug-induced-photosensitivity/
Sun protection and vitamin D deficiency	The UK Department of Health issued guidance to health care professionals on the danger of vitamin D deficiency. This, in part, has been caused by the use of sunscreens. Guidance is not to stop using sunscreen, but certain patient groups should take supplements. https://www.nice.org.uk/guidance/ph56

Further reading

Gupta, A. K., Paquet, M., Villanueva, E., & Brintnell, W. (2012). Interventions for actinic keratoses. *Cochrane Database System Review*, 12:CD004415. <https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD004415.pub2/full>

Websites**Charities**

Cancer Research UK: <https://www.cancerresearchuk.org/home>
 Melanoma UK: <https://www.melanomauk.org.uk/>
 The Skin Cancer Foundation: <https://www.skincancer.org/>
 Images of atypical moles are available at www.dermnet.com/Atypical-Nevi.

Guidance

British Association of Dermatologists guidelines on 'The prevention, diagnosis, referral and management of melanoma of the skin', 2007: <http://www.bad.org.uk/shared/get-file.ashx?id=793&itemtype=document>
 National Institute for Health and Care Excellence (NICE). Guidance on skin cancer protection: <https://www.nice.org.uk/guidance/ph32>

General sites

Sunsmart website: <https://www.sunsmart.com.au/>
 Cancer Council Australia: <https://www.cancer.org.au/>
 Melanoma Research Foundation: <https://melanoma.org/>

Self-assessment questions

The following questions are intended to supplement the text. Two levels of questions are provided, multiple-choice questions and case studies. The multiple-choice questions are designed to test knowledge and the application of knowledge, and the case studies allow this knowledge to be put in context in patient scenarios.

Multiple-choice questions

- 8.1** In which condition is scaling the most prominent?
- Allergic dermatitis
 - Scabies
 - Fungal infection
 - Plaque psoriasis
 - Lichen planus
- 8.2** Actinic keratosis tends to least affect which part of the body?
- Hands
 - Head
 - Arms
 - Neck
 - Back
- 8.3** A lesion described as flat and less than 1 cm in diameter is known as which of the following?
- Papule
 - Macule
 - Patch
 - Comedone
 - Nodule
- 8.4** What lesion symptom or sign is not associated with suspected skin malignancy?
- Symmetry
 - Change in sensation
 - Change in colour
 - Irregular border
 - Lesion growth
- 8.5** Mrs LK, 20 years old, comes into your pharmacy seeking advice about a rash on her arm. She tells you that it appeared about 10 to 14 days ago and is mildly itchy. She has no other symptoms and suffers from no other medical conditions. What is the most likely cause of her symptoms?
- Contact dermatitis
 - Atopic dermatitis
 - Tinea corporis
 - Discoid eczema
 - Psoriasis
- 8.6** Which statement best describes severe acne?
- Lesions affecting the face only that are a mixture of pustules and nodules. Scarring is likely.
 - Lesions affecting the face only that cause pain.
 - Lesions affecting the face, back and chest, which are a mixture of pustules and nodules. Scarring is unlikely.
 - Lesions affecting the face, back and chest, which are a mixture of pustules and nodules. Scarring is likely.
 - Lesions affecting the back and chest, which are a mixture of pustules and nodules. Scarring is likely.
- 8.7** Mr SW, a 32-year-old man, asks for advice on a skin rash on his arm near his elbow. It is raised, pink, and mildly itchy. From the listed conditions, which is most likely?
- Psoriasis
 - Discoid eczema
 - Fungal infection
 - Atopic dermatitis
 - Seborrhoeic dermatitis
- 8.8** A middle-aged woman complains of red papules and pustules on her forehead and her cheeks. There are no open comedones present. These symptoms indicate which one of the following dermatological conditions?
- Shingles
 - Rosacea
 - Urticaria
 - Acne vulgaris
 - Seborrheic dermatitis
- 8.9** An adult patient presents to the pharmacy with a rash. It is located on the left leg. Based solely on location, which condition is it most likely to be?
- Shingles
 - Ringworm

- c. Urticaria
- d. Discoid eczema
- e. Seborrheic dermatitis

8.10 A woman in her 20s presents with hair loss. She has noticed a rapid loss of hair toward the occipital region of her head. Based on this information, what is the most likely diagnosis?

- a. Androgenetic alopecia
- b. Traction alopecia
- c. Postpartum alopecia
- d. Alopecia areata
- e. Tinea capitis

8.11 Basal cell papillomas are characterized by being which of the following?

- a. Itchy
- b. Exuding and crusting
- c. Colour changes
- d. Scaling
- e. Asymptomatic

Questions 8.12 to 8.16 concern the following medicines:

- A. Clotrimazole
- B. Miconazole
- C. Benzoyl peroxide
- D. Salicylic acid
- E. Nicotinamide
- F. Benzyl benzoate
- G. Minoxidil

Select, from A to G, which of the medicines:

- 8.12** Is best avoided in diabetics?
- 8.13** Can bleach clothing?
- 8.14** Can be used for oral fungal infections?

8.15 Can produce systemic side effects

8.16 Is most associated with skin irritation

Questions 8.17 to 8.25 concern the following conditions:

- A. Chickenpox
- B. Cold sores
- C. Impetigo
- D. Pityriasis versicolor
- E. Psoriasis
- F. Lichen planus
- G. Tinea corporis
- H. Fifth disease
 - I. Molluscum contagiosum
 - J. Pityriasis rosea

Select, from A to J, which of the conditions:

8.17 Is associated with a facial rash often resembling a 'slapped cheek'?

8.18 Can be mistaken for warts?

8.19 Is associated with moderate to severe itching?

8.20 Sunlight can trigger symptoms

8.21 Itching, burning or tingling symptoms precede appearance of the lesions

8.22 Reinfection results in shingles

8.23 Is associated with a herald patch?

8.24 Central clearing of the rash is often observed

8.25 Is bacterial in origin?

Answers

8.1 Answer: d

Rationale: Allergic dermatitis (a) and scabies (b) are associated with itch but not scaling; the others could cause scaling but plaque psoriasis (d), being due to increased cell turnover, exhibits scaling as an obvious clinical feature.

8.2 Answer: e

Rationale: Actinic keratoses are very common on sites repeatedly exposed to the sun, so the back is likely to have as much exposure as the other sites listed.

8.3 Answer: b

Rationale: Papules (a), comedones (d) and nodules (e) are all raised lesions. This leaves macules (b) and patches (c) as viable options. Patches are large, so macule is the correct answer.

8.4 Answer: a

Rationale: Malignancy can be assessed through checklists, such as ABCDE. Using this, changes should be viewed with suspicion. On that basis, symmetry (a) is the correct answer.

8.5 Answer: e

Rationale: Concentrating on mild itch, contact (a) and atopic dermatitis (b) and discoid eczema (d) can be eliminated because they have itch as a prominent symptom. Tinea corporis (c) is also itchy and varies from mild to severe. Psoriasis (e) is the correct answer because it tends to be a condition that does not cause itch or is sometimes only mildly itchy.

8.6 Answer: d

Rationale: Severe acne affects the face, back and chest and on this basis options a, b, and e can be discounted. Scarring is likely and therefore d is the right option.

8.7 Answer: a

Rationale: Based on location, discoid eczema (b; legs), seborrheic dermatitis (e; face), and fungal infection (c; mostly body) can be discounted. Mild itch is unlikely to be atopic dermatitis (d).

8.8 Answer: b

Rationale: Urticaria (c) and seborrhoeic dermatitis (e) do not present with papules; shingles (a), although it can occur on the face, is unlikely to have papules.

Acne and rosacea are possible but in the absence of comedones and the age of the patient, this strongly points to rosacea.

8.9 Answer: d

Rationale: Shingles (a) is usually back and face; ringworm (b) is usually body; urticaria (c) can affect any body part; seborrheic dermatitis (e) is face and chest.

8.10 Answer: d

Rationale: Rapid hair loss is the key to determining the cause and is only likely to be observed in alopecia areata; all other conditions would see more gradual hair loss.

8.11 Answer: e

Rationale: Basal cell papillomas are noticed with advancing age and often go unnoticed initially due to their symptomless presentation.

8.12 Answer: D

Rationale: Any product that could damage skin or be destructive is best avoided in diabetic patients. Salicylic acid works by destroying skin cells and should not be used.

8.13 Answer: C

Rationale: Peroxide-based products can have a whitening effect and are included in products for tooth whitening. It therefore can have a bleaching effect on clothes.

8.14 Answer: B

Rationale: Only A and B are suitable for fungal infections. Miconazole as Daktarin oral gel can be used to treat oral thrush.

8.15 Answer: G

Rationale: Although all products are topically applied, skin penetration will result in systemic absorption. This has been reported only with minoxidil from this list.

8.16 Answer: F

Rationale: Azoles (A and B) have very few reports of skin irritation, as has nicotinamide (E). Salicylic acid (D) can cause skin destruction and therefore if used incorrectly can cause skin pain and irritation; Benzoyl peroxide (C) is associated with skin irritation, especially when first applied or at high strength. However, benzyl benzoate is a known skin irritant and is most likely to cause this problem.

8.17 Answer: H

Rationale: Concentrating on the location of the face, the options that should be considered are chickenpox (A), cold sores (B), impetigo (C), and fifth disease (H). Cold sores and impetigo tend to be located around the mouth and nose rather than the cheek and, although chickenpox sores can appear on the cheeks, they appear as discrete vesicles and not as flat patchlike lesions, as in fifth disease.

8.18 Answer: I

Rationale: Warts are raised hyperkeratotic lesions. On that basis, all lesions on the list that are flat can be eliminated. This leaves chickenpox (A), cold sores (B), impetigo (C), psoriasis (E), and molluscum contagiosum (I) as options. A, B, and C have lesions that form exudate and can also be eliminated. Psoriasis has red raised lesions that do not resemble warts.

8.19 Answer: A

Rationale: Itch is a hallmark symptom of most skin rashes, although the severity experienced varies. Mild itch is seen with cold sores (B), psoriasis (E), pityriasis versicolor (D), and rosea (J). Tinea corporis (G) may show a moderate itch. However, a hallmark symptom of chickenpox (A) is intense and severe itching.

8.20 Answer: B

Rationale: Triggers sometime are associated with the development of skin rashes – most notably from the list, cold sores (B) and psoriasis (E). Psoriasis is, however, associated with injury.

8.21 Answer: B

Rationale: Few skin lesions are preceded with symptoms before the development of a rash. From the list, chickenpox (A), cold sores (B) and pityriasis rosea can show such symptoms. In chickenpox, coldlike symptoms are experienced, and in pityriasis rosea, a herald patch is seen.

8.22 Answer: A

Rationale: The herpes zoster virus is the cause of shingles. From the list (see answer 8.25) only A, B, D, H, and I are viral in origin. Of these, chickenpox (A) is caused by the herpes virus.

8.23 Answer: J

Rationale: Not many skin rashes start with a discrete lesion before the full rash develops. This is only seen in J; however, singular lesions of tinea could be mistaken.

8.24 Answer: G

Rationale: Chickenpox (A), cold sores (B), impetigo (C), and molluscum contagiosum (I) show a vesicular or papular-like rash and therefore can be discounted. All other conditions present with macular or patch-like lesions and so need to be considered. All but fungal infection show concolourous lesions.

8.25 Answer: C

Rationale: A, B, D, H, and I are viral causes; pityriasis (D) and tinea (G) are yeast or fungal infections; lichen planus (F) and pityriasis rosea (J) causes are still unclear; psoriasis (E) is multifactorial. Only impetigo is bacterial in origin.

Self-assessment questions

The following questions are intended to supplement the text. Two levels of questions are provided: multiple choice questions and case studies. The multiple choice questions are designed to test knowledge and application of knowledge, and the case studies allow this knowledge to be put in context in patient scenarios.

Multiple choice questions

- 8.1** Which medicine has not been proven to be efficacious in treating dandruff?
- Cetrimide
 - Coal tar
 - Ketoconazole
 - Selenium sulphide
 - Zinc pyrithione
- 8.2** Which form of psoriasis can be managed OTC?
- Guttate
 - Erythrodermic
 - Pustular
 - Plaque
 - Seborrhoeic
- 8.3** Which medicine causes hair loss more than rarely?
- Ibuprofen
 - Nifedipine
 - Ranitidine
 - Simvastatin
 - Warfarin
- 8.4** What symptom is least associated with plaque psoriasis?
- Itch
 - Papules
 - Raised plaques
 - Redness
 - Scaling
- 8.5** In which form of tinea infection are imidazoles ineffective?
- Athlete's foot
 - Infection involving the body
 - Infection involving the nail
 - Infection on the hand
 - Jock itch
- 8.6** A corn is caused by?
- Damage to the plantar fascia
 - Excessive pressure caused by ill-fitting shoes
 - Human papilloma virus
 - Sweating feet
 - Too much pressure caused by anatomical deformity
- 8.7** In which condition is itching the least prominent?
- Allergic dermatitis
 - Fungal infection
 - Lichen planus
 - Psoriasis
 - Scabies
- 8.8** What skin condition is characterized by silvery-white scaly lesions of salmon-pink appearance with well-defined boundaries?
- Contact dermatitis
 - Pityriasis versicolor
 - Plaque psoriasis
 - Rosacea
 - Seborrhoeic dermatitis
- Questions 8.9 to 8.11 concern the following conditions:
- Acne
 - Cold sores
 - Dermatitis
 - Fungal infection
 - Plaque psoriasis
- Select, from A to E, which of the above conditions:
- 8.9** Is characterized by itching and scaling?
- 8.10** Often has prodromal symptoms prior to the rash appearing
- 8.11** Has a strong genetic link?
- Questions 8.12 to 8.14 concern the following medicines for fungal infection:
- Amorolfine

- B. Bifonazole
- C. Clotrimazole
- D. Hydrocortisone
- E. Tolnaftate

Select, from A to E, which of the above medicines:

- 8.12 Is applied once daily?
- 8.13 Is applied once weekly?
- 8.14 Should be used for no longer than 1 week?

Questions 8.15 to 8.17: for each of these questions *one or more* of the responses is (are) correct. Decide which of the responses is (are) correct. Then choose:

- A. If a, b and c are correct
- B. If a and b only are correct
- C. If b and c only are correct
- D. If a only is correct
- E. If c only is correct

Directions summarized

A	B	C	D	E
a, b and c	a and b only	b and c only	a only	c only

8.15 For the following statements about cradle cap which is/are true?

- a. There is normally a family history
- b. Ear and eye involvement is common
- c. The rash tends not to itch

8.16 Warts and verrucas are:

- a. Caused by the human papilloma virus
- b. Infections that never affect adults
- c. Can develop in to pre-cancerous growths if left untreated

8.17 When supplying aciclovir, patients should be told to:

- a. Use the product five times a day
- b. Apply as soon as symptoms are experienced
- c. Wash their hands after application

Questions 8.18 to 8.20: these questions consist of a statement in the left-hand column followed by a statement in the right-hand column. You need to:

- Decide whether the first statement is true or false
- Decide whether the second statement is true or false

Then choose:

- A. If both statements are true and the second statement is a correct explanation of the first statement
- B. If both statements are true but the second statement is NOT a correct explanation of the first statement
- C. If the first statement is true but the second statement is false
- D. If the first statement is false but the second statement is true
- E. If both statements are false

Directions summarized

	1st statement	2nd statement	
A	True	True	2nd explanation is a correct explanation of the 1st
B	True	True	2nd statement is not a correct explanation of the 1st
C	True	False	
D	False	True	
E	False	False	
	First statement		Second statement
	8.18 Benzoyl peroxide should be used to treat mild acne		It should be used for at least 6 weeks
	8.19 Scabies is intensely itchy		The mite's faeces cause a hypersensitivity reaction
	8.20 Minoxidil is used to treat hair loss		It works on over 80% of patients

Answers

8.1 Answer: a

Rationale: All listed medicines can be found in products to treat dandruff. Options c, d and e are actively marketed for dandruff and have specific evidence of efficacy. Coal tar (b) has been shown to help with scalp conditions and itchy scalp.

8.2 Answer: d

Rationale: The only form of psoriasis that is commonly seen in pharmacies, and for which efficacious products are available is plaque psoriasis.

8.3 Answer: e

Rationale: Ibuprofen (a), nifedipine (b) and ranitidine (c) are not known to cause hair loss. Simvastatin (d) has rarely been known to cause this problem.

8.4 Answer: b

Rationale: Classically, plaque psoriasis is described as lesions that are red (d), raised (c) and show scale (e). Itch (a) is seen in some patients but is not prominent. Papules are not a clinical feature of plaque psoriasis although they can be seen in pustular forms.

8.5 Answer: c

Rationale: Imidazoles are highly effective at treating and eradicating tinea infection involving soft tissues (e.g., feet) (a), body (b), hand (d) and groin (e). They do not penetrate the nail plate (c).

8.6 Answer: b

Rationale: Corn formation is due to abrasion and pressure. Therefore HPV virus (c) and muscle damage (a) can be ruled out; excessive sweating (d) may worsen symptoms but is not a cause. b and e are both plausible, but the normal cause is due to ill-fitting shoes.

8.7 Answer: d

Rationale: Itching is a very common symptom associated with skin rashes and all of these conditions can show itching. Allergic dermatitis (a), fungal infection (b) and scabies (e) are described as intensely itchy. Lichen planus (c) and psoriasis (d) have similar presentations but itch is more prominent in lichen planus.

8.8 Answer: c

Rationale: Scaling is not associated with contact dermatitis (a), rosacea (d) or seborrheic dermatitis (e). Pityriasis versicolor (b) does exhibit fine superficial scale but is paler and browner in colour.

8.9 Answer: D

Rationale: Acne (a) does not itch; cold sores (b) do not show scaling; plaque psoriasis (e) shows scale and itch, but the condition is not characterized by these symptoms; dermatitis (c) is defined by itch and rash but the rash shows little scaling.

8.10 Answer: B

Rationale: There a few skin rashes that show other symptoms before the eruption of the rash. Only cold sores are generally preceded by other symptoms that herald the eruption of the characteristic cold sore vesicles.

8.11 Answer: E

Rationale: Acne (a) is linked to hormonal changes in puberty; cold sores (b) and fungal infection (d) are infective in origin; dermatitis (c) seems to multifactorial and possibly has a genetic link, but psoriasis has a clear genetic link to disease expression.

8.12 Answer: B

Rationale: Amorolfine (a) is a weekly application; hydrocortisone (d) is twice daily and clotrimazole (c) and tolnaftate (e) are applied at least twice a day.

8.13 Answer: A

Rationale: See answer 8.12

8.14 Answer: D

Rationale: All products should be used for a finite time depending on the condition they are being used to treat, and each individual product licence highlights this, but it is hydrocortisone that has a very limited length of time it can be used for; this restriction was placed on the product to allow deregulation from POM.

8.15 Answer: C

Rationale: Cradle cap predominantly affects the scalp but other facial involvement is possible. The rash does not itch and there is no apparent hereditary link.

8.16 Answer: D

Rationale: Warts and verrucas are caused by viral infection and although they are more common in children they can be contracted by adults. They are self-limiting

and eventually will clear through autoimmune response from the patient.

8.17 Answer: A

Rationale: Aciclovir is more effective as soon as symptoms are experienced and requires frequent administration. To prevent any cross contamination, hands should always be washed after each application.

8.18 Answer: B (True/True – statement 2 not correct explanation of statement 1)

Rationale: Benzoyl peroxide is effective in treating mild cases of acne but if the patient responds treatment has to continue for weeks to see clinical benefit.

8.19 Answer: A (True/True – statement 2 is a correct explanation of statement 1)

Rationale: The mites' faeces are the cause of itch in patients and is due to a local allergic reaction.

8.20 Answer: C (True/False)

Rationale: Whilst minoxidil is promoted for treating hair loss it has poor efficacy.

Case studies

CASE STUDY 8.1

Mr RJ and his 9-year-old son Jimmy want to buy something for Jimmy's verruca. Mr RJ thinks that Jimmy has had the verruca for about 4 to 6 weeks. He describes it as a circular discoloured piece of skin that looks like the verrucas he used to get.

a. What course of action are you going to take?

Try and directly question Jimmy. See if Jimmy knows how long the suspected verruca has been there. Ask if the lesion is causing any pain when walking. Instead of asking for further descriptions of what the lesion looks like and where it is positioned, ask if you can look at the lesion.

On further questioning and examination, you concur with the self-diagnosis of a verruca. The lesion is small (<0.5 cm in diameter) and causes minimal pain when direct pressure is applied.

b. What are you going to recommend?

A salicylic acid-based product is the most suitable product; you recommend Bazuka after first making sure that Jimmy is not a diabetic.

Mrs RJ returns with Jimmy 6 weeks later and demands to see the pharmacist. She says the stuff you recommended is rubbish and Jimmy's verruca is bigger than it was before!

c. How are you going to respond?

First, you must stay calm and not be defensive. Many patients have unrealistic expectations on how quickly the verruca will resolve with therapy. Did you tell them how long it would take before an effect will be seen? This is a vital piece of information to ensure that patients realize that treatment is not a quick cure.

You find out that Mrs RJ has been applying the Bazuka and doing everything the instruction leaflet says. You inspect Jimmy's feet again and from what you can remember, the lesion does look slightly larger.

d. Why might this be the case?

Salicylic acid is destructive in nature and, if the product comes into contact with nonaffected skin, it can

damage skin and appear to the patient that the lesion has indeed gotten bigger.

Mrs RJ wants to try Bazuka Extra Strength because the normal Bazuka is not helping.

e. What are you going to do?

You must try to stress to Mrs RJ that she should continue with the normal Bazuka because 6 weeks of therapy is not long enough to make a decision to alter therapy. Reluctantly, Mrs RJ accepts your advice and leaves the pharmacy promising she will try for a bit longer.

One week later she presents a prescription for Cuplex gel for Jimmy.

f. What are you going to do?

It appears that Mrs RJ was not satisfied or convinced with your advice and has decided to see her GP. You do not know whether Mrs RJ told the doctor about using an OTC product. You could ring the GP to tell him or her that Mrs RJ has been using a salicylic acid-based product already; however, this is likely to have little bearing on the outcome of product selection because Jimmy will still need to continue treatment with something for a few more weeks. The prescription should be dispensed and Mrs RJ counselled appropriately. It would be unprofessional to point out that Cuplex is unlikely to be any better than Bazuka.

When you hand Mrs RJ the Cuplex, she mentions that the doctor said this was stronger than Bazuka and should do the trick.

g. How do you reply?

Be diplomatic and nonjudgemental. It is likely that the doctor knows that Cuplex is no better than Bazuka, but if the parent is convinced that what she is now getting is superior to the previous product, her motivation to comply with directions might be better. It might be worth asking the doctor next time you have a conversation what the rationale was for prescribing Cuplex.

Case studies

CASE STUDY 8.1

Mr KD, a 54-year-old man, presents to the pharmacy with a rash on his knees.

a. What do you think will help this patient?

He mentions 'knees', so this suggests it is affecting both knees. This means that the rash sounds like it is symmetrically distributed. Certain rashes do present in this way and therefore need to be uppermost in your thinking. Additionally, it seems that this is the major area of presentation; again, certain conditions are predisposed to certain parts of the body. He is 54, so childhood and adolescent skin rashes can be excluded from your thinking.

b. What questions do you ask him?

Questions about the presenting symptoms:

- How is the rash distributed? Is the same rash anywhere else on the body?
 - Knowing the exact location and if other lesions are present is important. For example, the patient may complain of rash on the knees but fail to tell you about other lesions because those are less noticeable or bothersome. However, from your perspective, knowing about other lesions is valuable because it might allow differentiation among similar lesions.
- What is the appearance of the rash (colour, arrangement, feel of lesions and presence of scaling)?
 - Knowing what the rash looks like is extremely important. You should really examine the rash and not take a patient description, which is likely to be incomplete or inaccurate. Always try and look at the rash.
- Any associated symptoms?
 - Many lesions are associated with varying levels of itch and discomfort, and knowing this information can allow you to discriminate among lesions.
- When did the rash start?

- Does he have a past history of lesions?
 - Knowing if this is an acute or recurrent presentation again allows discrimination. For example, an infection is likely to be an acute occurrence, whereas eczema is likely to be recurrent and exhibits relapse and remission.

He tells you that the rash started around 2 weeks ago and has gradually gotten worse. It is present on both knees around the knee cap area. There is one large patch on each knee. The lesions are slightly itchy. They are pink in colour, with some flaking of the skin. He recalls having a similar rash involving his elbows and knees about 10 years ago, although he doesn't remember what he used to treat it.

c. Based on this information, what could the rash be?

The lesions are likely to be symptoms of plaque psoriasis based on their bilateral location, colouration, lack of prominent itch and superficial flaking.

d. How could the diagnosis be confirmed?

Asking about family history and seeing if the lesions exhibit the classic Auspitz sign (pinpoint bleeding when the area is scratched).

He has a history of hypertension, hypercholesterolaemia and migraines. He states he has an 'allergy' to enalapril because it caused a cough.

Medication	Indication	Length of use
Amlodipine, 10 mg daily	Hypertension	4 years
Simvastatin, 40 mg nocte	Hypercholesterolaemia	4 years
Propranolol, 40 mg bd	Migraine prophylaxis	6 months
Sumatriptan, 100 mg prn	Migraine treatment	2 years

CASE STUDY 8.1 (Continued)

- e. Knowing his current medication regimen, how does this influence your management of Mr KD?

Beta blockers are known to precipitate or aggravate psoriasis, although this is rare. He has been on propranolol for 6 months and, because he had a history of similar symptoms 10 years ago, it seems unlikely that propranolol is the cause but is still a possibility.

- f. What advice do you offer on the management of Mr KD's symptoms?

You could recommend that he use an emollient to help soften and hydrate the skin. This can be applied liberally to the affected areas, as frequently as required. A tar product could be tried if the symptoms do not respond to the emollient. If symptoms persist, he is best referred to the physician for a review. Cessation of the beta blocker may lead to the remission of symptoms.

CASE STUDY 8.2

Ms AH is the mother of an infant son aged 4 months. She asks for your help in treating the flaky skin on his scalp. She says he has had the problem on and off for the last 6 weeks. She hasn't yet tried anything except baby shampoo, as recommended by the health visitor. However, she now wants a cream or something to get rid of the problem once and for all.

- a. What further information do you require to be in a position to help her?

You need to know more about the severity of the problem; for example, whether any other areas of the baby's skin are affected. Does the baby appear to scratch at the rash, and what were the previous episodes like? Were they the same as this time or different? Also, is there a family history of atopy or other dermatological conditions in the family?

You decide the child has cradle cap.

- b. What treatment are you going to recommend?

The use of a mild tar-based product every other day until the scalp clears would be appropriate. In between using the tar-based product, the mother should be instructed to use the baby shampoo.

Ms AH returns to the pharmacy 2 weeks later with another of her children. Impressed that her son's scalp is now clear, she now wants some advice for her 7-year-old daughter. She has a sore on the corner of her mouth.

- c. What further information do you require to be in a position to help her?

You need to know:

- *How long has the sore been present?*
- *How did the sore first develop?*
- *What symptoms are associated with the sore*
- *The progression of the sore. Has it spread?*
- *Previous history of the rash and any family history*

You find out the sore appeared overnight and is now itchy. On inspection, the lesion appears to be weeping a clear exudate.

- d. What is the most likely diagnosis?

Based on this information, the likely diagnosis is a cold sore.

- e. What treatment, if any, are you going to recommend?

No treatment is necessary but if the parent insists on therapy, any product could be given. Although antiviral therapy is most effective, it is expensive, and the cost could be difficult to justify. In addition, advice on minimizing transmission could be given such as not sharing towels and trying to avoid kissing (e.g., mum and dad).

CASE STUDY 8.2

A young girl (about 17 years old) asks for a stronger acne cream because her spots are getting worse. This table details the information obtained by the pharmacist.

Information Gathering	Data Generated
How long she has had the symptoms	Months
Anywhere other than the face	A few spots on the top of her chest
Other symptoms, provoking factors	No
Previous history of presenting complaint	No
Past medical history	None
Drugs (OTC, prescription)	Used Clearasil for the last month
Allergies	Strawberries
Social history	Not happy; she wants to go out but feels embarrassed
Family history	Mum apparently had bad acne; she keeps telling me it will go away.
On examination	Active lesions on face; mixture of papules and pustules, with some visible blackheads

- a. What is your diagnosis based on the information in the table?

Mild acne.

- b. What is your management plan for her?

The young girl seems to have been using a product that is unlikely to help and has not used it long enough to see visible improvement. Low-strength benzoyl peroxide should be recommended. Make sure she knows that the whole face needs to be treated, not just active lesions. Importantly, in this case, she needs to be given correct advice on when she will see improvement so she can manage her expectations.

CASE STUDY 8.3

Mr RT, an older man, asks for some cream to help get rid of a rash he has over part of his chest. The following questions are asked, and responses received.

Information gathering	Data generated
How long had the symptoms	Rash started 3 days ago
What does it look like	Red and angry
Where exactly	Started on his left side below his armpit and now spread under the armpit
Other symptoms	Felt a bit unwell, slight loss of appetite and headache
Any itching or pain?	Some pain, rated as 4 on scale of 1 to 10
On examination	Clusters of papules and vesicles unilaterally along dermatome, affecting left chest and back

Information gathering	Data generated
Medicines (OTC, prescription)	Regular warfarin, bendroflumethiazide, and nifedipine; uses emollients and clobetasone when needed for eczema
Past medical history	Stroke 1 year ago; hypertension and eczema
Social history, which may include questions relating to smoking, alcohol intake, employment, personal relationships	Wife died 6 months ago, finding it difficult to cope at times; does not like to bother his children, who live locally; feels very low
Family history	Not asked

Below are summarized the expected findings for questions when related to conditions that can present with rash associated with soreness seen by community pharmacists.

Condition	Vesicles	Unilateral	Recurrent	Pain	Other symptoms
Herpes zoster	Yes	Yes	Unusual	Yes	Tingling, burning before eruption; general malaise
Contact dermatitis	Possible	Yes	Yes	Possible	Itch
Eczema	Possible	Possible	Yes	Possible	Itch

When this information is compared to our patient's symptoms, and linking this with known epidemiology, it should be possible to make a differential diagnosis.

CASE STUDY 8.3 (Continued)

Condition	Vesicles	Unilateral	Recurrent	Pain	Other symptoms
Herpes zoster	✓	✓	✓	✓	✓
Contact dermatitis	✓	✓	X	X?	X
Eczema	✓	✓	X	X	X

We see that the symptoms most closely match shingles (✓ represents symptom match). A diagnostic question to ask is about a previous history of chickenpox. If the patient has never had chickenpox, he cannot develop shingles. Shingles is an acute infection caused by reactivation of a latent varicella zoster virus. Following primary chickenpox infection, the virus lies dormant in the dorsal root ganglia of the spinal cord. When reactivated, it travels along the sensory nerve to affect one or more dermatomes, causing the characteristic shingles rash. Reactivation of the virus probably occurs following a

decrease in cell-mediated immunity (e.g., with increasing age, HIV infection, illness).

The patient could be given analgesics to help with pain but referred for possible antivirals. To 'safety net': the patient also seems to be showing signs of depression, which needs further investigation. It would be good practice, in this case, to try and speak with the doctor to arrange an urgent appointment for the patient to treat the rash but also mention your concerns over the patient exhibiting signs of depressive illness.

CASE STUDY 8.4

Mr AC, a man in his late 20s or early 30s, presents with a very itchy rash on his left hand. He asks if you can give him a cream to stop the itching. The following questions are asked, and responses received.

Information gathering	Data generated
How long had the symptoms	Few days
Rash anywhere else	No
Other symptoms, provoking factors	Not really, just really itchy!
Additional questions	No exposure to chemicals or new tasks involving hand work
On examination	Left hand and wrist have obvious red papules but look like they have been scratched (confirmed by patient)

Information gathering	Data generated
Previous history of presenting complaint	No
Medicines (OTC, prescription)	Sodium valproate, 500 mg bd
Past medical history	Epilepsy – well controlled
Social history, which may include questions relating to smoking, alcohol intake, employment, personal relationships	Works for the National Health Service doing patient transports
Family history	Dad has eczema

Below are summarized the expected findings for questions related to rashes that cause itch involving the hands that can be seen by community pharmacists.

Condition	Location other than hands and wrists	Lesion appearance	Itch	Positive family or social history
Scabies	Unusual	Red papules through to vesicles	Intense	Yes
Dermatitis	Often (depends on type of dermatitis)	Red scaling rash that might crust over due to scratching	Moderate to intense	No
Insect bites	Often	Red papules through to vesicles	Moderate to intense	Possible
Pompholyx	Unusual	Vesicles	Intense	No

When this information is compared to our patient's symptoms, and linking this with known epidemiology of itching hands (see [Table 8.26](#)), it should be possible to make a differential diagnosis.

CASE STUDY 8.4 (Continued)

Condition	Location other than hands and wrists	Lesion appearance	Itch	Positive family or social history
Scabies	✓	✓	✓ (intensity points more to scabies than other conditions)	✓ (occupation exposes person to higher risk)
Dermatitis	✗?	✗	✓	✗
Insect bites	✗	✓	✓	✗?
Pompholyx	✓	✗?	✓	✗

We see that his symptoms most closely match scabies (✓ represents symptom match). Therapy could be started with permethrin cream, although it is expensive,

and referral to the GP might be considered. It is also important to try and trace the contact from which he has contracted scabies, and inform work.

CASE STUDY 8.5

A patient asks you for some OTC 1% hydrocortisone cream to treat some eczema on her face. She tells you that she has read on an Internet forum that it is much cheaper to buy this product than to get it on prescription, but that she has also heard that many pharmacists 'make a fuss' about selling this for use on the face.

What factors may have contributed to the development of this patient's view?

- Patients often expect to get what they want. Patients often see medicines as commodities and not medicines.
- You need to do the following:
Explain the legal and ethical position of the pharmacist.
Explain the risks.
Suggest other options.
Refuse sale.
- Patients may believe that they are well-informed through information read on the Internet. This is not always the case.

CASE STUDY 8.6

Atopic eczema, irritant contact dermatitis and allergic contact dermatitis can present in similar ways. For each condition, name the features and causative factors that are common to all three.

- All present as sore, red, itchy skin lesions but appear in different locations. Affected sites help diagnose the condition.
- A major factor in all three is the impaired barrier function of the epidermis, leading to increased loss of water – dry, cracked skin that allows entrance of irritants and allergens.
- Atopic eczema is due to internal factors. Causes are thought to involve genetics, environmental triggers, defects in the epidermal skin barrier and the immunological response.
- Irritant contact dermatitis is caused by exogenous (external) factors. An irritant must penetrate the outer skin layer to initiate the physiological response; for example, detergents, soaps, solvents, abrasives and oils.
- For allergic contact dermatitis, sensitization must occur: specific cell-mediated sensitization by an

allergen. Future exposure to the same allergen triggers memory T cells to initiate the inflammatory response. Lesions may appear at sites distant from the site of exposure; for example, nickel and chromate, cement, cosmetics, rubber, dyes and topical corticosteroids.

What other dermatological conditions need to be considered when differentiating eczema and dermatitis?

- Lichen planus: Thickened and scaly
- Psoriasis: General itch not present, distribution of lesions different
- Fungal infections: Clearly defined edge, central clearing
- Discoid dermatitis: Clear edges, circular or oval, symmetrical distribution
- Pompholyx: Intensely itchy vesicles and blisters on hands and soles of the feet
- Urticaria: Rash is itchy and red. Skin shows signs of oedema, and blanches if pressed.

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Musculoskeletal conditions

In this chapter

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History taking	299	Self-assessment questions	316

Background

The musculoskeletal system is comprised of hard (bone and cartilage) and soft (muscles, tendons, ligaments) tissues. It is responsible for mobility and provides protection to vital structures. Most musculoskeletal problems occur as a result of injury or organic illness. Most patients presenting to a community pharmacist will have an acute problem arising from injury, although chronic conditions such as osteoarthritis will be encountered routinely when issuing prescriptions to patients.

The key role of the pharmacist when dealing with patients with a musculoskeletal problem is to try and establish the cause, its severity, and whether it can be self-managed appropriately or requires further investigation.

General overview of musculoskeletal anatomy

The skeletal system of the human body is composed of 206 bones. At the point of contact between two or more bones, an articulation (joint) is formed. This system of bones and joints maximizes movement while maintaining stability. There are two basic types of joints:

- Synovial joints: allow considerable movement (e.g., shoulder or knee)
- Fibrocartilaginous joints: are completely immovable (e.g., the skull) or permit only limited motion (e.g., spinal vertebrae)

Bones and joints cannot move by themselves. The integrity of the musculoskeletal system depends on the interaction

between skeletal muscle and bones, and coordinated movement is only possible because of the way muscle is attached to bone. Tendons attach the end of the muscle to the bone or another structure on which the muscle acts. To perform such a function, tendons are composed of very dense fibrous tissue.

Joints require additional stability and support. Strong bands of fibrous tissue known as *ligaments* bind together bones entering a joint to provide this additional support and stability. It is often the integrity of the connecting structures that are damaged in a musculoskeletal injury. The simplified diagram of the medial aspect of the knee joint in Fig. 9.1 illustrates the relationship of the connective structures to the skeleton and musculature.

The knee joint is an example of a synovial joint. The femur, tibia, and fibula do not touch each other because they are covered with articular cartilage and separated by the synovial cavity. The knee joint also contains bursae, small fluid sacs, that provide protection at points in the joint where friction or pressure is high. These can become inflamed, leading to bursitis.

History taking

Obtaining an accurate history from the patient should provide enough information to determine whether the injury is within the scope of a community pharmacist. By the very nature of acute musculoskeletal injuries, if someone manages to come into the pharmacy, then the injury is unlikely to be serious. Information gathering should concentrate on when the problem occurred, what precipitated it, the level of discomfort, any restriction in range of motion, and whether the symptoms are worsening.

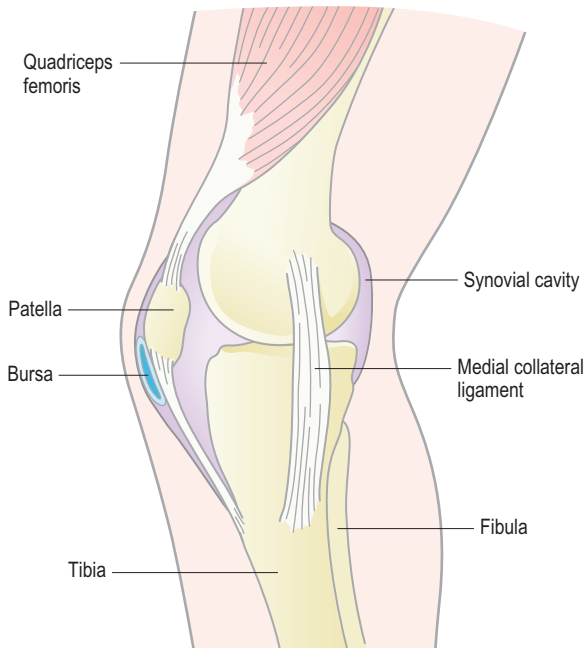


Fig. 9.1 The knee joint, medial view.

In general, any patient who presents with an injury that is causing extreme discomfort or an injury that adversely affects mobility and has been present for more than a week would probably be better managed by a doctor or physiotherapist/sports therapist.

Acute low back pain

Background

Low back pain is experienced in the lumbosacral area of the back, between the bottom of the ribs and the top of the legs. Acute back pain is classified as episodes lasting 6 weeks or less and chronic if symptoms persist beyond 6 weeks.

Over 50% of patients will be pain free within 6 to 12 weeks, although up to two thirds of patients will have a recurrence within 1 year after initial onset.

Prevalence and epidemiology

Low back pain is common. For example, in the US it is the fifth most common reason that patients see a medical practitioner and, in the UK, 7% to 8% of all adult general practitioner (GP) consultations are for low back pain. Latest UK statistics (Health and Safety Executive [HSE]) show that 6.6 million working days were lost through back pain in 2017.

Back pain is most common between the ages of 35 and 55 years, with prevalence rates similar for men and women, although 50% to 90% of pregnant women develop low back pain. Studies and statistical data have shown that in developed countries, 60% to 90% of adults will experience an episode of low back pain at some point in their adult lives. Back pain is most common in those with skilled manual, partly skilled, and unskilled jobs. Occupational risk factors in developing back pain include those who perform heavy manual labour, frequent bending, twisting, and lifting and people who remain in static positions for long periods of time such as truck and car drivers who drive long distances each year. Sports that involve excessive twisting, such as golf and gymnastics, can also lead to back pain. Other risk factors include obesity and psychosocial causes – for example, anxiety and depression.

Aetiology

Pain originates from the lumbosacral region and is often mechanical in origin (Fig. 9.2) although in many cases an exact cause cannot be determined, and it is often referred to as simple, nonspecific, or uncomplicated low back pain.

Arriving at a differential diagnosis

The vast majority of patients (95%) who present in the pharmacy will have simple back pain that will, in time, resolve with conservative treatment. The remaining cases will have back pain with associated nerve root compression. Serious underlying pathology is very rare, with infection and malignancy accounting for less than 1% of cases. It is worth noting that low back pain can be caused by gastrointestinal problems (e.g., peptic ulcer or pancreatitis) or genitourinary conditions (e.g., kidney stones, pyelonephritis) but low back pain is not the major presenting symptom.

Table 9.1 highlights conditions that can be encountered by community pharmacists and their relative incidence.

History taking should concentrate on questions regarding the pain, such as location, radiation, evidence of trauma, effect of pain on mobility, and factors that aggravate or relieve the pain (Table 9.2).

Clinical features of acute low back pain

Pain in the lower lumbar or sacral area is usually described as aching or stiffness. Depending on the cause, pain might be localized (e.g., lumbosacral strains after physical activity) or more diffuse (e.g., from postural backache after sitting incorrectly for a prolonged period). In cases of acute injury, the symptoms come on quickly, and there will be a reduction in mobility.

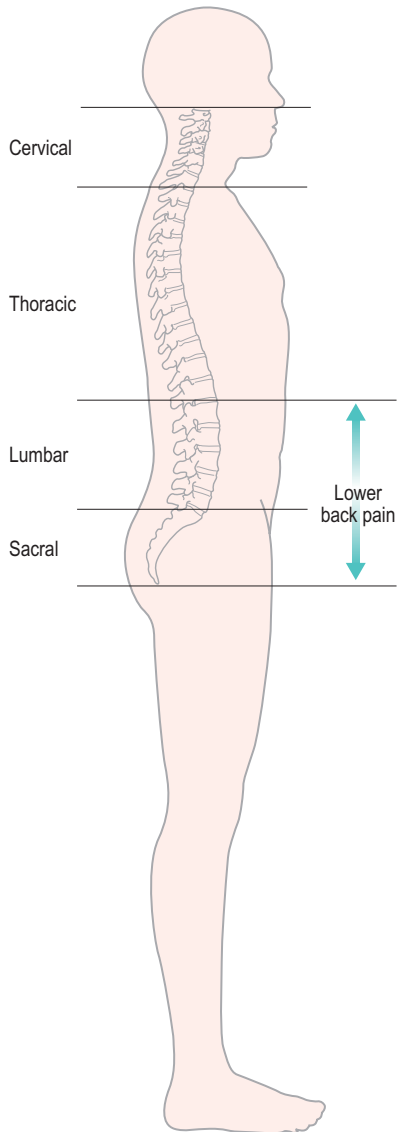


Fig. 9.2 Location and distribution of lower back pain – L4–L5, pain radiates down outer calf and onto the top of the foot; L5–S1, pain radiates to the outside and sole of the foot.

Bad posture when seated and poor lifting technique when performing daily tasks, such as cleaning or gardening, are very common predisposing factors.

Conditions to eliminate

Likely causes

Sciatica

Sciatica typically occurs in healthy, middle-aged adults. Pain is acute in onset and radiates to the leg. Pain starts in the lower

Table 9.1
Causes of back pain and their relative incidence in a community pharmacy

Incidence	Cause
Most likely	Simple back pain (usually associated with physical activity)
Likely	Sciatica, pregnancy
Unlikely	Osteoarthritis, osteoporosis
Very unlikely	Malignancy, osteomyelitis, ankylosing spondylitis

back and, as it intensifies, radiates into the lower extremities. Disc herniation usually involves those vertebrae between the L4 and L5 and L5–S1 (see Fig. 9.2), although most occur between L5 and S1. If disc herniation is minimal, pain is dull, deep, and aching. Pain spreads from the lumbar spine to the upper part of the leg. If the disc ruptures or herniates under strain, pain is usually lancinating in quality, shooting down the leg like an electric shock. Valsalva movements – for example, coughing, sneezing or straining at stool – often aggravate pain. Numbness, tingling, and muscle weakness in the distribution of a nerve root suggests nerve root compression. Referral is needed for confirmation of the diagnosis. Doctors can perform a straight leg raising test whereby the pain of sciatica can be induced by elevating the leg of the patient when lying down. Prognosis is good, although improvement and recovery are often slower than in simple low back pain alone.

Unlikely causes

Osteoarthritis

This is associated with advancing age, affecting up to one third of people older than 65 years, and is twice as common in women. It can be localized to a single joint or involve multiple joints; it most commonly affects the hands, knees, hips, neck, and low back. It is thought that an imbalance of synthesis and degradation of cartilage are responsible for the disease, which affects the whole joint. It is characterized by pain of insidious onset that progressively increases over months or years, is exacerbated by exertion, and is relieved by rest. The affected joints are painful when used and may show a restricted range of motion. Stiffness in the affected joint occurs typically in the morning and after rest, but usually only lasts for 15 to 30 minutes.

Osteoporosis

Often osteoporosis is asymptomatic and goes undiagnosed until a fragility fracture occurs, although nonspecific pain and/or localized tenderness is present if there is vertebral



Table 9.2
Specific questions to ask the patient: Back pain

Question	Relevance
Age	Age does influence the relative incidence of conditions seen in the population. <15 years: Although back pain is uncommonly reported in children, children do have a higher incidence of identifiable and potentially serious causes – for example, spondylolysis, malignancy, and Scheuermann disease (although pain is experienced in the upper back and neck, rather than the lower back). Also, studies have linked the weight of school bags and backpacks to back pain. It would seem prudent to refer all children unless backache is associated with recent participation in sport. 15–30: Prolapsed disc, trauma, fractures, pregnancy and ankylosing spondylitis most likely. 30–50: Degenerative joint disease (osteoarthritis), prolapsed disc, and malignancy most likely. >50 years: The incidence of serious underlying disorders increases, such as osteoporosis, malignancy, and metabolic bone disorders (Paget disease).
Location	Pain that radiates into the buttocks, thighs, and legs implies nerve root compression. If pain is felt below the knee, this is highly suggestive of sciatica.
Onset	Low back pain that is acute and sudden in onset is likely to be muscle strain in the lumbosacral region and not serious. However, acute low back pain in older adults should be referred, because even slight trauma can result in compression fractures. The patient will normally remember performing some recent exertion (e.g., playing sport, gardening) or say that the pain started when she or he bent forward. Low back pain that is insidious in onset should be viewed with caution.
Restriction of movement	People with disc herniation usually have difficulty in sitting down for long periods. Mechanical causes of pain are exacerbated with physical activity and relieved by rest. Systemic causes of backache are usually worse with rest and disturb sleep.
Weakness or numbness	Progressive muscle weakness must be referred for further evaluation.

fracture. The condition is most common in postmenopausal women.

Very unlikely causes

Infection (osteomyelitis)

Symptoms of osteomyelitis include bone pain, general malaise, and presence of a high-grade fever. There may be local swelling, redness, and warmth at the site of the infection. Patients also usually exhibit a loss of range of motion.

Ankylosing spondylitis

Spondylitis is characterized by thinning or loss of elasticity of the discs that cushion the vertebrae of the spine. Almost all cases occur before the age of 40, it is two to three times more common in men, and tends to run in families. Symptoms gradually worsen over a period of several months to several years. Patients commonly exhibit fatigue and have marked stiffness on awakening, with pain that can alternate

from side to side of the lumbar spine. Pain may awaken the person at night and worsens at rest, but improves with physical activity. Pain can be made worse by bending, lifting, and prolonged sitting in one position. Up to 40% of patients may also show inflammation of the eye.

Malignancy

Malignancy is very rare; it is more prevalent in patients older than 50 years, although rates are still low – 0.14% in patients younger than 50 and 0.56% in patients older than 50. Patients normally have symptoms for months before diagnosis due to the slow-growing nature of the tumour. A history of unexplained weight loss, presence of anaemia, and leg weakness might be seen in addition to low back pain.

Causes of low back pain not related to back pathophysiology

It must be remembered that acute illness – for example, colds and flu – can give rise to generalized aching or pain.

Likewise, prerash pain associated with shingles and referred pain from abdominal organs (e.g., pyelonephritis) can present as low back pain. A careful history of the presenting symptoms should enable exclusion of such conditions.

! TRIGGER POINTS indicative of referral

Symptoms/signs	Possible danger/ reason for referral	Urgency of referral
Numbness Fever Persistent and progressively worsening pain Weight loss Systemically unwell	Possible sinister spinal pathology	Immediate to general practitioner
Bowel or bladder incontinence	<u>Cauda equina</u> syndrome (rare and very unlikely to be seen by a pharmacist)	
Pain that radiates away from lower back area	Sciatica	As soon as practicable
Back pain from structures above the lumbar region	Outside scope of community pharmacist	
Failure of symptoms to improve after 4 weeks	Requires further investigation as pain that becomes subacute/chronic requires medical intervention	
Younger and older people (55 years old) with no identifiable cause	Suggests more sinister pathology	

Evidence base for over-the-counter medication

Pharmacists can appropriately treat patients with uncomplicated acute low back pain. The goal of treatment is to provide relief of symptoms and a return to normal mobility.

Conservative treatment

Bed rest was once widely prescribed for patients with low back pain. However, systematic reviews have now proven that prolonged bed rest is counterproductive (Dahm et al., 2010). The authors concluded that 'Moderate quality evidence shows that patients with acute LBP may experience small benefits in pain relief and functional improvement from advice to stay active compared with advice to rest in bed'.

Exercise programmes can help with acute back pain and have been shown to reduce recurrence.

Analgesics

Nonsteroidal anti-inflammatory drugs (NSAIDs) for 7 to 10 days is widely advocated. A systematic review of NSAIDs in acute or chronic LBP found that treatment with an NSAID produced significant short-term improvement compared with placebo (Roelofs et al., 2008). The review identified 65 trials, 28 of which were rated as high quality. The study failed to find any difference among the various NSAIDs. A further Cochrane review (involving 13 trials, of which 10 were rated high quality) looking at chronic LBP only found that NSAIDs were more effective than placebo in terms of pain intensity and, to a smaller extent, disability (Enthoven et al., 2016). Like Roelofs et al., the study failed to find any difference among the various NSAIDs.

Paracetamol when used for LBP has also been subject to a review (Saragiotto et al., 2016), which identified three trials involving 1825 patients. They found that paracetamol was no more effective than placebo in terms of pain reduction and improving quality of life. The authors concluded that paracetamol should not be used to manage acute LBP.

Compound analgesics

It is recognized that combination analgesics (paracetamol-codeine, aspirin-codeine, or paracetamol-dihydrocodeine) with high doses of opioids are effective for acute and chronic pain. However, in the UK, codeine and dihydrocodeine can only be prescribed over the counter (OTC) provided their respective maximum strengths do not exceed 1.5%, and the maximum dose does not exceed 20 or 10 mg, respectively. In practice, this equates to commercially available products with a maximum dose of 12.8 mg of codeine and 7.46 mg of dihydrocodeine. At these doses, their pain-killing effect has been called into question. In response to the ongoing concerns about codeine-containing products, the Medicines and Healthcare products Regulatory Agency (MHRA), in 2009, issued new guidance to restrict codeine-containing products for the short-term (3 days) treatment

of acute moderate pain that is not relieved by paracetamol, ibuprofen or aspirin alone.

Caffeine

It has long been claimed that caffeine enhances analgesic efficacy, and a number of proprietary products contain caffeine in doses up to 130 mg. A Cochrane review (Derry et al., 2014) identified 19 studies ($N = 7238$), which involved mainly paracetamol or ibuprofen, with 100 to 130 mg caffeine. Findings showed that there was a small but statistically significant benefit with caffeine used at doses of 100 mg or more, which was not dependent on the pain condition or type of analgesic. The authors concluded that the addition of caffeine (100 mg) to a standard dose of commonly used analgesics provides a small but important increase in the proportion of participants who experience a good level of pain relief. In light of this data, if recommending caffeine-containing products, only those with 100 mg or more of caffeine should be given.

Topical NSAIDs

A 2015 systematic review identified 61 studies comparing topical NSAIDs to oral NSAIDs and placebo (Derry et al., 2015). The review found that topical NSAIDs were significantly better than placebo in achieving 50% pain relief. It also found that the number needed to treat was less than 4 for all the NSAIDs examined compared with placebo and ranged from 1.8 (diclofenac [Emulgel]) to 3.9 (ibuprofen). The review authors stated there was insufficient data to reliably compare topical NSAIDs with each other, or with oral NSAIDs, but concluded that NSAIDs can provide good pain relief in acute musculoskeletal conditions without the adverse events seen with oral NSAIDs. Furthermore, certain formulations, mainly gel formulations of diclofenac, ibuprofen, and ketoprofen, provide the best results. This finding was reinforced when Derry et al. (2017) reviewed all Cochrane reviews investigating topical analgesics.

Rubefacients

Rubefacients (also known as *counterirritants*) have been incorporated into topical formulations for decades. They cause vasodilation, producing a sensation of warmth that distracts the patient from experiencing pain. It has also been hypothesized that increased blood flow might help disperse chemical mediators of pain, although this is unsubstantiated. Numerous chemicals are listed as being rubefacients.

Rubefacients containing salicylates have been reviewed (Derry et al., 2014). Any evidence of efficacy was reported from older smaller studies; the larger, more recent studies

have shown no effect. The authors concluded that current evidence does not support the use of salicylate-containing rubefacients.

Capsaicin

Capsaicin is approved for postherpetic neuralgia and painful diabetic neuropathy (Axsain, capsaicin, 0.075%) and symptomatic relief in osteoarthritis (Zacin, capsaicin, 0.025%) in the UK via prescription. Although these are not available OTC, a number of OTC products do contain capsaicin (e.g., Radian B Muscle Rub). Systematic reviews of the efficacy of capsaicin show mixed results (Mason et al., 2004; Zhang & Po, 1994). A review by Mason et al. (2004) concluded that capsaicin appears to have only poor to moderate efficacy in chronic musculoskeletal and neuropathic pain. They indicated that it may be a useful second-line agent for those who do not respond to or are intolerant of other treatments; however, capsaicin often causes local side effects (e.g., itching or rash).

Enzymes

Heparinoid and hyaluronidase are included in a number of products. Theoretically, they are supposed to disperse fluids in swollen areas, reducing swelling and bruising, but this is unproven.

Complementary therapies

Back pain accounts for more visits to a complementary practitioner than any other pain condition. In one study, 10% of people complaining of back pain had visited a complementary practitioner (e.g., osteopath, chiropractor, acupuncturist; Maniadas & Gray, 2000).

A limited but growing body of evidence exists to assess whether complementary therapies are effective. In light of the growing public interest and the expanding volume of literature, four Cochrane reviews have been conducted on heat and cold therapy (French et al., 2006), herbal remedies (Oltean et al., 2014), acupuncture (Furlan et al., 2005), and massage (Furlan et al., 2015), respectively.

Superficial heat and cold

Applying heat or cold to superficial musculoskeletal injuries, such as nonspecific back pain, is a popular lay recommendation. These range from hot water bottles, heat pads, and infrared lamps to ice packs. The Cochrane review identified nine trials that met their inclusion criteria (six trials involved heat; three trials involved cold therapy). The authors concluded that many of the studies were of poor methodological quality, but evidence exists that continuous heat wrap

therapy reduces pain and disability in the short term to a small extent. No conclusions could be drawn on cold therapy due to the limited nature of the three trials reviewed.

Herbal remedies

Several herbal medicines are promoted as treatments for various types of pain, some of which have been tested for the relief of symptoms of LBP. The Cochrane review reported on five active constituents – *Harpagophytum procumbens* (devil's claw), *Salix alba* (white willow bark), *Capsicum frutescens* (cayenne), *Solidago chilensis* (Brazilian arnica), and *Symphytum officinale* (comfrey root extract). Devil's claw (standardized daily dose of 50 or 100 mg harpagoside) reduced pain more than placebo, and a standardized daily dose of 60 mg was equally as effective as 12.5 mg of rofecoxib (now withdrawn from the market). Similarly, willow bark (standardized daily dose of 120 mg and 240 mg of salicin) was also more effective than placebo, and 240 mg of salicin was as effective as 12.5 mg of rofecoxib. Cayenne (as a cream or plaster) reduced pain more than placebo. One trial of arnica ($N = 20$) found very low-quality evidence of reduction in perception of pain and improved flexibility. Likewise, only one trial ($N = 120$) examined comfrey root extract but found low-quality evidence. The authors concluded that the best evidence was for the use of cayenne. It therefore appears that these products can be used as viable alternatives if conventional medicine has no effect.

Acupuncture

The available evidence for acupuncture in acute LBP does not support its use, although, if used in chronic back pain, acupuncture is more effective for pain relief than no treatment in the short term.

Massage therapy

Twenty-five randomized control trials (RCTs; $N = 3096$) were identified for the review, although all were considered to be of low quality (Furlan et al., 2015). Only one trial included participants with acute back pain; all others involved people with subacute or chronic back pain. Findings appear to show benefit compared to placebo in the short-term but not long-term. However, authors concluded they had 'little confidence' that massage is an effective treatment for LBP.

Glucosamine

Although glucosamine is not used for acute low back pain, it is widely advertised to the general public as a treatment for osteoarthritis. Glucosamine is naturally found in the body, especially in cartilage, tendons and ligaments, and must be synthesized by the body because significant amounts are not found in the diet. Its active form, D-glucosamine, is used

in the manufacture of glycosaminoglycan, a precursor to cartilage tissue. Early reviews of glucosamine reported favourable decreases in pain and increase in joint function. However, a review by Towheed et al. (2005), including 20 studies with 2570 patients with osteoarthritis, found mixed results. When studies of sound methodological quality were used, the review failed to find any difference between glucosamine and placebo with regards to pain and changes in the Western Ontario and McMaster Osteoarthritis Index (WOMAC) function score. It still remains uncertain whether the two salts of glucosamine available, sulphate and hydrochloride, are equally active. Studies so far have also been relatively short (2–3 months), and any long-term benefits are still uncertain.

Chondroitin

Early research into the benefit of chondroitin in reducing pain and improving functionality in people with osteoarthritis showed chondroitin to be beneficial. Recent research that involved larger trials has shown no significant benefit. Based on evidence, current UK guidelines advise avoidance of glucosamine and chondroitin (NICE, 2014).

Arnica (*Arnica montana*)

There are only limited studies with arnica, and these have shown mixed results, with it having little or no effect on bruising and swelling in soft tissue injuries. Although generally well tolerated, arnica has been reported to produce allergic reactions in some people (Natural Medicines Comprehensive Database, 2015).

Summary

Based on evidence, patients with acute LBP should be encouraged to keep active and be given a 7-day course of a systemic or topical NSAID unless contraindicated. If a complementary therapy is tried then cayenne has the best evidence.

Practical prescribing and product selection

Prescribing information relating to systemic analgesics is discussed and systemic proprietary products summarized in [Table 9.3](#); useful tips relating to systemic analgesics are given in 'Hints and Tips' in [Box 9.1](#).

Paracetamol

Paracetamol is the safest analgesic. It can be given to all patient groups, has no significant drug interactions, and side effects are very rare. Patients with LBP will benefit most from taking paracetamol regularly at its maximum dose of 4 g (eight tablets) per day. It is the drug of choice in pregnancy and breastfeeding.

Table 9.3
Systemic proprietary analgesics available OTC (excludes paediatric formulations and products for period pain)

Product	Aspirin (mg)	Paracetamol (mg)	Ibuprofen (mg)	Codeine (mg)	Other (mg)	Children
Alka-Seltzer Original	324					>16 years
Alka-Seltzer XS	267	133			Caffeine, 40	>16 years
Anadin Extra caplets; Sol Tabs	300	200			Caffeine, 45	>16 years
Anadin Ibuprofen; Anadin Joint Pain; Anadin Ultra			200			>12 years
Anadin Paracetamol		500				>6 years
Anadin Original	325				Caffeine, 15	>16 years
Care Ibuprofen Tablets			200			>12 years
Care Maximum Strength Tabs			400			>12 years
Codis 500	500			8		>16 years
Combogesic	500		150			>18 years
Cuprofen			400			>12 years
Disprin and Disprin Direct	300					>16 years
Feminax Express (ibuprofen lysine 342)			200			>12 years
Flarin 200 mg (ibuprofen)						
Mandanol		500				>6 years
Nurofen			200 & 400			>12 years
Nurofen Back Pain SR Caps			300			>12 years
Nurofen Plus			200	12.8		>12 years
Nuromol		500	200			>18 years
Panadol Advance		500				>10 years
Panadol Actifast		500				>12 years
Panadol Actifast Sol		500				>10 years
Panadol Extra Advance Tabs and Extra Sol Tabs		500			Caffeine 65	>12 years
Panadol Night Pain		500			Diphenhydramine 25	>16 years
Panadol Period Pain		500			Caffeine 65	>12 years
Paracodol Sol Tabs		500		8		>12 years
Paramol Tabs		500			Dihydrocodeine 7.46	>12 years
Solpadeine Plus Tablets; Capsules and Soluble Tablets		500		8	Caffeine 30	>12 years

Table 9.3
Systemic proprietary analgesics available OTC (excludes paediatric formulations and products for period pain)
(Continued)

Product	Aspirin (mg)	Paracetamol (mg)	Ibuprofen (mg)	Codeine (mg)	Other (mg)	Children
Solpadeine Max Tabs		500		12.8		>12 years
Solpadeine Max Soluble Tablets		500		12.8	Caffeine 30	>12 years
Solpadeine Headache Sol. Tabs.		500			Caffeine 65	>12 years
Syndol		450		10	caffeine 30; doxylamine 5	>12 years
Ultramol Soluble, Tablet		500		8	Caffeine 30	>12 years
Veganin Tablets		500		8	Caffeine 30	>12 years

^aAll deliver 200 or 400 mg of ibuprofen as base. Many products now formulated as lysine salt and marketed to show amount of salt which is higher than the base – for example, Nurofen Maximum Strength Migraine Pain 648 Caplets. Formulations include tablets, caplets, melt-tabs, and liquid capsules.

HINTS AND TIPS BOX 9.1: ANALGESIC ADVICE

Children and aspirin	Aspirin-taking in children has been linked to Reyes' syndrome, a rare syndrome in which encephalopathy occurs and, if not diagnosed early, can lead to death.
Caffeine-containing analgesics	These might have a mild stimulant effect and should therefore be avoided before going to bed.

Aspirin

Unlike paracetamol, aspirin is associated with problems in its use. Children younger than 16 years should avoid any products containing aspirin (although children with LBP should be referred). It can cause gastric irritation and is associated with gastric bleeds, especially in older adults. For this reason, aspirin should not be given to this patient group or any patient with a history of peptic ulcer. In a small minority of asthmatic patients, aspirin can precipitate shortness of breath, so any asthmatic who has previously had a hypersensitivity reaction to aspirin should not take it. It should be avoided in patients taking warfarin because bleeding time is increased. Aspirin is best avoided in pregnancy because adverse effects to the mother and foetus have been reported. It should also be avoided in breastfeeding.

Nonsteroidal antiinflammatory drugs

The choice of oral OTC NSAIDs in the UK is limited to ibuprofen (naproxen is currently only licensed for period pain).

The recommended dosage of ibuprofen in adults is 200 to 400 mg (one or two tablets), three times a day, although most patients will need the higher dose of 400 mg, three times a day.

NSAIDs are best avoided in certain patient groups, such as older adults, because they are more prone to gastrointestinal (GI) bleeds and have reduced renal function. Patients with a history of peptic ulcers and asthmatics who are hypersensitive to aspirin should also avoid NSAIDs. NSAIDs can be used in pregnancy but may delay labour; the use of NSAIDs, particularly in the last trimester, should be under medical supervision. They can be used in breastfeeding.

For most patients, NSAIDs are well tolerated, although gastric irritation is a well-recognized side effect. They can interact with many medicines and, although most of these interactions are not significant, NSAIDs can alter lithium levels so that where possible, an alternative analgesic should be recommended. If an NSAID is given with lithium, the patient's serum lithium level needs to be monitored more closely than normal.

Topical NSAIDs

Topical NSAIDs provide an alternative to patients who should avoid systemic NSAID therapy. They have fewer side effects than systemic therapy, with the most commonly reported adverse events being skin reactions (maculopapular rash or itching) at the site of application. GI side effects have been reported but are rare. Low plasma levels probably explain the low incidence of adverse systemic effects. Most manufacturers recommend avoiding use during pregnancy because of the same potential adverse effects as oral NSAIDs, although the risks should be generally far lower than with oral NSAIDs.

Topical NSAIDs come in a range of formulations, including cream, gel, spray, and mousse. Table 9.4 highlights all UK commercially available NSAIDs (as of October 2019) and summarizes their prescribing information.

Rubefacients

Most rubefacients (e.g., Deep Heat, Radian B ranges) are only licensed for people older than 12 years, although there are a few that can be used from the age of 5 (e.g., Deep Heat range) or 6 years (e.g., Radian B Muscle Rub). They have no drug interactions, and side effects are localized to excessive irritation at the site of application. Most products contain two or more compounds, although most contain nicotines and/or salicylates. Other compounds in rubefacients include menthol, camphor, capsaicin, and turpentine oil. They can be used in all patient groups.

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Table 9.4
Proprietary topical nonsteroidal antiinflammatory drug (NSAID) analgesics available over the counter (OTC)

Product	Formulation	Strength	Dosage	Children
<i>Ibuprofen</i>				
Care	Gel	5% and 10%	qd	> 14 years
Deep Relief	Gel	5%	td	> 12 years
Fenbid	Gel	5%	Up to qd	> 12 years
Fenbid Forte	Gel	10%	Up to qd	> 12 years
Ibugel	Gel	5%	td	> 12 years
Ibuleve	Gel	5%	td	> 12 years
Ibuleve Maximum Strength	Gel	10%	td	> 12 years
Ibumousse	Mousse	5%	td–qd	> 12 years
Ibuleve Speed Relief	Gel	5% and 10%	td	> 12 years
Ibuleve Speed Relief	Spray	5%	Up to qd	> 12 years
Ibuspray	Spray	5%	td–qd	> 12 years
Mentholatum	Gel	5%	td	> 14 years
Nurofen Joint and Back pain relief ^a	Gel	5% and 10%	qd	> 12 years
Phorpain	Gel	5%	qd	> 12 years
Phorpain maximum strength	Gel	10%	qd	> 12 years
Radian B Ibuprofen	Gel	5%	qd	> 14 years
<i>Other NSAIDs</i>				
Diffiam (benzydamine)	Cream	3%	td but max of six times	No lower age limit stated
Movelat (mucopolysaccharide polysulphate + salicylic acid)	Cream and gel	0.2% and 2.0%	qd	> 12 years
Traxam Pain Relief (Felbinac)	Gel	3%	bd–qd	> 12 years
Voltarol Osteoarthritis Joint Pain Relief; Voltarol Back and Muscle Pain Relief; (Diclofenac)	Gel	1.16%	td–qd	> 14 years
Voltarol Joint pain relief; 12 hr joint pain relief	Gel	2.32%	bd	> 14 years

^aNurofen medicated plaster are available that also contains ibuprofen (>16 years, one patch every 24 hours).

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Activity- and sports-related soft tissue injuries

This section will discuss common conditions affecting the shoulder, elbow, knee, ankle, and foot.

Background

Muscles, tendons, ligaments, fascia, and synovial capsules are all soft tissue structures. Damage to any of these structures will result in pain and/or inflammation. Most patients will present to a doctor physiotherapist, or casualty department rather than the pharmacy.

Prevalence and epidemiology

Most injuries are a direct result of physical activity or accident. Prevalence is therefore higher in people who actively participate in sports, and injuries involving the lateral ligaments of the ankle account for 25% of all sports injuries.

Aetiology

The aetiology of soft tissue injury depends on the structures affected. Sprains are due to forcing a joint into an abnormal position that overstretches or twists ligaments and can vary from damage of a few fibres to complete rupture. Strains involve tearing of muscle fibres, which can be partial or complete, and are usually a result of overexertion when the muscle is stretched beyond its usual limits.

Arriving at a differential diagnosis

Patients will often state that they have sprained or strained something. It is important to confirm their self-diagnosis because these terms are often used wrongly and interchangeably. Although sprains and strains can be graded according to the severity of the injury, it is of little practical value because it has no therapeutic consequence; therefore, the major role of the pharmacist is to determine whether the patient can manage the injury or whether referral is needed. This will be primarily based on questions asked (Table 9.5) that can be supported with the aid of a basic physical examination.



Table 9.5
Specific questions to ask the patient: Soft tissue injuries

Question	Relevance
When did it happen, and when did the patient present	The closer these two events are, the more likely the patient will be suffering from a problem that is outside the remit of the pharmacist (unless the injury was sustained in close proximity to the pharmacy and the patient has asked for first aid).
Presenting symptoms	Marked swelling, bruising, and pain occurring right after injury are suggestive of more serious injury, and referral to casualty for x-rays and further tests is needed.
Nature of injury	If the injury occurred in which impact forces were great, then fracture becomes more likely. Sudden onset associated with a single traumatic event suggests a mechanical problem such as tendon or ligament tearing. If the person has a foot injury and is unable to bear full weight while walking, then referral is needed.
Range of motion	If the affected joint shows marked reduction in normal range of motion, this requires referral for fuller evaluation.
Nature of pain	Referred pain suggests nerve root compression – for example, a shoulder injury in which pain is also felt in the hand. Pain that is insidious in onset and progressive is more likely to be due to some form of degenerative disease and requires referral.
Age of patient	<i>Children:</i> Bones are softer in children and therefore more prone to greenstick fractures (fracture of the outer part of the bone) and should be referred to exclude such problems. <i>Older adults:</i> Risk factors for fracture, such as osteoarthritis and osteoporosis, should be established.

Clinical features of soft tissue injury

In general, patients will present with pain, swelling, and bruising. The extent and nature of symptoms will be determined by the severity of the injury.

Shoulder-specific conditions

The shoulder provides the greatest range of motion of any joint. It is a very mobile and complex interconnected structure (Fig. 9.3); consequently, there are a number of commonly encountered shoulder injuries, such as frozen shoulder, impingement syndromes, and rotator cuff syndrome. The prevalence of shoulder-related problems is uncertain, although estimates range from 4% to 20%, with rotator cuff syndrome accounting for up to 70% of shoulder problems.

Within the confines of the community pharmacy, the patient can be asked to perform certain arm movements that will allow the range of motion of the shoulder to be determined (Fig. 9.4). Patients who show marked loss of motion should be referred.

Rotator cuff syndrome

The rotator cuff refers to the combined tendons of the scapula muscles that hold the head of the humerus in place. Rubbing of these tendons causes pain. It is most often seen in patients older than 40 and is associated with decreased range of motion. Pain is worsened with repetitive overhead activity,

and can also worsen at night leading to sleep disturbances. Reaching behind the back also tends to worsen pain, and the patient cannot normally initiate abduction.

Frozen shoulder

Pain is gradual in onset causing aching in the upper arm that can become severe, radiate down the arm to the elbow, and disturb sleep. Over time (usually months), marked stiffness and restriction in all the major ranges of motion is observed. This can make daily activities difficult, such as putting on clothes, although pain tends to be less prominent than on initial presentation. It is a relatively uncommon cause of shoulder pain, accounting for 2% to 5% of cases. It often occurs without warning or explanation and can vary in severity from day to day. NSAIDs could be offered but if symptoms fail to respond with treatment after 5 days, referral for alternative treatment and physiotherapy should be considered.

Elbow-specific conditions

Community pharmacists are only likely to see three elbow problems – tennis elbow (lateral epicondylitis), golfer's elbow (medial epicondylitis), and student's elbow (bursitis). Epicondylitis of the elbow is a condition associated with repetitive forearm and elbow activities. Tennis elbow is characterized by pain and tenderness felt over the outer aspect of the elbow joint that might also spread up the upper arm. The patient should have a history of gradually increasing pain and tenderness. If the patient tries to extend the wrist against resistance, pain increases. In comparison, the pain of golfer's elbow is noticed on the inner side of the elbow and can radiate down the forearm.

Knee-specific conditions

The knee is the largest joint in the body and is subject to extreme forces. To help maintain stability, the knee has three main pairs of ligaments – the medial collateral ligament, which connects the femur to the tibia; the lateral collateral ligament, which connects the femur to the fibula; and the anterior cruciate ligament, which prevents the tibia from sliding forward on the femur (Fig. 9.5). Traumatic knee injuries are common in young patients and, unsurprisingly, it is one of the most common sites of sport injuries, especially among footballers.

Ligament damage

If the injury occurred when twisting, this implies damage to the medial meniscus (incomplete rings of cartilage that promote joint stability) because the medial collateral ligament is attached to the meniscus and forces applied to the ligament result in tears of the meniscus. This is less serious than damage to the anterior cruciate ligament, which usually occurs

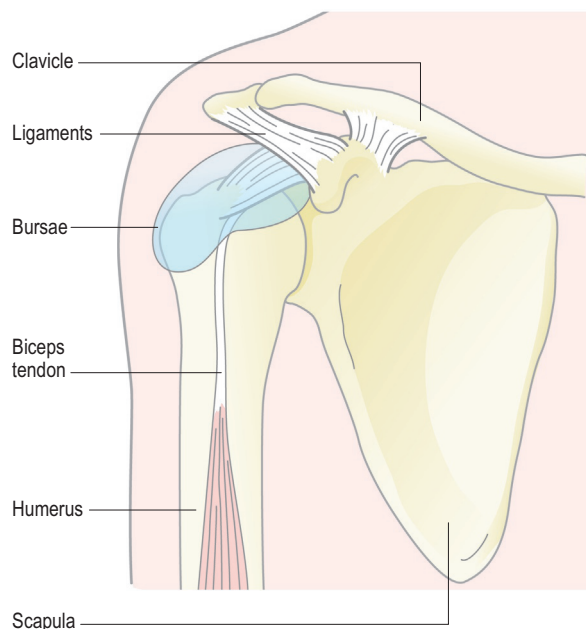


Fig. 9.3 Basic shoulder anatomy.

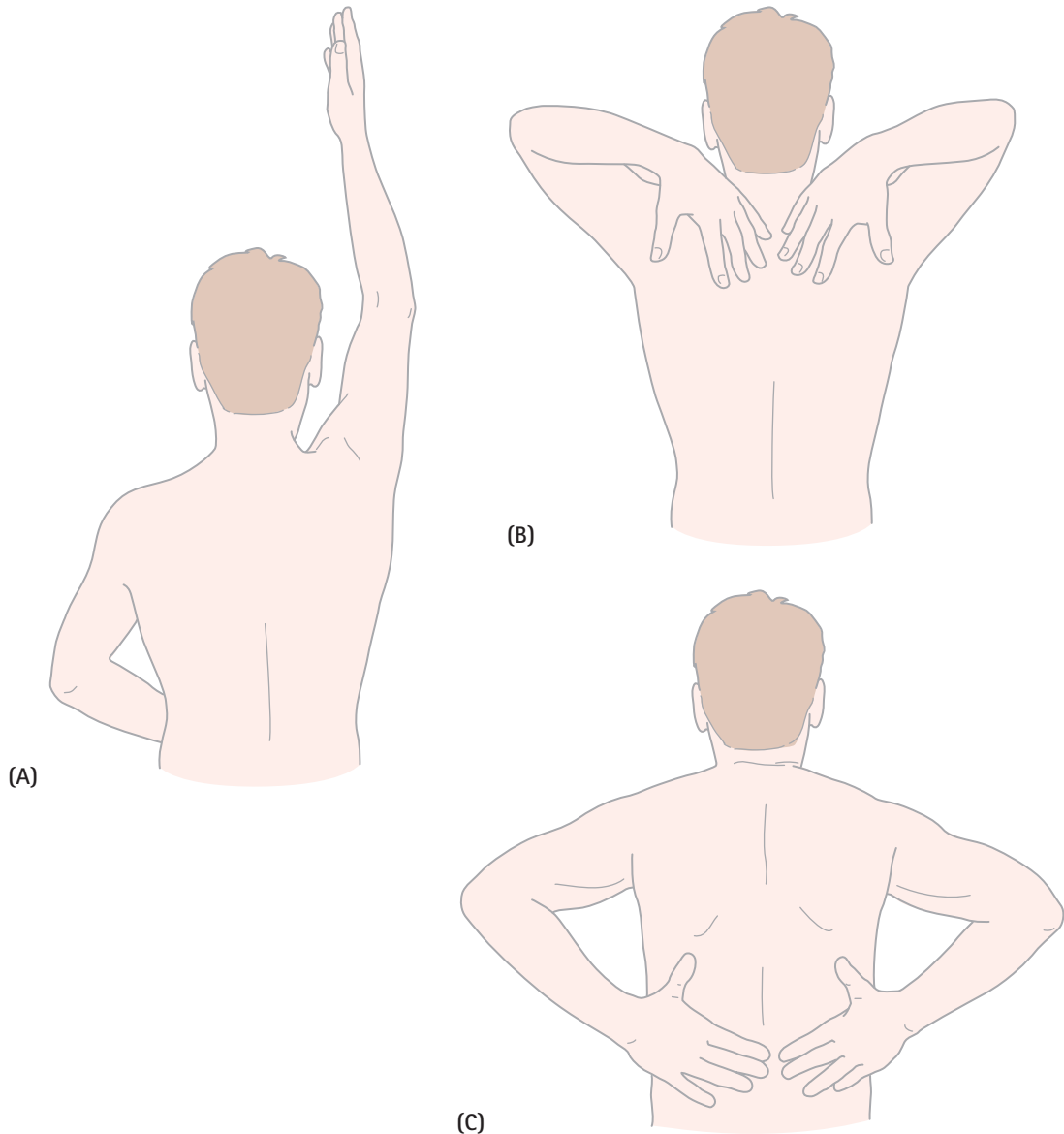


Fig. 9.4 Determining the shoulder's range of motion: (A) ask the patient to raise the arm, as if going to ask a question at school; (B) ask the patient to touch the back of the neck with both hands; (C) ask the patient to touch the back of the scapulae with both hands.

when the person receives a blow to the back of the knee. The former can usually respond to NSAIDs and physiotherapy, whereas the latter can take months to heal and might stop people from playing competitive sport.

Runner's knee (chondromalacia)

This is most commonly noted in recreational joggers who are increasing their mileage, for example, training to run a marathon. It develops insidiously with pain being the predominant symptom. Pain is experienced usually at the front of

the knee or behind the kneecap. Pain can be aggravated by prolonged periods of sitting down in the same position or going up and down stairs. Treatment depends on the severity of pain, from NSAIDs if the pain is mild, to total rest and stopping running if severe.

Ankle- and foot-specific conditions

The majority involve sprained ankles whether through sporting activity or just as a result of accidents.

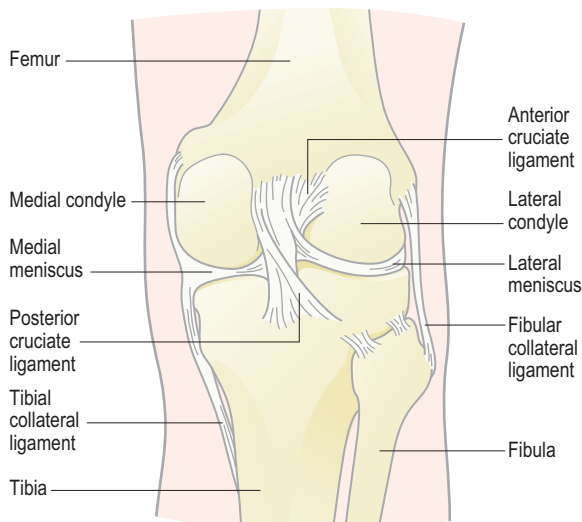


Fig. 9.5 Basic knee anatomy.

Ankle sprains

The ankle acts as a hinge joint permitting up and down motion. Three sets of ligaments provide stability to the joint: the deltoid, lateral collateral and syndesmosis. The majority of ankle sprains involve the lateral ligamentous structures due to inversion of the joint leading to injury (Fig. 9.6). Patients usually describe an accident when they 'went over their ankle'. Most patients will walk with a limp because the ankle cannot support their full weight.

Achilles tendon injuries

Injuries to the structures associated with the Achilles tendon are usually seen in runners or athletes involved in jumping sports. Pain is felt behind the heel, just above the calcaneus, and progressively worsens the longer the injury lasts. It often occurs when runners increase their mileage or run over hilly terrain. Depending on the severity of the injury, treatment could be anything from NSAIDs, complete rest or having a cast fitted. If the injury is recent in onset and pain not too severe, the pharmacist could suggest NSAID therapy and rest. If this fails, then the person should be referred.

Plantar fasciitis

The plantar fascia extends from the calcaneus to the middle phalanges of the toes. Runners are most prone to plantar fasciitis, although it can affect older people. Patients will present with tenderness and pain felt along the plantar surface of the foot and heel. Pain is insidious and progressively worsens, which can limit activity.

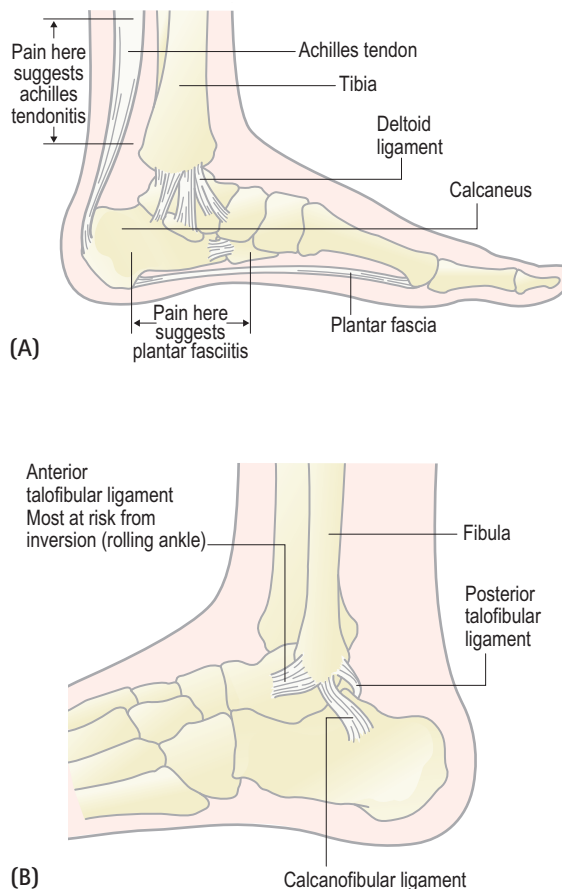


Fig. 9.6 Basic anatomy of the ankle: (A) medial view; (B) lateral view.

Common muscle strains

Thigh strains

Tears of the quadriceps (front of the thigh) and hamstring (back of the thigh) are very common. Patients will not always be able to recall a specific event that has caused the strain. Pain and discomfort are worsened when the patient tries to use the muscle, but daily activities can usually be performed. Rest, ice, compression and elevation (RICE) followed by NSAID treatment will usually resolve the problem; however, referral is needed if daily activities are compromised.

Delayed onset muscle soreness

This is a common problem and follows unaccustomed strenuous activity. For example, the patient might describe playing football for the first time in a long while or having just started going to aerobic classes. Pain is felt in the muscles, which feel stiff and tight. Pain is experienced within 24 to

48 hours and will resolve within 5 to 7 days. Palpation of the muscle is painful.

Patients should be encouraged to properly stretch before exercising to minimize the problem. No treatment is necessary.

Conditions to eliminate

Shin splint syndrome

Recreational runners and people unaccustomed to regular running can experience pain along the front of the lower third of the tibia. Pressing gently on this area will cause considerable pain. It is caused by over stretching the tibial muscle and is usually precipitated by running on hard surfaces. Pain is made worse by continued running or climbing stairs. Treatment involves running less frequently or for shorter distances and NSAID therapy for approximately 1 week.

Bursitis

Bursae can become inflamed, which leads to accumulation of synovial fluid in the joint. Housemaid's knee and student's elbow are such examples. Clinically, joint swelling is the key feature, with associated pain and local tenderness over the bursa.

Stress fractures

These are most commonly associated with the foot. Patients experience a dull ache along the affected metatarsal shaft that changes to a sharp ache behind the metatarsal head. It is often seen in those patients that have a history of increased activity or a change in footwear.

Gout

Acute attacks of gout are exquisitely painful, with patients reporting that even bedclothes cannot be tolerated. Approximately 80% of cases affect the big toe. Gout is more prevalent in men, especially those older than 50.

Carpal tunnel syndrome

At the base of the palm is a 'tunnel' through which the median nerve passes; this narrow passage between the forearm and hand is called the carpal tunnel. If the median nerve becomes trapped, it can cause numbness and tingling in the hand. Often, the patient will awaken in the night with numbness and tingling pain that radiates to the forearm, which sometimes extends to the shoulder.

Repetitive strain injury

This condition, also termed *chronic upper limb pain syndrome*, often results after prolonged periods of steady hand

movement and involves repeated grasping, turning and twisting. Pain is experienced in all or one part of the arm. Usually, the person's job will involve repetitive tasks such as keyboard operations.



TRIGGER POINTS indicative of referral: Soft tissue injury

Symptoms/signs	Possible danger/ reason for referral	Urgency of referral
Acute injuries that show immediate swelling and severe pain	Suggests fracture or complete ligament tear	Consider direct referral to emergency department
Marked decrease or excessive range of movement in any joint	May suggest major ligament disruption or complete tear	
Patients unable to bear any weight on an injured ankle or foot		
Children <12 years and older adult patients	Fractures more likely	

Evidence base for over-the-counter medication and practical prescribing and product selection

Prescribing information relating to medication for soft tissue injuries is the same as for acute low back pain (see earlier discussion). However, nondrug treatment plays a vital and major role in the treatment of acute soft tissue injuries. Standard advice follows the acronym RICE:

Rest	Rest allows immobilization, enhancing healing and reducing blood flow.
Ice	Ice should be applied while the injury feels warm to the touch. Apply until the skin becomes numb, and repeat at hourly intervals. Bags of frozen peas wrapped in a towel are ideal to use on the injury because they conform to body shape and provide even distribution of cold.

- Compression** A crepe bandage provides a minimum level of compression. Tubular stockings (e.g., Tubigrip) are convenient and easy to apply, but fail to give adequate compression.
- Elevation** Ideally the injured part should be elevated above the heart to help fluid drain away from the injury.

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Website

Society of Sports Therapists: <https://society-of-sports-therapists.org/>

Self-assessment questions

The following questions are intended to supplement the text. Two levels of questions are provided, multiple-choice questions and case studies. The multiple-choice questions are designed to test knowledge and application of knowledge, and the case studies allow this knowledge to be put in context in patient scenarios.

Multiple-choice questions

- 9.1** Which of the following symptoms is commonly associated with sciatica?
- Pain that radiates to the thoracic vertebrae
 - Pain that radiates to the quadriceps
 - Pain that radiates down the hamstring
 - Pain that radiates to the groin
 - Pain that radiates to sacroiliac junction
- 9.2** A strain is defined as:
- An injury to a ligament
 - An injury to the muscle
 - An injury to a tendon
 - An injury that affects both the muscle and the ligament
 - An injury that affects both the ligament and tendon
- 9.3** A fit young man (early 20s) played football for the first time in over a year, 2 days ago. He telephones the pharmacy for advice – he cannot walk properly because he has stiff legs. Which condition is he most likely to be experiencing after his football activities?
- Shin splint syndrome
 - Thigh strain
 - Hamstring strain
 - Delayed onset muscle soreness
 - Chondromalacia
- 9.4** Which anatomical structure attaches bone to muscle?
- Ligament
 - Tendon
 - Bursae
 - Cartilage
 - Fibrous tissue
- 9.5** Mr Smith, a 47-year-old hypertensive and asthmatic patient, asks for a painkiller because he has 'turned his ankle' while playing golf. Which treatment is most suitable?
- Aspirin
 - Ibuprofen
 - Heat rub
 - Paracetamol
 - Arnica
- 9.6** Which one of the following muscles extend the elbow:
- Biceps
 - Triceps
 - Pronator teres
 - Brachioradialis
 - Extensor carpi radialis longus
- 9.7** Mrs Williams comes in to the pharmacy wanting to get some paracetamol for her 10-year-old daughter, Aimee, and also asks for a heat pad to ease the pain in her ankle because she has just fallen over and twisted it while at school. Which one of the following is the most appropriate advice?
- Aimee should avoid heat but elevate her foot and use a cold compress.
 - Advise that a heat spray rather than a rub would be better because it has a quicker onset of action.
 - Don't do anything, and go to the doctor straight away.
 - Use heat and paracetamol but also elevate the foot.
 - Don't do anything, and visit the local emergency department because children are more likely to have a fracture.
- 9.8** A sprain is defined as:
- An injury to a ligament
 - An injury to the muscle
 - An injury to a tendon
 - An injury that affects both the muscle and the ligament
 - An injury that affects both the ligament and tendon
- 9.9** Which ligament is most often damaged in a sprained ankle?
- Cruciate ligament
 - Deltoid ligament
 - Medial collateral ligament
 - Posterior talofibular ligament
 - Anterior talofibular ligament

9.10 In which of the following conditions is pain most likely to disturb sleep?

- a. Rotator cuff syndrome
- b. Frozen shoulder
- c. Lateral epicondylitis (tennis elbow)
- d. Medial epicondylitis (golfer's elbow)
- e. Housemaid's knee

Questions 9.11 to 9.18 concern the following conditions

- A. Lateral epicondylitis
- B. Medial epicondylitis
- C. Rotator cuff syndrome
- D. Bursitis
- E. Plantar fasciitis
- F. Chondromalacia
- G. Stress fracture
- H. Sciatica

Select, from A to H, which symptom is most associated with:

9.11 Radiating pain

9.12 Increased pain when sedentary

9.13 Decreased range of motion

9.14 Joint swelling

9.15 Pain over the outer elbow

9.16 Repetitive overhead activity

9.17 Insidious pain aggravated by rest

9.18 Acute injury

Questions 9.19 to 9.25 concern the following medicines:

- A. Paracetamol
- B. Aspirin
- C. Naproxen
- D. Ibuprofen
- E. Diclofenac
- F. Caffeine
- G. Codeine
- H. White willow bark

Select, from A to H, which of the above medicines:

9.19 Is only available topically?

9.20 Is safest for pregnant women?

9.21 Has a stimulant effect?

9.22 Analgesic effect is not fully proven?

9.23 Is restricted to a maximum 3 days duration?

9.24 Is licensed for pain relief but not for low back pain?

9.25 Has no reported pain killing action?

Answers

9.1 Answer: c

Rationale: Sciatica is associated with referred pain that moves away to the lower extremities from the lumbar and sacral vertebrae. This means options a, d and e are incorrect; b or c could be correct because the pain is described as moving down the leg. Typically, this extends to the foot, and on that basis, c is the correct answer.

9.2 Answer: b

Rationale: Strains relate to muscles; therefore, options a, c and e can be eliminated. This leaves b and d as viable options. However, strains involve tearing of muscle fibres only so b is the correct answer.

9.3 Answer: d

Rationale: People who take part in unaccustomed physical activity can experience acute pain. Shin splint syndrome (a) and chondromalacia (e) are more long-term problems and can be ruled out. Strains (b and c) and delayed muscle soreness could be the cause of the person's symptoms. However, if the cause was a strain, the pain would normally be experienced shortly after activity and not after a couple of days.

9.4 Answer: b

Rationale: Fibrous tissue (e) is obviously incorrect. Ligaments (a) bind bones together; bursae (c) act as cushions in joints; cartilage (d) is a tissue that helps with structural support.

9.5 Answer: d

Rationale: Ideally, using aspirin (a) and ibuprofen (b) should be avoided due to him being asthmatic. Heat rubs (c) will not help reduce pain, and arnica (e) has very little evidence of a pain-relieving effect.

9.6 Answer: b

Rationale: The triceps is the only extensor of the elbow joint. The biceps (a) and brachioradialis (d) flex the elbow. The pronator teres (c) pronates the forearm, and the extensor carpi (e) extends and abducts the wrist.

9.7 Answer: a

Rationale: RICE is the standard treatment for acute injuries; heat is therefore not appropriate and rules out options b and d. The injury appears to be manageable through self-care and thus options c and e are also incorrect.

9.8 Answer: a

Rationale: Sprains relate to ligament damage only.

9.9 Answer: e

Rationale: Option (a) and (c) are not ligaments of the ankle; the deltoid ligament is an ankle ligament but is much stronger than options (d) and (e). With ankle strains it is the ligament which is anterior which is more commonly affected because it absorbs most of the negative impact when the ankle twists in an unnatural way.

9.10 Answer: b

Rationale: Pain is observed in all conditions and a to d are associated with repetitive actions. Epicondylitis (c and d) are not associated with night pain, and neither is housemaid's knee (e). Rotator cuff and frozen shoulder can wake the patient but it is frozen shoulder (b) that is the more likely of the two to cause this problem.

9.11 Answer: H

Rationale: Of the options listed below lateral (A) and medial (B) epicondylitis and sciatica (H) are associated with radiating pain, although it is a more prominent symptom in sciatica than epicondylitis.

9.12 Answer: F

Rationale: See answer 9.17.

9.13 Answer: C

Rationale: All conditions will cause pain and discomfort that can limit movement to some degree, but very characteristic of rotator cuff syndrome is the person's inability to move the arm over the head and behind the back.

9.14 Answer: D

Rationale: Joint swelling usually is caused by increased fluid in synovial spaces or direct inflammation of local structures. Swelling in joints therefore is often due to bursae inflammation.

9.15 Answer: A

Rationale: Only the two types of epicondylitis need to be considered. In medial epicondylitis, pain is seen on the inner aspect compared to the outer aspect in lateral epicondylitis.

9.16 Answer: C

Rationale: Epicondylitis is linked with repetitive activities but not usually overhead activities. Discounting these options only leaves rotator cuff syndrome that is seen with repetitive activities.

9.17 Answer: F

Rationale: Insidious pain is a characteristic of plantar fasciitis (E) and chondromalacia (F); however, this can be worsened in chondromalacia with rest.

9.18 Answer: G

Rationale: Most options are a result of repeated activity, and only in fracture would symptoms be sudden and acute in onset, although bursitis can develop quickly on occasion.

9.19 Answer: E

Rationale: Diclofenac was available as an OTC oral product until withdrawn due to concerns over rare cardiac side effects and so is now only available topically under the brand of Voltarol.

9.20 Answer: A

Rationale: Paracetamol has the best safety record of all analgesics.

9.21 Answer: F

Rationale: Options A to E, and G all relate to compounds that have proven analgesic efficacy. White willow bark (H) has some (low-quality) evidence of pain relief. Only caffeine has no analgesic effect but does have stimulant effects.

9.22 Answer: H

Rationale: See answer to 9.21.

9.23 Answer: G

Rationale: Recent MHRA announcements have restricted the sale of codeine.

9.24 Answer: C

Rationale: Naproxen has a specific OTC licence for primary dysmenorrhoea.

9.25 Answer: F

Rationale: See answer to 9.21.

Self-assessment questions

The following questions are intended to supplement the text. Two levels of questions are provided: multiple choice questions and case studies. The multiple choice questions are designed to test knowledge and application of knowledge, and the case studies allow this knowledge to be put in context in patient scenarios.

Multiple choice questions

9.1 Which of the following is not used in topical formulations for musculoskeletal disorders?

- a. Capsaicin
- b. Choline
- c. Hyaluronidase
- d. Nicotines
- e. Nonsteroidal antiinflammatories

9.2 Which of the following statements is true of osteoarthritis?

- a. Inflammation is a key pathological finding
- b. Morning stiffness usually lasts less than 30 minutes
- c. Osteoarthritis commonly affects small joints
- d. Pain is eased by movement
- e. Pain is usually worst in the morning

9.3 Which patient group is most suitable to take ibuprofen in treating an ankle sprain?

- a. Asthmatics
- b. Children under 16
- c. Elderly
- d. Patients with heart failure
- e. Patients with a peptic ulcer

9.4 Vertebrae most associated sciatica are:

- a. L1–L2
- b. L2–L3
- c. L3–L4
- d. L4–L5
- e. T12–L1

9.5 A strain is said to affect which structure?

- a. Bursa
- b. Cartilage
- c. Ligament
- d. Muscle
- e. Tendon

9.6 From the following list, what common name is given to inflammation of the bursa?

- a. Golfer's elbow
- b. Repetitive strain injury
- c. Shin splints
- d. Student's elbow
- e. Tennis elbow

Questions 9.7 to 9.9 concern the following groups of people:

- A. Footballers
- B. Occasional gardeners
- C. Runners/Joggers
- D. Squash players
- E. Swimmers

Select, from A to E, which of the above groups of people are more prone to:

- 9.7** Anterior cruciate ligament damage
- 9.8** Plantar fasciitis
- 9.9** Tennis elbow

Questions 9.10 to 9.12 concern the following OTC medications:

- A. Codis tablets
- B. Ibugel
- C. Panadol Advance tablets
- D. Radian B muscle rub
- E. Voltarol Emulgel

Select, from A to E, which of the above medicines:

- 9.10** Can only be given to children older than 16?
- 9.11** Has no evidence of efficacy?

9.12 May cause constipation?

Questions 9.13 to 9.17: for each of these questions *one or more* of the responses is (are) correct. Decide which of the responses is (are) correct. Then choose:

- A. If a, b and c are correct
- B. If a and b only are correct
- C. If b and c only are correct
- D. If a only is correct
- E. If c only is correct

Directions summarized

A	B	C	D	E
a, b and c	a and b only	b and c only	a only	c only

9.13 Which of the following measures should be recommended to a patient who has just suffered an acute soft tissue injury?

- a. Heat and massage of the affected area
- b. Elevation of the affected area
- c. Compression of the affected area by means of an elastic bandage or support

9.14 Acute low back pain is characterized by:

- a. Insidious onset and progressively worsening pain
- b. Radiating pain toward the thoracic vertebrae
- c. Decreased mobility

9.15 Children under 12 with a soft tissue injury should be referred to the GP because:

- a. 'RICE' is only suitable for adults
- b. OTC medication is contraindicated
- c. More prone to greenstick fractures than adults

9.16 In which scenario should the patient be referred when presenting with low back pain?

- a. Radiating pain
- b. Numbness
- c. General malaise

9.17 Carpal tunnel syndrome causes:

- a. Pain that radiates into the hand

- b. Tingling sensation in the hand
- c. Numbness in the hand

Questions 9.18 to 9.20: these questions consist of a statement in the left-hand column followed by a statement in the right-hand column. You need to:

- Decide whether the first statement is true or false
- Decide whether the second statement is true or false

Then choose:

- A. If both statements are true and the second statement is a correct explanation of the first statement
- B. If both statements are true but the second statement is NOT a correct explanation of the first statement
- C. If the first statement is true but the second statement is false
- D. If the first statement is false but the second statement is true
- E. If both statements are false

Directions summarized

	1st statement	2nd statement	
A	True	True	2nd explanation is a correct explanation of the 1st
B	True	True	2nd statement is not a correct explanation of the 1st
C	True	False	
D	False	True	
E	False	False	
	<i>First statement</i>	<i>Second statement</i>	
9.18	Carpal tunnel syndrome causes hand numbness	Medial nerve impingement results in symptoms	
9.19	Low back pain with associated fever should be referred	Malignancy is the likely cause	
9.20	NSAIDs are the mainstay of systemic treatment for soft tissue injuries	They should be used for 7–10 days. If symptoms do not improve referral is needed	

Answers

9.1 Answer: b

Rationale: Topical formulations marketed for the treatment of soft tissue injuries contain a variety of ingredients; the majority of which have little or no evidence to support their effectiveness. However, choline is used to treat pain in other conditions, such as oral pain.

9.2 Answer: b

Rationale: Larger joints are often affected and osteoarthritis results from the breakdown of supporting connective tissues. Stiffness is associated with lack of movement; e.g. rest, but eases on movement.

9.3 Answer: b

Rationale: NSAIDs have the ability to cause bleeds; therefore they should be avoided in patients with peptic ulcer (e), also the elderly are more prone to bleeds caused by NSAIDs (c); they can also precipitate asthma (a) and heart failure (d) in susceptible patients.

9.4 Answer: d

Rationale: Sciatica causes pain in the buttocks and legs due to nerve entrapment of the lumbar vertebrae. Most implicated are the L4–L5 vertebrae.

9.5 Answer: d

Rationale: Damage to any of these structures will cause pain and inflammation; strains are associated with muscle damage.

9.6 Answer: d

Rationale: Repetitive strain injury (b) and shin splints (c) involve muscle and ligamental structures; of the 'elbow' conditions listed, golfer's (a) and tennis elbow (e) involve the epicondyle.

9.7 Answer: A

Rationale: The ACL is located behind the knee and is only damaged through blunt trauma. From the list, this is most likely when playing contact sports such as football.

9.8 Answer: C

Rationale: The plantar fascia is a large ligament that runs from the heel to the front of the foot. If this becomes aggravated then pain is felt in this region. It is therefore

most seen when this ligament is 'overworked'; this is therefore common in runners.

9.9 Answer: D

Rationale: As stated above inflammation of the epicondyle can cause golfer's and tennis elbow and is associated with repeated movement; therefore it is seen commonly in racket sports.

9.10 Answer: A

Rationale: Ibugel can be given from the age of 12; Panadol Advance from 10 yrs; Radian B (D) from 6 yrs; and Voltarol from 14 years.

9.11 Answer: D

Rationale: Most products marketed for pain relief available OTC have good evidence of efficacy. Codis' (combination of paracetamol/codeine) pain-relieving properties can be called in to question with regard to its codeine content, but the paracetamol component does obviously help with pain relief. Radian B contains multiple ingredients that have a rubefacient effect but have no proven pain-killing effect.

9.12 Answer: A

Rationale: The only product with an ingredient that is known to be constipating is codeine, which is found in Codis.

9.13 Answer: C

Rationale: Rest, Ice, Compression and Elevation (RICE) is recommended for acute soft tissue injuries. Therefore options B and C are appropriate; thus the answer is C.

9.14 Answer: E

Rationale: Low back pain is acute in onset and pain is prominent from the outset. If the pain radiates it tends to radiate downward toward the buttocks or legs.

9.15 Answer: E

Rationale: RICE is a standard treatment for all ages and simple analgesia or NSAIDs are given.

9.16 Answer: A

Rationale: Radiating pain suggests some level of nerve entrapment, as does numbness. These symptoms require

further investigation, and referral is the best course of action. General malaise could be a sign of infection if an association with the back pain is suspected, and again should be referred.

9.17 Answer: E

Rationale: Numbness rather than tingling is associated with carpal tunnel. Pain that radiates can occur but radiates toward the forearm rather than the hand.

9.18 Answer: A (True/True - statement 2 is a correct explanation of statement 1)

Rationale: Hand numbness is a classic symptom with carpal tunnel syndrome and is caused by nerve entrapment.

9.19 Answer: C (True/False)

Rationale: Low back pain does not normally also present with fever, and fever could suggest infection rather than malignancy.

9.20 Answer: B (True/True – statement 2 not correct explanation of statement 1)

Rationale: Injuries with obvious inflammation best respond with NSAID treatment with symptoms resolving within 2 weeks.

Case studies

CASE STUDY 9.1

Mrs BB, a 69-year-old woman, hobbles into your pharmacy, supported by her husband. She has just slipped off the pavement edge and believes she has sprained her ankle.

- a. To ascertain if referral is necessary, describe the questions you would ask Mrs BB.

Find out the exact nature of the pain and its location. It is likely that the anterior talofibular ligament has been damaged. Symptoms that would warrant referral to an ED are if severe pain is present and if Mrs BB is unable to walk unsupported for at least four steps.

You decide that Mrs BB has indeed sprained her ankle, but referral is unnecessary. Mrs BB asks to purchase some OTC analgesia to alleviate her pain. Her regular medication is as follows:

- Bendroflumethiazide 2.5 mg od, used to treat hypertension; taken for 5 years
- Fybogel sachets, 1 bd, taken for 4 years for constipation
- Lansoprazole 15 mg od, maintenance therapy in treatment of gastro-oesophageal reflux disease (GORD) associated with hiatus hernia.

- b. Which OTC systemic analgesic would be most suitable for Mrs BB? Explain how you arrived at your choice and why you eliminated others.

- Aspirin can cause GI disturbance; Mrs BB has GORD, so aspirin is contraindicated.
- Ibuprofen – NSAIDs can cause fluid retention and Mrs BB has hypertension. However, this is unlikely to be

clinically significant, especially if NSAIDs are recommended for only a few days. Like aspirin, ibuprofen can cause GI disturbances and bleeds in older adults. Although both aspirin and NSAIDs will have an anti-inflammatory action, they are best avoided for Mrs BB.

- Paracetamol (with or without codeine) could be offered, but the analgesic effect of codeine is questionable, and the codeine content is likely to worsen her already existing constipation. This leaves paracetamol as the medicine of choice for Mrs BB.

Mrs BB asks if she should also use a cream on her ankle.

- c. Describe which would be suitable to recommend to Mrs BB. Give the reasons for your decision(s).

Rubefacients contain essential oils, salicylates, nicotines, capsicum, camphor, turpentine, and menthol. Evidence is lacking with regard to their efficacy in decreasing pain but they help in masking pain symptoms. These could be recommended to Mrs BB but ideally recommend a product with no salicylate present because there is a low risk of systemic absorption and gastric irritation.

Topical NSAIDs – relatively low doses reach the bloodstream, and there is therefore less risk of GI problems than with systemic NSAIDs. Use of topical NSAIDs are unlikely to cause side effects if used for short periods of time (5–10 days) and could be given to Mrs BB, even though she has GORD. However, she should be told that if she experiences any indigestion-type symptoms to stop using the product.

Case study

CASE STUDY 9.1

Mrs SD, a 71-year-old woman, presents to the pharmacy requesting pain relief for lower back pain. She is visiting from Australia to see relatives and asks for Mersyndol because she has been told that it is stronger than Panadol.

a. What do you first need to do?

You need to find out what the active ingredient's is (are) in Mersyndol. In the UK, you remember there used to be an OTC painkiller called Syndol, so you suspect it is something similar. You would need to look in standard reference sources such as Martindale.

You find out that it contains paracetamol (450 mg), codeine phosphate (9.75 mg), and doxylamine (5 mg).

b. How would you respond to her request?

First, you will need to tell her it is not available in the UK, and there is no similar or equivalent OTC remedy. Panadol in the UK just contains paracetamol and is equivalent to the Australian version of Panadol.

You need to find out more about her pain and why she feels she needs a stronger pain killer.

c. What do you therefore need to know to help Mrs SD?

- *Why does she feel the need for a stronger pain killer (this depends on if she has taken Panadol)?*

- *Establish the severity of pain in relation to previous pain episodes:*
 - *Knowing this information should allow you to establish the need for pain relief. Of course, it does not address the underlying cause of the pain and this should be your next line of enquiry.*

Questions should be asked about the following:

- *What is the site of the pain, and is there any radiation of the pain?*
- *What is the character of the pain (e.g., sharp, dull, aching)?*
- *Does anything aggravate or relieve the pain?*
- *How long has she had the pain?*
- *Are there any other associated symptoms (e.g., fever, vomiting, nausea)?*

She tells you that the pain started in the morning while she was working in her daughter's garden. It came on very suddenly when she bent down to pick up her watering can. She describes the pain as 'quite bad' and sharp in nature. The pain is worse on movement. She does not recall having pain like this before.

Given this information, it appears to be a simple back strain.

She goes on to tell you she takes quite a few medicines and the pharmacist back home always wants to know what she takes before giving her anything.

Her current medications are as follows:

Medication	Indication	Length of use
Methotrexate, 10 mg weekly (Monday)	Rheumatoid arthritis	8 years
Folic acid, 5 mg weekly (Tuesday)	While on methotrexate	8 years
Perindopril, 7.5 mg daily		7 years
Indapamide, 1.5 mg SR	Hypertension	4 years
Simvastatin, 40 mg nocte	Hypercholesterolaemia	4 years
Pantoprazole, 40 mg daily	GORD (gastro-oesophageal reflux disease)	6 years
Fish oil, 1-g capsules, nine capsules daily	Rheumatoid arthritis	5 years
Paracetamol 1g qd prn	Rheumatoid arthritis	10 years

CASE STUDY 9.1 (Continued)

- d. Given her medical history, does this alter your opinion of your differential diagnosis?

Simple back strain is still most likely but caution should now be exercised in that she is postmenopausal and suffers from arthritis. The risk of an osteoporotic fracture will be higher for Mrs SD compared to others.

- e. What management do you suggest?

You cannot eliminate the chances of pain being caused by an osteoporotic vertebral fracture.

Therefore, it is best to refer her to a physician for further investigation.

You suggest that she continues using paracetamol for now, but should discuss other pain management options with the GP. Because she is on an angiotensin-converting enzyme (ACE) inhibitor and a diuretic, nonsteroidal antiinflammatory drugs (NSAIDs) should be avoided. In addition, she has GORD and is being treated with a proton pump inhibitor (PPI), and therefore NSAIDs should be avoided.

CASE STUDY 9.2

Mr JD, a 47-year-old man, asks you for something for low back pain. On questioning, you find out the following:

Information gathering	Data generated
Describe the pain.	Pain described as aching and dull and spreads to bottom on the right-hand side
How long have you had the symptoms?	Came on about 2 days ago; woke up with the pain
Where is the pain?	Pain is diffuse over low back
Any other symptoms?	No other symptoms
When do you get the symptoms?	Constant
Does the pain move anywhere?	Top of the bum
Does anything make the symptoms better or worse?	Pain made worse if sitting over a long period of time
Level of pain	Severity – 5 or 6 out of 10

Information gathering	Data generated
Any obvious reasons what triggered the pain	Cannot remember doing anything to precipitate it.
Previous history of presenting complaint	No
Medicines (OTC, prescription)	Esomeprazole 1 od for last year to help with indigestion
Past medical history	None
Social history, which may include questions relating to smoking, alcohol intake, employment, personal relationships	Works in an office No lifestyle changes
Family history	Not asked

Below summarizes the expected findings for questions related to the conditions in which back pain is implicated and can be seen by community pharmacists.

Condition	Age	Radiation of pain	Onset	Absence of systemic or neurological signs	Precipitating factors
Simple back pain	All adults	No	Acute	Yes	Yes
Sciatica	>30 years	Yes (buttocks and leg)	Acute	Yes	Yes
Osteoarthritis	>30 years but more common with increased age	No	Chronic	Yes	No
Osteomyelitis	All ages	No	Acute	No	No
Ankylosing spondylitis	>50 years	Yes (side to side of back)	Chronic	Yes	No
Malignancy	>50 years	No	Chronic	No	No

When this information is compared to our patient's symptoms, and linking this with known epidemiology

on back pain (see [Table 9.1](#)), it should be possible to make a differential diagnosis.

CASE STUDY 9.2 (Continued)

Condition	Age	Radiation of pain	Onset	Absence of systemic or neurological signs	Precipitating factors
Simple back pain	✓	✗	✓	✓	✗
Sciatica	✓	✓	✓	✓	✗
Osteoarthritis	✓	✗	✗	✓	✓
Osteomyelitis	✓	✗	✓	✗	✓
Ankylosing spondylitis	✗?	✓	✗	✓	✓
Malignancy	✗?	✗	✗	✗	✓

We see that his symptoms most closely match sciatica (✓ represents symptom match). The acute onset and radiation are very suggestive of this condition, despite there being no obvious cause. Referred pain is usually an indication to refer the patient. However, analgesia could be tried to and relieve symptoms in the short term, and because he takes a proton pump inhibitor, it would be best to recommend paracetamol.

Paediatrics

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Background

A number of conditions are encountered much more frequently in children than the rest of the population. It is these conditions that this chapter focuses on. A small number of conditions that affect all age groups but are often associated with children are not included – for example, middle ear infection. Such conditions are covered in other chapters and, where appropriate, will be cross-referenced to the relevant sections in the text.

History taking

In most cases, pharmacists will be heavily dependent on getting details about the child's problem from their parents or an adult responsible for the child's welfare. This presents benefits and problems to the pharmacist. Parents will know when their child is not well, and asking the parent about the child's general health will help determine how poorly the child actually is. For example, a child who is running around and lively is unlikely to be acutely ill, and referral to a doctor is less likely. The major problem faced by all healthcare professionals is the difficulty in gaining an accurate history of the presenting complaint. This poses difficulties in assessing the quality and accuracy of the information because children find it hard to articulate their symptoms. If the child can be asked questions, these often have to be posed in either closed or leading formats to elicit information.

As a rule of thumb, any child who appears visibly ill should always be seen by the pharmacist, and referral might well be needed, whereas children who are acting normally

and appear generally well will often not need to see the doctor and can be managed by the pharmacist.

Head lice

Background

Humans act as hosts to three species of louse: *Pediculus capitis* (head lice), *Pediculus corporis* (body lice), and *Pediculus pubis* (pubic lice). Only head lice are discussed in this section.

Prevalence and epidemiology

Head lice is most prevalent in children aged 4 to 11 years, especially girls. Studies conducted in schools show wide variation of current lice infestation, ranging from 4% to 20% of pupils. Head lice can occur at any time and do not show any seasonal variation. Most parents will have experienced a child who has head lice or received letters from school alerting parents to head lice infestation in the school.

Aetiology

Head lice can only be transmitted by head to head contact. Fleeting contact will be insufficient for lice to be transferred between heads. Once transmitted lice begin to reproduce; the adult louse lives for approximately 1 month. Throughout this time, the female louse lays several eggs at the base of a hair shaft each night. Eggs hatch after 7 to 10 days, leaving the egg case attached to the hair shaft (known as a *nit*). In the

course of maturing to adulthood, the young louse (the nymph) undergoes three moults. Shortly after maturing, the female louse is sexually mature and able to mate.

Arriving at a differential diagnosis

Most parents will diagnose head lice themselves or be concerned that their child has head lice because of a recent local outbreak at school. Occasionally, parents will also want to buy products to prevent their child contracting head lice. It is the role of the pharmacist to confirm a self-diagnosis and stop inappropriate sales of products. It should also be remembered that an itching scalp in children is not always due to head lice. Asking a number of symptom-specific questions should enable a diagnosis of head lice to be easily made (Table 10.1).

Clinical features of head lice

Observation of live lice is diagnostic. They are commonly found in the occipital and postauricular areas. Scalp itching is seen in approximately one third of patients. Itching is caused by an allergic response of the scalp to the saliva of the lice and can take weeks to develop.



Table 10.1
Specific questions to ask the patient: Head lice

Question	Relevance
Have live lice been seen?	<p>The presence of live lice is diagnostic. Pharmacists can advise patients on how best to check for infection. Currently, both wet and dry combing are advocated.</p> <p>Dry combing:</p> <ol style="list-style-type: none"> 1. Straighten and untangle the dry hair using an ordinary comb. 2. Once the hair moves freely, switch to a detection comb. Starting from the back of the head, comb the hair from the scalp down to the end of the hair. 3. After each stroke, examine the comb for live lice. 4. Continue to comb all the hair in sections until the whole head has been combed. <p>This process can take 5 or more minutes in people with shoulder-length hair.</p> <p>Wet combing:</p> <ol style="list-style-type: none"> 1. Wash the hair with a normal shampoo. 2. Apply hair conditioner. 3. Repeat steps 1–4 as for dry combing. 4. Rinse out the conditioner. <p>Wet combing is more time-consuming than dry methods and can take up to 10–15 minutes.</p>
Empty egg shells (nits)	<p>This does not constitute evidence of current infestation. This is a common misconception held by the general public, and the pharmacist must ensure that parents seeking treatment have observed live lice. Egg shells are not removed by using insecticides. Patients need to be reassured that the presence of egg shells does not mean treatment failure.</p>
Presence of itching	<p>Itching is not always present in head lice. Inspection of the scalp should be made to check for signs of dandruff, psoriasis or seborrhoeic dermatitis.</p>

Conditions to eliminate

Dandruff

Dandruff can cause irritation and itching of the scalp. However, the scalp should be dry and flaky. Skin debris might also be present on clothing.

Seborrhoeic dermatitis

Typically, seborrhoeic dermatitis will affect areas other than the scalp, most notably the face. If only scalp involvement is present, the child might complain of severe and persistent dandruff. In infants, the child will have large yellow scales and crusts of the scalp (cradle cap).



TRIGGER POINTS indicative of referral: Head lice

Parents who find cost of treatment prohibitive

Evidence base for over-the-counter medication

Treatment options include insecticides, wet combing, and physical agents. All treatments available in the UK have

shown varying degrees of clinical effectiveness, but it is difficult to assess which is most effective because very few comparative trials have been performed, and insecticidal resistance varies from region to region. No treatment is 100% effective, and failure has been linked with poor adherence to each treatment regimen.

Insecticides

Of the treatment approaches, insecticides have been most studied, but only malathion should be now be used because all other insecticides show very poor cure rates.

Wet combing

Wet combing is an alternative treatment option; however, cure rates are reported to be only 40% to 60%, with the low cure rates attributed to poor adherence (Hill et al., 2005; Roberts et al., 2005).

Physical agents

Dimeticone is a relatively recent introduction to the market and is thought to work by coating the lice internally and externally, which leads to disruption in water excretion, causing the gut of the lice to rupture from osmotic stress (Burgess, 2009). Its inclusion in treatment options seems to stem from one robust trial conducted by Burgess et al. (2005). Dimeticone was compared against phenothrin with cure rates determined at days 9 and 14. Dimeticone was shown to have comparable cure rates to phenothrin (69% compared with 78%). The study has been criticized for using dry detection methods and using different detection days (days 5 and 12 as recommended by the Department of Health); however, a further trial in 2007 supports the 2005 trial results.

In the latter study, 4% dimeticone lotion, applied for 8 hours or overnight, was compared with 0.5% malathion liquid applied for 12 hours or overnight. The results indicated that dimeticone was significantly more effective than malathion, with 30/43 (70%) participants cured using dimeticone compared with 10/30 (33%) using malathion.

Dimeticone is also available in a much higher concentration (92%) marketed as NYDA. A randomized controlled trial compared the efficacy of a product containing dimeticone 92% to a permethrin 1% lotion. Both products were applied twice, 7 days apart, and the results showed that cure rates on day 9 were 97% with dimeticone and 68% with permethrin, but cure rates were not given for day 14 (Heukelbach et al., 2008).

Isopropyl myristate is another physical insecticide product; it works by blocking the tracheal breathing system and coating the surface of lice with a thin film of fluid (Drugs and Therapeutics Bulletin, 2009). Evidence of efficacy comes

from two trials that compared isopropyl myristate with permethrin. Results found that isopropyl myristate was significantly more effective than permethrin (82% vs. 19%). Although these results seem impressive, the comparator drug was permethrin, a product not recommended due to its poor efficacy.

In summary, the treatment used will be driven by individual preference, the patient's medical history, and previous exposure to treatment regimens. Wet combing (available as bug-busting kits) is time-consuming and requires patient motivation but is helpful in areas of high insecticidal resistance. Insecticides, dimeticone, and isopropyl myristate are simpler to use than bug-busting kits and appear to have higher cure rates.

Based on current evidence, it seems dimeticone is the treatment of choice.

Practical prescribing and product selection

Prescribing information relating to medicines for head lice is discussed and summarized in [Table 10.2](#); useful tips relating to patients presenting with head lice are given in Hints and tips [Box 10.1](#). All products have to be used more than once; insecticides have to be repeated 7 days after first application. This is based on expert opinion, because the second application is intended to kill nymphs emerging from eggs that have survived the first application. Physical agents should also be reapplied in 7 days' time, and wet combing used every 4 days for at least 2 weeks. All products, except isopropyl myristate, can be used on children older than 6 months. Dimeticone or wet combing is recommended for pregnant and breastfeeding women. When applying all products, pay particular attention to the areas behind the ears and at the nape of the neck because these areas are where lice are most often found.

Below highlights application details for products recommended in the UK (as of April 2020).

Malathion (Derbac-M liquid)

Derbac-M should be applied to dry hair and left for a minimum of 12 hours before washing off.

Dimeticone

4% Lotion and Spray

When using dimeticone 4% lotion and spray (Hedrin), the lotion is applied to dry hair, ensuring that it is spread evenly from the hair root to the tips. The spray should be applied approximately 10 cm from the hair, making sure it is evenly distributed over dry hair. Both need to be left on for a minimum of 8 hours (overnight is preferable) before being washed out with shampoo.



Table 10.2
Practical prescribing: Summary of head lice medicines

Name of medicine	Use in children	Very common (>1/10) or common (>1/100) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
Malathion	>6 months		None	None	OK
Dimeticone Isopropyl myristate	>2 years	None reported			

HINTS AND TIPS BOX 10.1: HEAD LICE

Who to treat?	Only those individuals with an active head lice infestation should be treated.
Products for prevention	No credible evidence exists for any product marketed for prevention. The patient and/or parent should be counselled on when treatment is required.
Treatment failure?	It is recommended that detection combing be performed after any treatment to confirm head lice eradication. For wet combing: Wet combing should be continued if necessary until no full-grown lice have been seen for three consecutive sessions. For insecticides, dimeticone and isopropyl myristate: Perform detection combing (wet or dry) 2–3 days after completing treatment. If no adult or nymph lice are found, repeat detection, combing 8–10 days after treatment. Treatment is successful if no lice are found in both detection combing sessions after treatment.
Myths	Public misconceptions about head lice need to be dispelled. Head lice are not only associated with dirty hair. Head lice do not only affect children. Children should not be kept from attending school.

Dimeticone 4% Gel (Hedrin Once Spray gel)

4% gel (Hedrin Once Liquid gel) is applied in the same way as the lotion but only needs to be left on the hair for 15 minutes.

Dimeticone 92% Spray (NYDA)

The hair should be combed with a fine-toothed comb before applying the spray over the entire head. Once applied, leave the hair for at least 30 minutes to kill the head lice, then comb the hair carefully with a fine-toothed lice comb to remove the suffocated lice. Once applied, it should be left on the hair and scalp for 8 hours or overnight and then washed out using shampoo.

Isopropyl myristate in cyclomethicone

Full Marks Solution Spray is applied in the same manner as dimeticone, but the manufacturers recommend contact time of only 5 minutes. It is only recommended for adults and children older than 2 years.

Isopropyl alcohol aerosol & isopropyl myristate (Vamousse)

Like Full Marks, this is only recommended for those older than 2 years. Contact time is, however, 15 minutes.

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Connolly, M. (2003). Recommended management of headlice and scabies. *The Prescriber*, 2013, 17–29.

Websites

Community Hygiene Concern: <https://www.chc.org/>

Pediculosis.com: <http://www.pediculosis.com/>

Once a week – take a peek: <http://www.onceaweektakeapeek.com/>

Threadworm

Background

Worm infections are extremely common in both the developed and developing world. In Western countries, the most common worm infection is threadworm (*Enterobius vermicularis*), known in some countries as *pinworm*, which is a condition that causes inconvenience and embarrassment. Social stigma surrounds the diagnosis of threadworm, with many patients believing that infection implies a lack of hygiene. This belief is unfounded because infection occurs across all social strata. The patient might benefit from reassurance, explaining that the condition is very common and is nothing to be ashamed or embarrassed about.

Prevalence and epidemiology

Threadworm is the most common helminth infection throughout temperate and developed countries. Threadworm prevalence is difficult to establish due to the high number of people who self-medicate or are asymptomatic. However, UK prevalence rates have been estimated at 20% in the community, rising to 65% in institutionalized settings. Threadworms are much more common in school or preschool children than adults because of their inattention to good personal hygiene.

Aetiology

Eggs are transmitted to the human host primarily by the faecal-oral route (autoinfection) but also by retroinfection and inhalation. Faecal-oral transmission involves eggs

lodging under fingernails, which are then ingested by finger sucking after anal contact. Retroinfection occasionally occurs when larvae hatch on the anal mucosa and migrate back into the sigmoid colon. Finally, threadworm eggs are highly resistant to environmental factors and can easily be transferred to clothing, bed linen and inanimate objects (e.g., toys), resulting in dust-borne infections. Once eggs are ingested, duodenal fluid breaks them down and releases larvae, which migrate into the small and large intestines. After mating, the female migrates to the anus, usually at night, where eggs are laid on the perianal skin folds, after which the female dies. Once laid, eggs are infective almost immediately. Transmission back into the gut can then take place again via one of three mechanisms outlined, and so the cycle is perpetuated.

Arriving at a differential diagnosis

Threadworm diagnosis should be one of the simpler conditions to diagnose because patients present with very specific symptoms.

Clinical features of threadworm

Nighttime perianal itching is the classic presentation (caused from the mucous produced by females when laying eggs). However, patients might experience symptoms ranging from a local tickling sensation to acute pain. Any child with nighttime perianal itching is almost certain to have threadworm. Itching can lead to sleep disturbances, resulting in irritability and tiredness the next day. Diagnosis can be confirmed by observing threadworm on the stool, although they are not always visible.

Complicating factors such as excoriation and secondary bacterial infection of the perianal skin can occur due to persistent scratching. The parent should be asked if the perianal skin is broken or weeping.

Conditions to eliminate

Other worm infections

Roundworm and tapeworm infections are encountered occasionally. However, these infections are usually contracted abroad when visiting poor and developing countries, with patients experiencing non-specific abdominal symptoms such as loss of appetite, nausea and altered bowel habit.

Contact irritant dermatitis

Occasionally, dermatitis can cause perianal itching (especially in adults). If there is no recent family history of threadworm or there is no visible sign of threadworm on the faeces, dermatitis is possible.

**TRIGGER POINTS indicative of referral: Threadworm**

Symptoms/signs	Possible danger/ reason for referral	Urgency of referral
Medication failure	Possible misdiagnosis	As soon as practicable
Secondary infection of perianal skin due to scratching	Need for assessment and possible systemic antibiotics	

Evidence base for over-the-counter medication

Mebendazole is available OTC for the treatment of threadworm. There is a large body of evidence to support the effectiveness of mebendazole in roundworm infections but, for other worm infections, including threadworm, cure rates are lower. For threadworm, cure rates between 60% and 82% for single-dose treatment of mebendazole have been reported (Rafi et al., 1997; Sorensen et al., 1996).

Practical prescribing and product selection

Prescribing information relating to mebendazole is summarized in [Table 10.3](#); useful tips relating to patients

presenting with threadworm are given in Hints and tips [Box 10.2](#).

Treatment should ideally be given to all family members, and not only the patient with symptoms, because it is likely that other family members will have been infected, even though they might not show signs of clinical infection. A repeated dose 14 days later is often recommended to ensure that worms maturing from ova at the time of the first dose are also eradicated.

Mebendazole should be avoided in pregnancy because foetal malformations have been reported; however, it appears to be safe in breastfeeding women. Pregnant women should be advised to practise hygiene measures for 6 weeks to break the cycle of infection.

Mebendazole

The dose of mebendazole (e.g., Ovex) for adults and children older than 2 years is 100 mg (a single tablet or 5 mL of suspension). Young children might prefer to chew the tablet, and it has been formulated to taste of orange (suspension is banana flavoured). Side effects include abdominal pain and discomfort (most commonly reported side effect), diarrhoea, and flatulence. It does interact with cimetidine, increasing mebendazole plasma levels, but this is of little clinical consequence. Phenytoin and carbamazepine decrease mebendazole plasma levels, and the dose of mebendazole may need to be increased.



Table 10.3
Practical prescribing: Summary of medicines for threadworm

Name of medicine	Use in children	Very common (>1/10) or common (>1/100) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy & breastfeeding
Mebendazole	>2 years	Abdominal pain	Phenytoin and carbamazepine	None	Avoid in pregnancy; OK in breastfeeding

HINTS AND TIPS BOX 10.2: THREADWORM

Hygiene measures	Complementary to drug treatment is the need for strict personal hygiene. Nails should be kept short and clean. Careful washing and nail scrubbing before meals and after each visit to the toilet are essential to prevent autoinfection. Bed linen, towels and sleepwear should be washed on the first day of treatment. Underwear should be worn underneath night clothes to prevent scratching. Shower daily, immediately on rising, washing around the anus. Damp dusting and daily vacuuming are recommended to remove eggs.
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Colic

Background

There is no universally agreed definition of colic. A widely used definition of colic is that proposed by Wessel et al. (1954) and has come to be known as the *rule of threes*. Wessel proposed that an infant could be considered to have colic if he or she cries for more than 3 hours a day for more than 3 days a week for more than 3 weeks. However, the definition by Wessel is arbitrary, and few parents are willing to wait 3 weeks to see if the infant meets the criteria for colic. As a result, in the clinical setting, colic is usually defined because as episodes of excessive and inconsolable crying in an infant who otherwise appears to be healthy (NICE, 2015).

Prevalence and epidemiology

Due to no universally accepted definition of colic, its prevalence is difficult to determine, and estimates vary widely from 3% to 40%, depending on which definition is used. Studies reporting lower figures strictly applied Wessel's criteria, whereas higher figures used wider definitions. It is likely that prevalence falls between the two extremes and affects 10% to 20% of infants.

Colic starts in the first few weeks of life and usually resolves by the age of 3 to 5 months old.

Aetiology

The cause of colic is poorly understood but seems to be multifactorial. It has been linked to a disorder of the gastrointestinal (GI) tract, where spasmodic contraction of smooth muscle causes pain and discomfort, which might be caused by allergy to cow's milk, lactose intolerance, or inadequate amounts of lactobacilli. It has also been suggested that it might stem from emotional, behavioural, and social problems that include underdeveloped parenting skills, inadequate social network, postpartum depression, and parental anxiety and stress.

Arriving at a differential diagnosis

It can be difficult to determine whether the baby has colic or is just excessively crying because the diagnosis of the condition is dependent on qualitative descriptions. However, the term *colic* is often wrongly applied to any infant who cries more than usual. Asking a number of symptom-specific questions should enable a diagnosis of colic to be made (Table 10.4).

Clinical features of colic

Excessive crying and inconsolable crying are obvious clinical features, accompanied by facial flushing and drawing up of the legs. Pain may be mild, merely causing the child to be restless in the evenings or severe, resulting in rhythmic screaming attacks lasting a few minutes at a time, alternating with equally long quiet periods in which the child almost goes to sleep before another attack starts. Attacks appear to be more common in the early evening, giving rise to the name *6:00 PM colic*.



Table 10.4
Specific questions to ask the patient: Colic

Question	Relevance
History of crying	Excessive crying is not isolated and will have been present for some time. Acute infections are normally sudden in onset, and the baby will not exhibit a long-standing history of excessive crying
Aggravating factors	Infants may cry excessively for reasons other than a medical cause, for example, hunger, thirst, being too hot or cold and trapped wind. These should be explored as part of your questioning strategy before diagnosing colic

Conditions to eliminate

Acute infection

Colic and acute infections of the ear or urinary tract can present with almost identical symptoms. However, in acute infection, the child should have no previous history of excessive crying and have signs of systemic infection such as fever.

Intolerance to cow's milk protein

Colicky pain in infants is sometimes due to intolerance to cow's milk protein. This is far less common than generally believed but should be considered if the infant is failing to thrive.

Gastro-oesophageal reflux disease

Infants frequently have regurgitation that is accompanied with excessive crying. A diagnosis of gastro-oesophageal reflux disease (GORD) is usually made if regurgitation happens more than five times a day and is associated with failure to gain weight and refusal to feed.

! TRIGGER POINTS indicative of referral: Colic

Symptoms/signs	Possible danger/ reason for referral	Urgency of referral
The infant is not thriving, or symptoms are not starting to improve or are worsening after 4 months of age	This may indicate GORD or intolerance to cow's milk	As soon as practicable
Overanxious parents	Parents might need further reassurance	

Evidence base for over-the-counter medication

Parents should be reassured that the child's symptoms will subside over time, that their baby is well, and they are not

doing something wrong. Most parents will want some form of treatment. Treatments include simeticone, lactase enzymes, low-lactose milk formulas, and Gripe mixtures. None have a credible evidence base.

Simeticone is reported to have antifoaming properties, reducing surface tension and allowing easier elimination of gas from the gut by passing flatus or belching. It is widely used yet has very limited evidence of efficacy. Of three trials reported, only one found a small improvement in the number of crying attacks. This trial was small ($N = 26$) and suffered from methodological flaws, so results should be viewed with caution (Joanna Briggs Institute, 2008).

Lactase breaks down lactose present in milk to glucose and galactose. This reduction in lactose concentration is reported to improve colic symptoms, but four small trials investigating its effect were inconclusive.

Low-lactose formulas should not be recommended because studies conducted to date have been of poor methodological quality. No trial data exist for Gripe mixtures and therefore should be avoided.

Summary

Although evidence for simeticone and lactase enzymes is not strong, it would seem unreasonable not to let parents try either for a trial period of 1 week if they are finding it difficult to cope. If no response is seen, referral to a doctor or health visitor would be advisable.

Practical prescribing and product selection

Prescribing information relating to simeticone is discussed and summarized in [Table 10.5](#); useful tips relating to colic are given in Hints and tips [Box 10.3](#).

Simeticone

Simeticone (e.g., Infacol, Dentinox) is pharmacologically inert; it has no side effects, drug interactions, or precautions in its use and can therefore be safely prescribed to all infants. The dose for Infacol is 0.5 to 1.0 mL and for Dentinox the dose is 2.5 mL.



Table 10.5
Practical prescribing: Summary of medicines for colic

Name of medicine	Use in children	Very common (>1/10) or common (>1/100) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
Simeticone	Infant upwards	None	None	None	Not applicable
Lactase					

HINTS AND TIPS BOX 10.3: COLIC

Review feeding technique Before recommending a product, it is worth checking the feeding technique. Underfeeding the baby can result in excessive sucking and in air being swallowed, leading to colic-like symptoms. Additionally, if bottlefeeding, the teat size of the bottle should be checked. When the bottle is turned upside down, the milk should drop slowly from the bottle.

Lactase enzyme (Colief)

The dose of lactase enzyme (Colief) differs, depending if the baby is formula or breast-fed. If breastfeeding, four drops should be added to a small amount of expressed milk and the baby breastfed as normal; if using an infant formula, the feed should be made up as usual and four drops added to warm, but not hot, formula. If making up the formula in advance, then add two drops of Colief and store in the fridge for 4 hours.

Reference

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 Kanabar, D. (2008). Current treatment options in the management of infantile colic. *The Prescriber*, 24–29.

Websites

- CRY-SIS: <https://www.cry-sis.org.uk/> National telephone helpline (0845 122 8669).
 The Breastfeeding Network: <https://www.breastfeedingnetwork.org.uk>

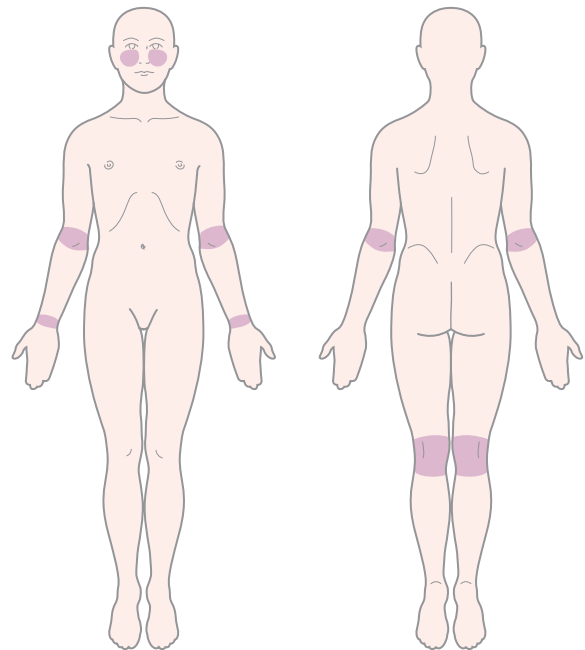


Fig. 10.1 Typical distribution of atopic dermatitis.

out' of the condition by their early teens. However, in a small number of patients, atopic dermatitis persists into adulthood, where the condition becomes chronic. Atopic dermatitis can impair the quality of life of patients and their families. A typical distribution of atopic dermatitis is illustrated in Fig. 10.1.

Atopic dermatitis**Background**

Atopic dermatitis is a chronic noninfective inflammatory skin condition characterized by an itchy red rash. It usually starts within the first 6 months of life and predominantly affects young children. Most patients (60%–70%) will 'grow

Prevalence and epidemiology

The prevalence of atopic dermatitis is unclear. Rates vary from country to country. In the UK, prevalence rates have been rising, and it now affects 15% to 30% of children, although over 80% are reported to have mild disease. The condition usually presents in infants aged between 2 and 6 months, but it can occur in older children. Upwards of 60% of children will have onset within the first year, rising to 70% to 90% within the first 5 years.

Aetiology

Atopic dermatitis has a strong genetic component, although the precise genetic cause is unknown. Two thirds of people with the disease have a family history of atopic dermatitis, asthma, or hay fever. Atopic dermatitis is present in approximately 80% of children where both parents are affected and in 60% if one parent is affected. In addition, a number of environmental factors have been implicated in the development or worsening of the condition and include certain foods (e.g., dairy products), stress, extremes of heat and humidity, and irritants such as detergents and chemicals.

Arriving at a differential diagnosis

An itchy rash with very early childhood onset is indicative of atopic dermatitis (Figs. 10.2 and 10.3). To help with diagnosis, criteria-based protocols are available; for example, National Institute for Health and Care Excellence (NICE) guidelines state that atopic dermatitis is likely if the person has had an itchy skin condition, plus three or more of the following:

- Onset before the age of 2 years
- History of dry skin in the last 12 months



Fig. 10.2 Atopic dermatitis in an infant. From Zitelli, B. J., & Davis, H. W. (1997). *Atlas of pediatric physical diagnosis* (3rd ed.). Mosby.



Fig. 10.3 Atopic dermatitis in the popliteal fossa (bend of knee). From Gawkrödger, D. J. (2007). *Dermatology: An illustrated colour text* (4th ed.). Churchill Livingstone.

- History of eczema in the skin creases (and also the cheeks in children <18 months)
- Visible flexural eczema involving the inside elbows or behind knees (or involvement of the cheeks or forehead and outer limbs in children <18 months)
- Personal history of other atopic disease

Asking a number of symptom-specific questions should enable a diagnosis of atopic dermatitis to be made (Table 10.6).

Clinical features of atopic dermatitis

A typical presentation is an irritable child with dermatitis of varying severity. Itching is the predominant symptom, which can induce a vicious cycle of scratching, leading to skin damage, which in turn leads to more itching – the so-called itch scratch itch cycle. The child might have had the symptoms for some time, and the parent has often already tried some form of cream to help control the itch and rash. Scratching can lead to broken skin, which can become infected. There is a tendency to have dry sensitive skin, even in those who have outgrown the disease.

Once a diagnosis has been established, and before treatment is considered, it is important to make an assessment on the severity and social impact of the condition (<https://www.nice.org.uk/guidance/cg57>).

Conditions to eliminate

Seborrhoeic dermatitis

Seborrhoeic dermatitis in infants typically occurs in the first 6 months. Itching is generally not present, and the condition usually spontaneously resolves after a few weeks and seldom



Table 10.6
Specific questions to ask the patient: Atopic dermatitis

Question	Relevance
Is itching present?	Atopic dermatitis is typically associated with itching that can be severe. Lack of itch strongly suggests that the rash is not atopic dermatitis.
Distribution of rash	Varies according to age (see Fig. 10.1) but in infants, the nappy area is not involved and is a useful distinction between atopic dermatitis and seborrhoeic dermatitis. Babies: Facial involvement (the cheeks) is common, along with patchy red scaly lesions on the wrists and hands (see Fig. 10.2). Toddlers and older children: The antecubital (in front or at the bend of the elbow), popliteal fossae (behind the knee), and ankles are more commonly involved (see Fig. 10.3).
Family history of atopy	If a parent has eczema, hay fever, or asthma, the likelihood of atopic dermatitis rises.



Table 10.7
Practical prescribing: Summary of medicines for atopic dermatitis

Name of medicine	Use in children	Very common (>1/10) or common (>1/100) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
Emollients	Birth onwards	None	None	None	Not applicable
Sedating antihistamines					
Chlorphenamine	>1 year	Sedation	Increased sedation with opioid analgesics, anxiolytics, hypnotics, and antidepressants. However, it is unlikely a child will be taking such medicines	None	Not applicable
Clemastine	>1 year				
Cyproheptadine	>2 years				
Promethazine	>2 years				

recurs. It usually affects the scalp, face, and nappy (diaper) area. Large yellow scales and crusts often appear on the scalp and are often referred to as *cradle cap* (see Fig. 8.10).

Psoriasis

Psoriasis can be mistaken for atopic dermatitis because the rash is erythematous and can occur on parts of the body such as the scalp, elbows, and knees, which is a common location for atopic dermatitis in older children. However, the rash is raised and has well-defined boundaries with a silvery-white, scaly appearance that is typically symmetrical. Itch, if present, is mild (For further information on psoriasis see Chapter 8 and Fig. 8.3).

Allergic contact dermatitis

A red, itchy skin rash can be seen at any site related to exposure (see Fig. 8.27). Allergic contact dermatitis can be a trigger factor of atopic eczema. For further information on contact dermatitis, see Chapter 8.

Fungal infection

The rash is a pink or red, itchy, slightly raised annular patch, with a well-defined inflamed border (see Fig. 8.14). It can occur on all body surfaces. For further information on fungal infection see Chapter 8.


TRIGGER POINTS indicative of referral: Atopic dermatitis

Symptoms/signs	Possible danger/reason for referral	Urgency of referral
Children with moderate or severe atopic dermatitis	Outside scope of community pharmacist; patient probably needs corticosteroid therapy	As soon as practicable
Medication failure – patient suffers two or more flare-ups per month		
Presence of secondary infection (weeping and crusting lesions)	Potentially needs systemic antibiotics	Same day referral to GP

Evidence base for over-the-counter medication

The mainstay of treatment for atopic dermatitis consists of avoiding potential irritants, managing dry skin, controlling itching, and using topical corticosteroids to treat flare-ups. Unfortunately, the latter option is not available to children younger than 10 years due to OTC license restrictions.

Avoiding irritants

Where practical, factors that worsen dermatitis should be avoided. The use of highly perfumed soaps and detergents should be discouraged and replaced with soap substitutes (e.g., Alpha Keri, Neutrogena, Dove).

Emollients

It is believed that emollients add moisture to the skin and repair the lipid barrier function while also helping prevent

penetration by irritants and decreasing the need for steroids. Despite a lack of high-quality, randomized controlled trials, emollients are well established as first-line treatment for atopic dermatitis. No trials appear to have addressed whether one emollient is superior to another. Patients might have to try several emollients before finding one that is most effective for their skin.

Antihistamines

There appears to be no clinical trial data on the use of sedative antihistamine for reducing pruritus in atopic dermatitis; however, they are often prescribed to children to help with itching. The American Academy of Dermatology guidelines on the treatment of atopic dermatitis report that there is little evidence for the use of antihistamines; however, sedating antihistamines may be useful when there is significant sleep disruption due to itching (Hanifin et al., 2004).

Corticosteroids

A substantial body of evidence exists for corticosteroids in controlling all types of dermatitis, including atopic dermatitis. If the symptoms warrant corticosteroid therapy, children need to be referred to the doctor. Usually mild steroids, such as hydrocortisone (1%–2.5%), preferably in an ointment base, should be prescribed twice daily.

Practical prescribing and product selection

Prescribing information relating to medicines for atopic dermatitis is discussed and summarized in [Table 10.7](#); useful information regarding emollients containing lanolin is given in Hints and tips [Box 10.4](#).

Emollients

There is a plethora of emollient products marketed and which one a patient uses will be dictated by patient response and acceptability. All emollients should be regularly and liberally applied, with no upper limit on how often they can be used. They should be routinely used, even when the skin is clear.

HINTS AND TIPS BOX 10.4: ATOPIC DERMATITIS

General self-help	If possible, avoid scratching. Keep nails short and rub with fingers to alleviate itch to minimize skin trauma.
Lanolin-containing emollients	Emollients that contain lanolin (e.g., Keri Lotion and E45) should be patch tested before use because they are known to cause sensitization.
Applying emollients	They are best applied when the skin is moist, for example, during bath times. Apply as frequently as possible. The more oily the emollient, the more effective it tends to be.

All are chemically inert and therefore can be safely used from birth upwards. For a summary of emollient products, see Table 8.38.

Sedating antihistamines

Chlorphenamine

Chlorphenamine (e.g., Piriton Allergy Tablets and Syrup) can be given from 1 year upwards (2.5 mL [1 mg] twice daily). The dose is every 4 to 6 hours for all age groups. Children 2 to 6 years of age should take 2.5 mL (1 mg); children 6 to 12 years of age should take 5 mL (2 mg or half a tablet).

Clemastine

Clemastine (Tavegil) is taken twice a day by children older than 1 year. Those aged between 1 and 3 years should take 250 to 500 µg (one-quarter to one-half a tablet), children aged between 3 and 6 years should take 500 µg (one-half a tablet), and for those older than 6 years, the dose is 500 µg to 1 mg (one-half to one tablet).

Cyproheptadine

Children between the ages of 2 and 6 years should take 2 mg (half a tablet) of cyproheptadine (Periactin) and for children older than 7 years, the dose is 4 mg (one tablet) two or three times a day.

Promethazine

Children between the ages of 2 and 5 years should take promethazine (Phenergan, 5 mg/5 mL, and 10- and 25-mg tablets) 5 to 15 mg (5–15 mL) daily in one to two divided doses. For those older than 5 years, the dose is 10 to 25 mg daily in one or two divided doses.

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- National Institute for Health and Care Excellence (NICE). (2007). CG57. *Atopic eczema in under 12s*. <https://www.nice.org.uk/guidance/cg57>.

Websites

- National Eczema Society: <http://www.eczema.org/>
General dermatology site: <http://www.dermatologist.co.uk/index.html>

Fever

Background

Fever is simply a rise in body temperature above normal. Normal oral temperature is 37°C (98.6°F), plus or minus 1°C, although rectal temperature is about 0.5°C higher and underarm temperature is 0.5°C lower than oral temperature. During the course of 24 hours, minor fluctuations in temperature are observed. Fever is often classified as being mild (low-grade; up to 39°C) or high (>39°C).

In a practice setting, for those younger than 5 years, the best temperature to take is under the arm using an electronic or chemical dot thermometer. Infrared tympanic thermometers are also advocated. Forehead strip thermometers are popular because they are easy to use, but should be avoided because they are unreliable.

Prevalence and epidemiology

Fever is a common symptom of many conditions; in children, viral and to a lesser extent bacterial causes are most commonly implicated. It has been reported that fever is probably the most common reason for a child to be taken to a doctor.

Aetiology

Body temperature is regulated closely because temperature changes can significantly alter cellular functions and, in extreme cases, lead to death. Thermoregulation is a balance between heat production and heat loss. Cellular metabolism produces heat and this means that energy, in the form of heat, is produced continually by the body. This heat production is lost through the skin by radiation, evaporation, conduction, and convection. The thermoregulation centre located in the

hypothalamus controls the whole process. When body temperature reaches its *set point* ($\sim 37^{\circ}\text{C}$), mechanisms to lose or conserve heat are activated. When a person suffers from a fever, this suggests that there is some defect in the temperature-regulating control system. In fact, the system is functioning normally but with an adjusted higher set point. This process is complex but involves the production of pyrogens (fever-causing substances) that alter the set point.

Arriving at a differential diagnosis

Establishing fever is usually a subjective perception by the parent that the child feels warm or is off-colour. The importance of the parent's perception should not be underestimated or dismissed if the child's temperature has not been taken. Many health care professionals often place too much value on an empirical figure when in many cases the look of the child is more important than the height of the fever. Asking a number of symptom-specific questions should enable the pharmacist to treat or refer the child with fever (Table 10.8).

NICE recommends using a traffic light system to assess the seriousness of fever (<https://www.nice.org.uk/guidance/ng143>). In a pharmacy setting, any child who shows symptoms or signs of intermediate (amber) or high (red) risk should be referred to the doctor.

Clinical features of fever

A child with fever will generally be irritable, off his or her food, and seek greater parental attention. Other signs that might be seen include facial flushing and shivering.

Likely causes

Urinary tract infection

One of the most common causes of fever in children is a urinary tract infection. Often, the child will present only with fever. Other symptoms can be present and include irritability,

poor feeding, vomiting, or abdominal pain. Referral is needed.

Roseola infantum (sixth disease)

Roseola infantum is probably caused by a neurodermotropic virus and is most prevalent in children younger than 1 year. Onset is with a sudden high fever (40°C) that usually subsides by the third or fourth day once the rash, which blanches when pressed, appears on the trunk and limbs. The condition is self-limiting.

Vaccine reaction

A recent history of vaccination plus injection site pain is typical.

Unlikely causes

Upper respiratory tract infections

It is rare for upper respiratory tract infections to present with fever alone. Cough, cold, or sore throat is usually present. Treatment can be offered, and referral is generally not needed unless secondary bacterial infection is suspected; earache symptoms might suggest this.

Medicine-induced fever

A number of medicines can elevate body temperature and should be considered if no other cause can be determined. Penicillins, cephalosporins, macrolides, tricyclic antidepressants, anticonvulsants, and anti-inflammatory drugs, when associated with hypersensitivity, have all been associated with increasing temperature.

Pneumonia

Children exhibit cough, chest pain, and increased respiration rate.

Glandular fever

Glandular fever is most commonly seen in young adults rather than children, but any patient who has a long-standing



Table 10.8
Specific questions to ask the patient: Fever

Question	Relevance
How old is the child?	Children <3 months should be referred automatically because diagnosis can be very difficult, and serious complications can arise unless associated after routine vaccinations.
How poorly is the child?	The parent will know how poorly the child is relative to normal behaviour. A child might have a high temperature but appear relatively normal, whereas a child with a mild temperature might be quite poorly.
Associated symptoms	Viral upper respiratory tract infections are usually accompanied with one or more symptoms including cough, cold, and sore throat. If no other symptoms are present, this suggests a bacterial infection, often a urinary tract infection.

history of fatigue and a low-grade fever should be referred for further evaluation.

Very unlikely causes

Meningitis

Meningitis should be considered in any feverish child who is obviously systemically unwell and exhibits symptoms such as severe headache, photophobia, lethargy, drowsiness, and neck stiffness. The classic textbook sign of a nonblanching rash is often seen late in symptom presentation and should not be routinely expected to be seen in children. Further information is provided under infectious childhood conditions.

Scarlet fever

Twelve to 48 hours prior to the rash developing, patients may present with sore throat, headache, and low-grade fever. Further information is provided under infectious childhood conditions.

! TRIGGER POINTS indicative of referral: Fever

Symptoms/signs	Possible danger/ reason for referral	Urgency of referral
Any feverish child <3 months old Fever accompanied with no other symptoms Fever of 5 days or longer Febrile convulsions, seizures	Outside scope of community pharmacist; person requires further assessment	Immediate to GP
Stiff neck Obviously ill child or child who fails to respond to stimuli	Suggests meningitis	Immediate to E&D

Signs of dehydration that fall in 'amber' or 'red' categories (see https://www.nice.org.uk/guidance/ng143)	Oral rehydration may be inadequate; intravenous fluids may be needed	Immediate to GP
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Evidence base for over-the-counter medication

Paracetamol and ibuprofen are effective in reducing fever, but UK guidelines recommend they should only be used in children who are unwell or distressed. Either could be used as monotherapy and, if the first is not helping, switch to the other. If both appear to be ineffective, consider alternating between the two (Wong et al., 2013).

Nonpharmacological intervention – tepid sponging

Two reviews by Meremikwu and Oye-Ita (2002, 2003) considered the effect of physical cooling methods – for example, tepid sponging for reducing fever. Conclusions from both reviews were guarded in stating effectiveness due to the small number of trials reviewed that met their inclusion criteria. This does not mean to say that these approaches are ineffective but that better, larger trials are required.

Practical prescribing and product selection

Prescribing information relating to medicines for fever is discussed and summarized in Table 10.9; useful tips relating to patients presenting with fever are given in Hints and tips Box 10.5.



Table 10.9
Practical prescribing: Summary of medicines for fever

Name of medicine	Use in children	Very common (>1/10) or common (>1/100) side effects	Drug interactions of note	Patients in whom care is exercised	Pregnancy and breastfeeding
Paracetamol ^a	>3 months	None	None	None	Not applicable
Ibuprofen		GI disturbances		Children with known hypersensitivity to NSAIDs	

^aNote: Paracetamol from 2 months for postimmunization pyrexia.

HINTS AND TIPS BOX 10.5: FEVER

Drinking fluids Children should be told to drink additional fluids to prevent dehydration because a fever will make them sweat more than usual.

Paracetamol

Paracetamol (e.g., Calpol is available in a number of dosage forms – liquid, soluble tablets, sachets, and melt tabs). Dosing of paracetamol in children falls into a number of age groups (Table 10.10).

For all age groups, the maximum number of doses per day is four. Paracetamol has no commonly occurring side effects, does not interact with any medicines, and so can be safely taken by all children.

Ibuprofen

Ibuprofen (e.g., Nurofen, Calprofen) can be given to children older than 3 months. Doses for ibuprofen, like paracetamol, are age-dependent. The dosing schedule that follows is taken from the British National Formulary (note that some OTC products' dosing schedules are different than these):

- Age, 3 to 5 months: 50 mg, three times a day.
- Age, 6 to 11 months: 50 mg, three or four times a day.
- Age, 1 to 3 years: 100 mg, three times a day.
- Age, 4 to 6 years: 150 mg, three times a day.
- Age, 7 to 9 years: 200 mg, three times a day.
- Age, 10 to 11 years: 300 mg, three times a day.

Ibuprofen can cause gastrointestinal side effects, such as nausea and diarrhoea, and also interacts with many other medicines, although medicines that interact with ibuprofen are very unlikely to be taken by children. Any child who has previously taken a nonsteroidal antiinflammatory drug

Table 10.10
Dosing schedule for paracetamol

3–5 months	2.5 mL	120 mg/5 mL
6–23 months	5.0 mL	
2–3 years	7.5 mL	
4–5 years	10 mL	
6–7 years	5 mL	250 mg/5 mL
8–9 years	7.5 mL	
10–11 years	10 mL	

(NSAID) and had an allergic reaction to it should avoid ibuprofen.

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Infectious childhood conditions**Background**

A number of infectious diseases are more prevalent in children than the rest of the population. Many of these diseases are now vaccine-preventable, and the provision of immunization programmes has almost eradicated them from developed countries. However, some conditions have no vaccine or incomplete vaccine cover is provided, which means contraction of the disease is still possible. This usually results in the child suffering from mild symptoms from which a full and speedy recovery is made but, in some cases (e.g., measles and meningitis), infection can result in death.

Most likely conditions to be encountered**Chickenpox**

Chickenpox is very common and is probably the most likely infectious childhood rash seen in community pharmacy (in

the UK, >80% of people have been infected by the age of 10 years). It is the primary infection observed when the patient contracts the varicella zoster virus, which is transmitted by droplet infection or with contact with vesicular exudates. The incubation period ranges from 10 to 20 days and, before the rash develops, the patient might experience up to 3 days of prodromal symptoms that could include fever, headache, and sore throat. The rash typically begins on the face, stomach, and back before spreading to other parts of the body. Initially, lesions appear as small red lumps that rapidly develop into vesicles, which crust over after 3 to 5 days. New lesions tend to occur in crops of three to five for the first 4 days; at the height of infectivity, lesions appear in all stages of development (Fig. 10.4). The vesicles are often extremely itchy, and secondary bacterial infection due to the vesicles being scratched is not unusual. Chickenpox is highly contagious, from a few days before the onset of rash until all lesions have crusted over. Reinfection results in people suffering from shingles (Fig. 10.5). A vaccination has been available since the mid-1990s and has shown to be 70% to



Fig. 10.4 Chickenpox. From White G. (2004). *Color atlas of dermatology* (3rd ed.). Churchill Livingstone: Elsevier.



Fig. 10.5 Typical dermatomal distribution of herpes zoster. From Wilkinson, W., Shaw, S., & Orton, D. (2004). *Dermatology in focus*. Churchill Livingstone: Elsevier.

90% effective. It is part of standard vaccination schedules in countries such as the United States and Australia but currently not the UK.

Molluscum contagiosum

Caused by a pox virus, molluscum contagiosum is usually transmitted by indirect contact – for example, sharing towels – although it is not very contagious. The face and axillae are common sites of infection. They generally appear in crops and appear as pink, pearl-like spots usually less than 0.5 cm in diameter. All lesions have a central punctum that is a diagnostic feature (Fig. 10.6). Confusion should not arise with other conditions other than viral warts (for further information on warts, see Chapter 8). The condition will spontaneously resolve (usually within 12 months) but if



Fig. 10.6 Molluscum contagiosum. From Gawkrödger, D. J. (2007). *Dermatology: An illustrated colour text* (4th ed.). Churchill Livingstone: Elsevier.



Fig. 10.7 Impetigo. From Habif, T. B. (2010). *Clinical dermatology: A color guide to diagnosis and therapy*. Mosby: Elsevier.

the parent or child is anxious, referral to the GP should be made because liquid nitrogen can be used to remove the lesions.

Impetigo

Impetigo is caused by a bacterial infection, most notably *Staphylococcus aureus* or *Streptococcus pyogenes*. It presents mainly on the face, around the nose and mouth. It usually starts as a small, red, itchy patch of inflamed skin that quickly develops into vesicles that rupture and weep. The exudate dries to a brown-yellow sticky crust (Fig. 10.7). It is contagious, and children should be kept off school until the lesions have healed, dried, and crusted over. General hygiene measures should include not sharing towels, which will help stop household contacts contracting the infection. Treatment involves topical or systemic antibiotics (e.g., fusidic acid or flucloxacillin), which currently are not available OTC in most Western countries.

Unlikely conditions to be encountered

Scarlet fever

Scarlet fever is a notifiable infectious disease caused by the bacteria *Streptococcus pyogenes*. Twelve to 48 hours prior to the rash developing, patients may present with sore throat, headache, and low-grade fever. The rash, which is blanching, starts on the abdomen before spreading to the neck, limbs, and extremities. The rash has a rough, sandpaper-like texture.

Erythema infectiosum

Erythema infectiosum is also called *slapped cheek disease* or *fifth disease*. It is caused by parvovirus B19 and

predominantly affects children between the ages of 3 and 15 years. Coldlike symptoms appear a couple of days before the rash appears. Typically, the rash appears on the cheeks and presents as red and inflamed marks (like the person has been slapped). Itch is often present, and the rash can spread to the arms and legs. Low-grade fever may also occasionally be present.

Glandular fever

Glandular fever (infectious mononucleosis) is caused by the Epstein-Barr virus and is most commonly seen in patients aged between 15 and 24 years. In Western countries, it is rare in children younger than 5 years and less frequent in those aged between 5 and 14.

It is transmitted from close salivary contact and is also known as the *kissing disease*. It has an incubation period of 4 to 7 weeks. Symptoms are vague but characterized by fatigue, headache, sore throat, and swollen and tender lymph glands. A macular rash can also occur in a small proportion of patients. The symptoms tend to be mild but can linger for many months.

Roseola infantum

Roseola infantum (also called *sixth disease*) is caused primarily by human herpesvirus (HHV)-6. It is most commonly seen in children aged 6 to 24 months. Children develop a high-grade fever that lasts 3 to 5 days before a macular rash develops on the trunk, which can spread to proximal extremities.

Very unlikely conditions to be encountered

Meningitis

The peak incidence of contracting meningitis is between 6 and 12 months old. Signs and symptoms are nonspecific in the early stages of the disease and are similar to flu. Symptoms range from fever, nausea, vomiting, headache, and irritability. Symptoms can develop quickly, in a matter of hours, and can be unpredictable, especially in infants and young children. Symptoms of fever, lethargy, vomiting, and irritability are common in children aged between 3 months and 2 years. In infants, floppiness and a dislike of being handled are also common features. Symptoms more common in older children include severe headache, stiff neck, and photophobia. Any child who experiences neck pain when asked to place the chin on the chest must be immediately referred.

In the latter stages of the disease, a petechial or purpuric nonblanching rash characteristically develops in meningococcal infection. Since the introduction of the UK vaccine schedule, the numbers of confirmed meningitis cases have

fallen to an all-time low, with less than 1000 cases seen in 2017–2018.

Measles

Measles is caused by an RNA virus and spread by droplet inhalation. Approximately 7% of patients develop respiratory complications such as otitis media and pneumonia, but encephalitis is seen in about one in every 600 to 1000 cases of measles.

Measles has an incubation period of between 7 to 14 days, which is then followed by 3 or 4 days of prodromal symptoms, where the child will have a fever, head cold, cough, and conjunctivitis. Small white spots are visible on the inner cheek and gums, like grains of salt, and are known as *Koplik's spots*; these are diagnostic for measles. A blotchy maculopapular rash appears around the ears before moving to the trunk and limbs. Immediate referral to the GP is needed.

Mumps

Mumps is caused by a paramyxovirus and is transmitted by airborne droplets from the nose and throat. It is the least contagious of the childhood diseases and requires close personal contact before infection can occur. There is an incubation period of 16 to 21 days, after which symptoms of fever and malaise typically occur a day or so before swelling of the parotid glands. The child will experience pain when the mouth is opened.

Mumps is much more unpleasant if contracted as an adult, and in 20% to 30% of men the disease affects the testicles, with a serious infection possibly causing sterility. The most serious complication from mumps is meningitis (seen in ~10% of people).

German measles (rubella)

Rubella is caused by an RNA virus and spread by close personal contact or airborne droplets. It is less contagious than measles and, if contracted, many people suffer from mild symptoms, and the infection can pass undiagnosed. After the incubation period of 14 to 21 days, the child experiences up to 5 days of prodromal symptoms, which include coldlike symptoms and swollen glands in the neck before a rash appears on the face, which quickly moves to the trunk and extremities. The rash tends to be pinpoint and macular. The biggest threat posed by rubella is to women in early pregnancy because foetal damage is possible.

To aid the differential diagnosis of childhood conditions, see [Table 10.11](#).

Websites

Charities: <https://www.meningitis.org> and <https://www.meningitisnow.org>

Nappy (diaper) rash

Background

Nappy rash (also known as *nappy dermatitis* or *diaper rash*) is a nonspecific term used to describe inflammatory eruptions in the nappy area.

Prevalence and epidemiology

The incidence and prevalence of nappy rash are difficult to determine because of variability among studies, but in one UK study 25% of infants younger than 1 month had an episode of nappy rash, and most newborns will exhibit some skin breakdown in the first few weeks.

Aetiology

Friction and maceration of the skin are key to its cause. This is compounded by excessive heat and moisture combined with the effect of faecal and urinary enzymes when in prolonged contact with the skin (faeces breakdown produces ammonia, and is considered a contributory cause, because ammonia is only an irritant when in contact with damaged skin). Greater exposure of skin surfaces to moisture impairs the skin's barrier function and makes the skin more susceptible to secondary infection.

Arriving at a differential diagnosis

The diagnosis is straightforward, although identifying the cause can be more difficult. There are four forms of nappy rash, with irritant nappy rash being the most common. [Table 10.12](#) highlights the key differences in symptom presentation among the four forms.

Clinical features of irritant nappy rash

The rash affects primarily the buttocks (the area in contact with the irritant) but can involve the lower abdomen and upper thighs. The flexures, which are protected from exposure, are usually spared.

Conditions to eliminate

Secondary infection

An environment that is wet and warm creates an ideal breeding ground for opportunistic infections. Most commonly secondary infections are caused by *Candida albicans* (but other pathogens such as *S. aureus* can be involved). Candidiasis is associated with satellite lesions (i.e., away from the main skin involvement). The lesions tend to be papular or pustular.

Table 10.11
Differential diagnosis of childhood conditions

Sign or symptom	Measles	German measles	Meningitis	Glandular fever	Chickenpox	Molluscum contagiosum	Mumps	Impetigo	Erythema infectiosum	Scarlet fever	Roseola
Prodromal stage											
Fever	Yes	No	Yes	Yes	Yes, in older individuals	No	Yes	No	No	Yes	Yes
Swollen glands	No	Yes	No	Yes	No	No	Yes	No	No	No	No
Coldlike symptoms	Yes	Yes	No	No	No	No	No	No	Yes	Yes	No
Other signs	Koplik's spots	Malaise	Lethargy, stiff neck, vomiting, photophobia	Malaise, headache	Malaise, headache	None	None	None	None	None	None
Rash											
Location	Ears and face, progressing to trunk and limbs	Face moving quickly to trunk	Trunk and limbs	Trunk	On trunk and face; rarely on extremities	Face and axillae	Not applicable	Facial area, especially around nose and mouth	Face before moving to arms and legs	Abdomen before spreading to the neck, limbs, extremities	Trunk and limbs
Character	Maculopapular	Macules, often pinpoint by day 2	Purplish blotches; do not blanch	Maculopapular; ~10% have rash	Lesions discrete and appear in crops	Pink pearl-like spots with central punctum ^a	Vesicles that exude forming yellow crusts	'Slapped' skin	Blanching	Blanching	Blanching
Epidemiology											
Age group most affected	Children and adolescents	Children <12 years	90% before age of 5	15- to 24-year-olds most at risk	Very common in children	Young children	Children <12 years	School-aged children	Children, adolescents	Children <8 years	<1 year
^a Diagnostic.											

Table 10.12
Differences in symptom presentation between the four causes of nappy rash

Presentation	Irritant	Candidal	Seborrhoeic	Psoriasiform
Flexure involvement	No	Yes	Yes	Yes
Satellite lesions	No	Yes	No	No
Other sites involved	No	Yes	Yes	Yes
Rash description	Red, raw	Bright red and well demarcated	Shiny/greasy	Atypical for psoriasis as usually no scaling is present

Seborrhoeic dermatitis

Seborrhoeic dermatitis presents as a rash, which is bright red and confluent. The flexures are not spared, and the rash can take on a diffuse, red, shiny or greasy look. It is common for other sites to be involved, such as the scalp and face.

Psoriasiform nappy eruptions

Infants usually develop this form of nappy rash within the first 4 months of life. It presents as well-demarcated erythematous plaques. It can show scaling that resembles psoriasis, although this is uncommon. Involvement away from the nappy area is common and affects the limbs, face, and scalp.

! TRIGGER POINTS indicative of referral: Nappy rash

Symptoms/signs	Possible danger/reason for referral	Urgency of referral
Involvement of rash away from nappy area	Suggests other causes such as psoriasis	As soon as practicable
OTC treatment failure	Requires prescription-only treatments	
Severe rash		

Evidence base for over-the-counter medication

Management centres on reducing skin irritation (Box 10.6), applying a protective layer of barrier cream, and reducing any inflammation and/or eliminating infection. Barrier creams are designed to rehydrate and soothe the skin. A number of chemical constituents have been formulated into barrier creams and include silicone, antiseptics, and protectorants. Many proprietary products are available and often consist of a combination of ingredients. Secondary infection with *Candida* can be treated with imidazole products.

Practical prescribing and product selection

Barrier creams and protectorants should be applied to all skin surfaces, including the skin folds, after each nappy change. They have no side effects, although some products do contain potential sensitizing agents; it is best to patch-test an area of skin before application. Commonly prescribed products include Drapolene, Metanium, and Sudocrem.

For cases causing discomfort (in general, those that are secondarily infected with *Candida*), the use of an imidazole twice a day is recommended. Parents should be told not to use a barrier cream until the infection has settled.

Further reading

Baer, E. L., Davies, M. W., & Easterbrook, K. (2006). Disposable nappies for preventing napkin dermatitis in infants. *Cochrane Database System Review*, 3:CD004262. <https://doi.org/10.1002/14651858.CD004262.pub2>. <https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD004262.pub2/full>.

HINTS AND TIPS BOX 10.6: NAPPY RASH

Preventive measures	<p>Leave the nappy off for as long as possible each day.</p> <p>Avoiding using soaps for cleaning.</p> <p>Washed nappies should be thoroughly rinsed to ensure that they do not contain residues of soap and detergent.</p> <p>Change nappies as soon as they have been soiled.</p>
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Self-assessment questions

The following questions are intended to supplement the text. Two levels of questions are provided, multiple-choice questions and case studies. The multiple-choice questions are designed to test knowledge and application of knowledge, and the case studies allow this knowledge to be put in context in patient scenarios.

Multiple-choice questions

- 10.1** A 12-week-old baby is brought to the pharmacy by his mother. He has a sore mouth. What is the most likely diagnosis?
- Teething
 - Mouth ulcer
 - Thrush
 - Leukoplakia
 - Herpes simplex
- 10.2** Which measurement of fever does NICE (National Institute of Health and Clinical Excellence) recommend for children younger than 5 years?
- Underarm
 - Forehead
 - Oral
 - Anal
 - Either oral or under arm
- 10.3** Mrs Ng tells you that while combing her daughter's hair, she saw a head louse. You decide to advise a dimeticone lotion, and Mrs Ng asks how to use it. Which one of the following is the most appropriate way to apply the lotion?
- Apply once only.
 - Apply today, then reapply every 7 days for the next 2 weeks.
 - Apply today, then reapply in 7 days' time.
 - Apply today, then reapply at 3- to 4-day intervals for the next 2 weeks.
 - Apply today, then reapply twice more at 14-day intervals
- 10.4** What confirms the presence of a head louse infection?
- Presence of egg cases (nits) in the hair
 - An itchy scalp
 - A live louse
 - Louse faeces on the pillow
 - Dead lice on a pillow
- 10.5** Which statement concerning threadworm management is incorrect?
- All family members should be treated.
 - Mebendazole can be given from 6 months upwards.
 - A repeated dose after 14 days is recommended.
 - Mebendazole can cause GI upset.
 - Bed linens should be washed at start of treatment.
- 10.6** Nappy rash that becomes secondarily infected with *Candida* is most commonly associated with which of the following?
- Itch and pain
 - Shiny, bright red lesions
 - Satellite lesions
 - Flexure involvement
 - Scaling lesions
- 10.7** Which sign or symptom represents high risk in children younger than 5 years with fever?
- Decreased activity
 - Respiration rate of less than 50 breaths/min
 - Reduced urine output
 - Pallor
 - Reduced skin turgor
- 10.8** At what age does colic usually resolve?
- Within the first few weeks of birth
 - Before 6 months old
 - Between 6 and 12 months
 - Between 12 and 18 months
 - Before the age of 2 years old
- 10.9** Mrs Brown requests treatment for her 7-year-old son, James. He has confirmed active head lice infection. James has not had a previous infection. He has asthma and uses a salbutamol inhaler when required and beclometasone 100- μ g inhaler, two puffs twice daily. Which one of the following is the most appropriate treatment?

- a. Dimeticone 4% lotion, applied to the hair for 8 hours before rinsing and repeated after 7 days.
- b. Lyclear Spray & Comb, applied to the hair for 15 minutes before rinsing and repeated after 14 days.
- c. Permethrin 1% creme rinse, applied to the hair for 10 minutes before rinsing and repeated after 7 days
- d. Bug buster kit to be used immediately and repeated after 7 days
- e. Malathion 1% cream shampoo, applied to the hair for 10 minutes before rinsing and repeated after 7 days

10.10 Young children are prone to otitis media. Which of the symptom clusters best reflects the signs and symptoms of otitis media in this age group?

- a. Irritability and crying
- b. Irritability, crying, and pain
- c. Irritability, crying, fever, and pain
- d. Irritability and pain
- e. Irritability and fever

10.11 A mother of a 5-year-old daughter wants some advice. Her daughter has developed a rash on her face. Based solely on this information, which is the most likely condition causing the rash?

- a. Pertussis
- b. Psoriasis
- c. Atopic dermatitis
- d. Erythema infectiosum
- e. Pityriasis rosea

10.12 Warts are a common skin condition seen in children. Which symptoms best describe warts?

- a. Raised smooth papules
- b. Raised hyperkeratotic papules
- c. Raised papules with central dimples
- d. Raised waxy lesions
- e. Raised crusty lesions

10.13 Itchy rash with which of the following symptom(s) or history is most indicative of atopic dermatitis?

- a. Family history of asthma
- b. Personal history of asthma
- c. Visible eczema
- d. Onset of symptoms before the age of 1 year
- e. Family history of eczema

10.14 Which infection is most likely to present with fever as the major symptom in children?

- a. Upper respiratory tract infection

- b. Lower respiratory tract infection
- c. Urinary tract infection
- d. Impetigo
- e. Atopic dermatitis

10.15 Which statement best describes the rash of measles?

- a. Rash appears around the ears before moving to the trunk and limbs.
- b. Rash appears on the face that quickly moves to the trunk and extremities.
- c. Rash starting on the abdomen before spreading to the limbs, and extremities.
- d. Rash appears on the trunk and limbs.
- e. Rash typically begins on the face, stomach, and back.

Questions 10.16 to 10.21 concern the following:

- A. Chickenpox
- B. Molluscum contagiosum
- C. Fifth disease (erythema infectiosum)
- D. Impetigo
- E. Psoriasis
- F. Atopic dermatitis
- G. Roseola infantum

Select, from A to G, which of the conditions:

10.16 Is associated with a facial rash, often resembling a 'slapped cheek'?

10.17 Can be mistaken for warts?

10.18 Can lead to shingles in later life?

10.19 Commonly affects cheeks and behind the knee

10.20 Is associated with high-grade fever?

10.21 Is caused by bacterial infection?

For questions 10.22 to 10.25, select the most likely diagnosis in each of the following scenarios:

- A. Chickenpox
- B. Measles
- C. Fifth disease (erythema infectiosum)
- D. Impetigo
- E. Rubella
- F. Scarlet fever
- G. Pertussis

10.22 A 7-year-old girl who is sent home from school because she developed multiple vesicles on her face and arms.

10.23 An 18-month-old boy appears irritable and unwell with a fever that lasts 2 days but then subsides, only to develop a maculopapular rash on his body.

10.24 A 5-year-old girl is sent home from school because she feels poorly. She has been suffering coldlike symptoms

the previous couple of days. Later that night, her mum notices a widespread rash on her face and body.

10.25 A 9-year-old girl has a sore throat, and examination reveals red spots on her palate. A day later, her father notices a fine red rash over the whole body.

Answers

10.1 Answer: c

Rationale: Based on age, leukoplakia (d) is associated with old age; mouth ulcer (b) and herpes simplex (e) are more likely with older children; teething (a) normally starts at around 6 months.

10.2 Answer: a

Rationale: NICE guidance states avoidance of oral and rectal routes (see section 3.2.1 of the guidance) due to unacceptability in clinical practice, and forehead thermometers are unreliable.

10.3 Answer: c

Rationale: All products need to be reapplied, thus discounting option (a). Option d is the schedule for wet combing; options (b) and (d) are incorrect because current recommendations state reapplication should only be done once.

10.4 Answer: c

Rationale: Faecal matter (d), dead lice (e), and egg cases (a) could suggest recent or current infection but are not diagnostic. Other causes of itchy scalp (b) are possible other than lice. Only confirmation of live lice (c) is truly diagnostic.

10.5 Answer: b

Rationale: Only (a) is not true. There is no need to treat asymptomatic people.

10.6 Answer: c

Rationale: Fungal infections tend to show involvement away from the presenting lesions (c). Itch and pain (a) are not associated with nappy rash; shiny lesions (b) and flexure involvement (d) are noted with seborrheic dermatitis (b); scaling lesions can be seen with psoriasis (e).

10.7 Answer: e

Rationale: Options (a), (c), and (d) are all amber risk, and (b) is green. Option (e) is classified as red – high risk.

10.8 Answer: b

Rationale: Colic is associated with infants, so options (c) to (e) can be ruled out. Option a is when colic starts rather than stops.

10.9 Answer: a

Rationale: Shampoos (e) and crème rinses (c) are no longer recommended; the dosing schedule for (d) is

incorrect. Options a and b are dimeticone products, and dosing is appropriate, but repeat applications are different, with a being right and b wrong.

10.10 Answer: c

Rationale: Pain is most commonly seen, so this eliminates options (a) and (e). Crying is also prominent and thus eliminates option d. Options (b) and (c) are both possible but fever is often seen; thus c is the correct option.

10.11 Answer: d

Rationale: Pertussis (a) does not have facial rash; psoriasis (b) can have scalp involvement but lesions away from the hairline are rare; pityriasis rosea (e) is associated with a rash on the body. This leaves atopic dermatitis (c) and erythema infectiosum (d); both could show facial lesions. Based on probabilities, erythema infectiosum (d) is more likely. Indeed, its alternative name is slapped cheek disease.

10.12 Answer: b

Rationale: All options have a descriptor of being raised, and hence is of no value. Warts are, however, associated with excessive cell turnover and results in hypertrophy; thus, the answer is (b). Option (a) could be a host of skin problems – the descriptor is very broad; (c) could be molluscum contagiosum because of the central dimple reference; likewise, (d) could be seborrheic warts because they are associated with wax-like lesions. Finally, (e) could suggest cancer-like growths.

10.13 Answer: d

Rationale: Although a family history of atopy (a and b) is associated with atopic dermatitis, in this case it is not most indicative. Visible flexural eczema is a symptom, but c only states visible eczema. Dry skin is associated with atopic dermatitis, but guidance states the last 12 months. Hence, option (d) is the correct answer.

10.14 Answer: c

Rationale: Atopic dermatitis (e) is not an infection so it can be ruled out straight away. Impetigo (d) is not associated with fever. Options a, b, and c could have fever as a symptom; however, from these options, only urinary tract infection (c) is likely to have fever as a prominent feature.

10.15 Answer: a

Rationale: Options (b) describes German measles; (c) is scarlet fever; (d) describes sixth disease, and (e) chickenpox.

10.16 Answer: c

Rationale: Facial lesions can occur with chickenpox (A), molluscum contagiosum (B), fifth disease (C), impetigo (D), and atopic dermatitis (F). Chickenpox, molluscum contagiosum, and impetigo and psoriasis have raised lesions. This leaves (C) as the correct answer.

10.17 Answer: B

Rationale: (C), (E), (F) and (G) are flat lesions and can be discounted; (A) is vesicular, and (D) is crusting and so can be eliminated. This only leaves (B).

10.18 Answer: A

Rationale: Shingles is caused by the herpes zoster virus, and so too is chickenpox. Hence, option (A) is the correct answer.

10.19 Answer: F

Rationale: Chickenpox (A) is seen on the face and trunk; molluscum contagiosum (B) is also seen on the trunk; fifth disease (C) and impetigo (D) is on the cheeks but not the knees; psoriasis (E) can be knees (but on the front, not back), and not the face; roseola infantum is the trunk and arms.

10.20 Answer: G

Rationale: Molluscum contagiosum (B), fifth disease (C), psoriasis (E), and atopic dermatitis (F) are not associated

with fever. Impetigo (D) can produce fever but is uncommon and low-grade; fever in chickenpox is also low grade.

10.21 Answer: D

Rationale: Chickenpox (A), molluscum contagiosum (B), fifth disease (C), and roseola infantum (G) are viral; psoriasis and atopic dermatitis (F) have mixed causes but viral causes are not implicated.

10.22 Answer: A

Rationale: Facial rash is seen in chickenpox (A), measles (B), fifth disease (C), impetigo (D) and rubella (E). However, the only condition that is vesicular is chickenpox.

10.23 Answer: B

Rationale: Impetigo (D) does not have prodromal symptoms and can be eliminated. Chickenpox (A) has a vesicular rash, and mumps (G) does not exhibit a rash. This leaves measles (B), fifth disease (C), rubella (E), or scarlet fever (F) as plausible options, but measles rash tends to be maculopapular.

10.24 Answer: E

Rationale: See answer 10.23; plus, rubella tends not to exhibit fever compared with measles.

10.25 Answer: F

Rationale: See answer 10.23, plus sore throat can be seen in chickenpox (A) and scarlet fever (F). Chickenpox rash tends to be facial and on the trunk rather than all over the body.

Self-assessment questions

The following questions are intended to supplement the text. Two levels of questions are provided: multiple choice questions and case studies. The multiple choice questions are designed to test knowledge and application of knowledge, and the case studies allow this knowledge to be put in context in patient scenarios.

Multiple choice questions

10.1 The common name of nits refers to:

- a. An adult female head louse
- b. An adult male head louse
- c. An immature head louse
- d. Egg cases
- e. Live eggs

- b. 5
- c. 7
- d. 10
- e. 14

10.2 Which antihistamine cannot be sold OTC for pruritus?

- a. Chlorphenamine
- b. Clemastine
- c. Cyproheptadine
- d. Loratadine
- e. Promethazine

Questions 10.7 to 10.9 concern the following conditions:

- A. Chicken pox
- B. German measles
- C. Glandular fever
- D. Impetigo
- E. Measles

10.3 A high-grade fever is defined as a temperature above?

- a. 37°C
- b. 37.5°C
- c. 38.5°C
- d. 39.5°C
- e. 40°C

Select, from A to E, which of the above conditions:

- 10.7 Is often caused by *Staphylococcus*?
- 10.8 Is characterized by a vesicular rash?
- 10.9 Is transmitted by close salivary contact?

10.4 What are the usual ages that children present with atopic dermatitis?

- a. In the first month of life
- b. Before 6 months
- c. Before 1 year
- d. Before 2 years
- e. Before 5 years

Questions 10.10 to 10.12 concern the following medicines:

- A. Chlorphenamine
- B. Clotrimazole
- C. Dimeticone
- D. Mebendazole
- E. Permethrin

10.5 Mebendazole can be given to patients from what age (years)?

- a. 1
- b. 2
- c. 3
- d. 4
- e. 5

Select, from A to E, which of the above medicines:

- 10.10 Is associated with sedation?
- 10.11 Is contraindicated in all trimesters of pregnancy?
- 10.12 Can cause abdominal pain?

10.6 How many days after initial treatment should a second application of insecticide be used to eradicate head lice?

- a. 3

Questions 10.13 to 10.17: for each of these questions *one or more* of the responses is (are) correct. Decide which of the responses is (are) correct. Then choose:

If a, b and c are correct

If a and b only are correct

If b and c only are correct

If a only is correct

If c only is correct

Directions summarized

A	B	C	D	E
a, b and c	a and b only	b and c only	a only	c only

10.13 Napkin dermatitis caused by an irritant presents with

- Flexural sparing
- Satellite lesions
- Skin scaling

10.14 Atopic dermatitis can be defined as itchy skin plus

- History of dry skin
- Flexural eczema
- A personal history of other atopic disease

10.15 Which statement(s) about head lice treatment is/are true

- Shampoos are not effective
- Physical agents are the current treatment of choice
- Insecticides can be used prophylactically

10.16 Which of the listed symptoms about headache in a young child would raise sufficient concern to refer to a doctor?

- Irritability
- Fever
- Photophobia

10.17 Which statements about treating fever with analgesia are true?

- Paracetamol is effective in reducing fever
- Alternating between paracetamol and ibuprofen is not recommended
- Evidence for tepid sponging is inconclusive

Questions 10.18 to 10.20: these questions consist of a statement in the left-hand column followed by a statement in the right-hand column. You need to:

- Decide whether the first statement is true or false
- Decide whether the second statement is true or false

Then choose:

- If both statements are true and the second statement is a correct explanation of the first statement
- If both statements are true but the second statement is NOT a correct explanation of the first statement
- If the first statement is true but the second statement is false
- If the first statement is false but the second statement is true
- If both statements are false

Directions summarized

	1st statement	2nd statement	
A	True	True	2nd explanation is a correct explanation of the 1st
B	True	True	2nd statement is not a correct explanation of the 1st
C	True	False	
D	False	True	
E	False	False	
	First Statement		Second statement
	10.18 Emollients are the mainstay of treatment of atopic dermatitis		Products with lanolin should be avoided
	10.19 Oral temperature is the most accurate measure of temperature		Normal body temperature is 37°C
	10.20 Measles is vaccine preventable		It is usually given as a triple vaccine

Answers

10.1 Answer: d

Rationale: Nits is the lay name the general public often use to describe a head lice infestation. In reality the 'nit' describes the empty yellow-white eggshells that are left when the lice hatch.

10.2 Answer: d

Rationale: Antihistamines are routinely used to help treat pruritus. Clemastine (b) and Cyproheptadine (c) have specific indications for pruritus; chlorphenamine is specifically indicated for the symptomatic relief of itch associated with chickenpox; promethazine (e) can be used to help pruritus associated with insomnia; Loratadine has no specific indication for pruritus.

10.3 Answer: e

Rationale: Normal body temperature is defined as 37°C (a); low grade fevers tend to be less than 40°C (options b–d).

10.4 Answer: b

Rationale: Epidemiological data shows that it usually starts within the first 6 months of life and predominantly affects young children.

10.5 Answer: b

Rationale: Convulsions in young children (under 1 year of age) have been reported on rare occasions. As mebendazole has been little studied in those under 2 years of age, the manufacturers only have a product licence from over this age.

10.6 Answer: c

Rationale: Reapplication of headlice treatment is recommended to ensure any larva hatched after the first treatment are killed; this is currently recommended after 7 days.

10.7 Answer: D

Rationale: The only condition listed that is bacterial in origin is impetigo (D); all others are viral.

10.8 Answer: A

Rationale: Glandular fever (C) rarely causes rash; measles (D) or German measles (B) are macular or maculopapular; impetigo (E) can be vesicular but rapidly exude and crust over.

10.9 Answer: C

Rationale: Chicken pox (A) is transmitted by droplet infection or with contact with vesicular exudates as is German measles (B); measles is via droplet infection; impetigo (E) is contracted through contact with exudate or items the infected person has touched.

10.10 Answer: A

Rationale: Clotrimazole (A), dimeticone (C) and Permethrin (E) are topical products and will not cause sedation; mebendazole, whilst associated with side effects such as abdominal pain (see Q10.12) is not associated with causing sedation.

10.11 Answer: D

Rationale: Contraindications tend to be when the patient takes medicines via the oral route. This only leaves chlorphenamine and mebendazole to consider. Chlorphenamine appears to be safe in pregnancy and is the recommended antihistamine.

10.12 Answer: D

Rationale: See answer to Q10.10

10.13 Answer: D

Rationale: As the cause is an irritant it will only affect the skin surface it comes into contact with; therefore areas of skin that are in the folds will not be affected; likewise, satellite lesions are lesions seen away from the main rash and are associated with infection. Irritants, as stated earlier, will only cause rash from direct contact.

10.14 Answer: A

Rationale: Criteria are available to establish if the person has atopic dermatitis. All three listed would be expected findings, with history of dry skin within the last 12 months.

10.15 Answer: B

Rationale: No products should be used as a preventative as this is ineffective, as are shampoos in the treatment. Currently, products containing ingredients such as dimeticone are the treatment of choice as they have relatively high cure rates and are comparable to or better than insecticides.

10.16 Answer: A

Rationale: Headaches in children are relatively uncommon and normally associated with viral infections associated with coughs and colds. Irritability and photophobia are certainly not symptoms that one would normally think of in a child presenting with headache. Fever associated with headache in a young child is possible (infection possible) but requires further investigation.

10.17 Answer: a

Rationale: Paracetamol can reduce fever, and evidence shows that a management strategy can be switching between paracetamol and ibuprofen. Reviews have also looked at tepid sponging, but numbers in trials are low to make any firm conclusions as to its effectiveness.

10.18 Answer: B (True/True – statement 2 not correct explanation of statement 1)

Rationale: Whilst emollients have little evidence, they are routinely used and recommended as the treatment of choice to control symptoms and skin dryness, and those with lanolin can cause sensitization so are best avoided.

10.19 Answer: D (False/True)

Rationale: Whilst normal body temperature is 37°C and is usually taken via the oral route, the most accurate way of measuring it in younger children is under the arm.

10.20 Answer: B (True/True – statement 2 not correct explanation of statement 1)

Rationale: Vaccination against measles is in the standard vaccination schedule (MMR vaccine) – measles, mumps and rubella.

Case studies

CASE STUDY 10.1

Ms JP, a young mother of two children, comes into the pharmacy one afternoon, clutching a letter from the children's primary school. The letter says that there is a head lice outbreak and instructs parents to treat their children for head lice.

a. How do you respond?

You need to find out if her children actually have head lice or she is trying to buy a product to stop them from getting head lice. She should be told that products cannot be bought to prevent her children contracting head lice, and she should inspect their heads regularly. Only when live lice are found should a product be bought. Ms JP should be told how to inspect her children's hair for signs of head lice.

Ms JP returns to the pharmacy 4 days later and says her youngest daughter now has head lice. She is 5 years old and suffers from no medical problems.

b. What product are you going to recommend?

Insecticides or a physical agent would be acceptable treatment options. Due to insecticidal resistance and

high cure rates seen with dimeticone, it would seem reasonable to use this as treatment of choice.

Ms JP says she has heard that you can use conditioner and that will get rid of the problem.

c. How do you respond?

Ms JP is probably referring to the 'bug-busting' technique. She should be told that the effectiveness of bug busting is dependent on how well people adhere to the regimen because poor compliance with the bug-busting method is probably why its effectiveness has been questioned.

Ms JP then asks you whether her older daughter, Samantha, should also be treated, even though she has not got head lice.

d. What do you say?

Only those with a live lice infestation should be treated. Ms JP should be asked to keep checking Samantha's hair on a regular basis.

Case study

CASE STUDY 10.1

A mother presents to your pharmacy with her 10-month-old girl. She asks you for some advice on treating her nappy rash.

a. What questions do you ask the mother?

- *What areas are affected?*
 - *Any involvement of the flexures, any satellite lesions, and any involvement of other sites away from the napkin area will all be helpful in differentiating the cause of the rash.*
- *What is the appearance of the rash?*
 - *Is it bright red or shiny and are there any pustules? Using this information in conjunction with the area affected will start to form a sign and symptom cluster that you can match up to the different causes of nappy rash.*
- *Was there a nappy change routine?*
 - *What type of nappies are being used?*
 - *What other things are done at nappy change time (e.g., use of wipes, use of barrier creams)?*
 - *How many changes per day?*
 - *This will help you to understand the level of occlusion and contact that faecal contents have with skin and again help with differentiation of the cause.*

The rash is primarily on the buttocks and does not go into the skin creases. It is red in colour. There are no other lesions. Her daughter is otherwise well, no past medical problems, and feeding normally. The mother uses disposable nappies.

You tell the mother that you think it is irritant nappy rash. She asks you what causes it.

b. What do you tell her about the cause of irritant nappy rash?

A number of factors contribute to the occurrence of nappy rash. However, friction and maceration (damage to the skin caused by prolonged exposure to moisture) appear to be the most important. Other factors, such as excessive heat and contact of faecal and urinary enzymes with the skin also play a role.

c. What advice do you give the mother regarding prevention of future episodes of nappy rash?

- *Leave the nappy off for as long as possible each day.*
- *Avoid using soaps for cleaning (use soap substitutes) or wipes that are perfumed or contain alcohol.*
- *Change nappies as soon as they have been soiled.*
- *The mother could apply a barrier cream to all skin surfaces, including the skin folds, after each nappy change.*

Unfortunately, the mother returns about a week later. She tells you that the rash has gotten worse. The rash has a distinct border, although there are also some small patches further out from the main rash, and the skin has a slightly pimply appearance. She thinks that the rash might be causing pain.

d. What do you think is the problem now?

There appears to be a secondary fungal infection.

e. The mother asks whether she should swap from disposables to cloth nappies because she has heard they are better for the baby and the environment. What do you say?

There is some evidence that disposable nappies are better for preventing nappy rash than cloth because they tend to keep the child dryer. The important thing is to make sure there are regular nappy changes.

f. What management for the nappy rash do you recommend?

The best treatment would be with a combination hydrocortisone/clotrimazole. Advise the mother to apply a thin layer two or three times a day, but this is not licenced for use in the UK OTC. The mother is therefore limited to reinforcing nappy change routines and using barrier creams to protect the skin and an antifungal cream to clear the infection. If inflammation remains a problem, then she needs to see the physician.

CASE STUDY 10.2

Mr PB is looking after his 4-year-old grandson for the weekend. He asks for some advice because he has noticed a rash on his grandson's body and wants something to help get rid of it.

a. What do you need to know?

You need to know:

- *The location of rash*
- *What the rash looks like*
- *When the rash appeared*
- *Associated symptoms such as itch*
- *General health of the child*
- *What symptoms, if any, the child had before the rash appeared*

All Mr PB is able to tell you is that his grandson has been with him for the past day and only noticed the rash this morning when he was dressing him. The rash is on his chest and back; Mr PB describes them as spots. He thinks it is probably itchy because he saw his grandson scratching this morning.

b. What do you think could be the problem?

Without seeing the child and the rash, it is always difficult to make a differential diagnosis from information from a third party, but it appears the child might have chickenpox, given his age, location of rash, and that the spots itch.

c. Are there any further questions you could ask the man to confirm your diagnosis?

Further questions you could ask are:

- *Are the spots coming out in groups?*
- *Have any of the spots turned into little blisters?*
- *Has he been exposed to other children with chickenpox?*

Knowing about the grouping and look of the spots is helpful because the chickenpox rash often appears in clusters. Knowing about prior exposure is very useful – this should help confirm your differential diagnosis.

d. Mr PB is unsure and concerned that his grandson is OK. What could you do?

It appears that his grandson is not doing poorly and, unless his condition deteriorates, there is probably no need to call the doctor. You could recommend an antihistamine to help with the itching and reassure him that his grandson will be OK, but if his symptoms become worse, the doctor should be contacted. You also tell him that the rash fits the description of chickenpox but without seeing the rash, you cannot be sure. It would therefore be useful if you could see the child or if the child could be seen by someone over the next couple of days to confirm your suspicions.

CASE STUDY 10.3

A mother of a 3-month-old girl asks for help with her baby; she seems to be crying all the time.

Information gathering	Data generated
Describe symptoms	Baby cries and will not be consoled, even after feeding, burping and nappy changes; brings knees to her chest as she cries
How long has she had the symptoms?	About 1 month but just not getting better.
Severity of pain, distress of child	Difficult to say, but she is obviously worse than other babies she knows about
Other symptoms or provoking factors?	Usually worse in the evening
Any previous symptoms?	Has always had times when she has cried a lot but is just far worse in the last month

Information gathering	Data generated
Additional questions	Baby is bottle-fed. Baby is gaining weight satisfactorily. No stomach distention, and baby is passing stool adequately. Mother has changed formula milk twice in the last month.
Past medical history	Bought a Gripe mixture last week on the advice of a relative. This seems to have had no effect.
Social history, which may include questions relating to smoking, alcohol intake, employment, personal relationships	Mother is frustrated and appears tired.
Family history	None for presenting complaint

Below summarizes the expected findings for questions when related to the different conditions that can cause excessive crying in infants seen by community pharmacists.

Condition	History	Weight gain	Systemic symptoms	Inconsolability
Colic	Weeks	OK	No	Yes
Infection	Days, hours	OK	Yes	Yes?
GORD	Weeks	OK	No	No
Intolerance to cow's milk protein	Weeks	Poor	No	No

When this information is compared to our patient's symptoms, we see that her symptoms most closely match a diagnosis of colic (✓ represents symptom match).

CASE STUDY 10.3 (Continued)

Condition	History	Weight gain	Systemic symptoms	Inconsolability
Colic	✓	✓	✓	✓
Infection	✗	✓	✗	✓?
GORD	✓	✓	✓	✗
Intolerance to cow's milk protein	✓	✗	✓	✗

GORD is possible and, to eliminate this, further questions about regurgitation and the duration of the crying could be asked.

Because colic is the likely cause, reassure the parent that symptoms are transient. Although something

has already been tried, it might be worth considering a dimeticone product or Colief for 1 week.

Safety net: If that fails to help, then referral to the GP is appropriate.

Specific product requests

In this chapter

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Background

Many patients will present in the pharmacy requesting a specific product rather than wanting advice on symptoms. Regardless of the reason why they are asking for the product, it is the responsibility of the pharmacist to ensure that the patient receives the most appropriate therapy. This chapter therefore deals with situations where patients ask for a particular product but where more information from the patient is needed before complying with their request.

Motion sickness

Background

Motion sickness is a symptom complex that is characterized by nausea, pallor, vague abdominal discomfort and occasionally vomiting. Symptoms of fatigue, weakness and an inability to concentrate can also be experienced. Symptoms tend to resolve over prolonged exposure to motion. For example, sea sickness disappears over time – a characteristic called adaptation or habituation. Motion sickness can affect any individual and involve any form of movement, from moving vehicles to fairground rides.

Prevalence and epidemiology

The exact prevalence of motion sickness is unknown. Children between the ages of 2 and 12 are most commonly

affected and it tends to affect women more than men. However, certain sectors of the population understandably show higher prevalence rates; for example, naval crew and pilots.

Aetiology

It is widely believed that motion sickness results from the inability of the brain to process conflicting information received from sensory nerve terminals concerning movement and position; the sensory conflict hypothesis. Motion sickness occurs when motion is expected but not experienced, or the pattern of motion differs from that previously experienced.

Evidence base for over-the-counter medication

First-generation antihistamines (cyclizine, cinnarizine and promethazine) and the anticholinergic hyoscine (also called scopolamine) are routinely recommended to prevent motion sickness. All have shown various degrees of effectiveness. A Cochrane review (14 studies, $N = 1025$) found scopolamine to be superior to placebo and metoclopramide, and as good as antihistamines (Spinks et al., 2011).

Ginger has long been advocated for use as an antiemetic. A review by Chrubasik et al. (2005) identified four studies with ginger in the prevention of motion sickness. The results suggested ginger was better than placebo, and similar in efficacy to other pharmacological agents. However, the studies involved small numbers of patients and were of uncertain quality; the authors of the review concluded that further studies are required to confirm the effectiveness of ginger.

Nonpharmacological approaches to prevent motion sickness are also available over-the-counter (OTC). Bruce et al. (1990) investigated the use of Sea Band acupressure bands versus hyoscine and placebo. Eighteen healthy volunteers were subjected to simulated conditions to induce motion sickness. The findings showed that while hyoscine exerted a preventative effect, Sea Bands were no more effective than placebo. Further trials have confirmed these findings, although one small trial by Stern et al. (2001) reported positive findings. Accurate placement of the pressure bands may be important because acupressure has shown positive effects for nausea and vomiting associated with pregnancy. However, another study examining two different acupressure bands (Refieband and Acuband) found no evidence of efficacy in reducing the development of motion sickness compared with placebo, irrespective of whether the bands were used appropriately or not (Miller & Muth 2004).

Summary

Current evidence indicates that hyoscine and first-generation antihistamines are effective. Choice between the various agents will be driven by patient acceptability.

Practical prescribing and product selection

Prescribing information relating to medicines for motion sickness reviewed in the section 'Evidence base for over-the-counter medication' is discussed and summarized in [Table 11.1](#). They are most effective when given before experiencing motion sickness and products should be selected based on matching the length of the journey with the duration of action of each medicine (see 'Hints and Tips' in [Box 11.1](#)).

Antihistamines

Antihistamines promoted for use in motion sickness are first-generation H₁ antagonists and are associated with sedation. They have the same side effects, interactions and precautions in use as other first-generation antihistamines used in cough and cold remedies.

Cyclizine

Cyclizine is now rarely used as it is subject to abuse and consequently many pharmacies do not stock it. If taken, adults and children over the age of 12 should take one tablet (50 mg) three times a day. The dose for children over the age of 6 is half the adult dose.



Table 11.1
Practical prescribing: Summary of medicines for travel sickness

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in which care is exercised	Pregnancy and breastfeeding
Cyclizine	>6 years	Dry mouth, sedation	Increased sedation with alcohol, opioid analgesics, anxiolytics, hypnotics and antidepressants	Angle-closure glaucoma, prostate enlargement	Standard references state OK, although some manufacturers advise avoidance
Cinnarizine (Stugeron 15)	>5 years				
Promethazine (Avomine)	>5 years				
<i>Hyoscine</i>		Dry mouth, sedation	Increased anticholinergic side effects with TCAs and neuroleptics	Angle-closure glaucoma, prostate enlargement	Avoid if possible in pregnancy In breastfeeding, may cause drowsiness, which would lead to poor feeding in long-term use but OK for short journeys
Joy-Rides	>3 years				
Kwells	>10 years				
Kwells Kids	>4 years				

HINTS AND TIPS BOX 11.1: TRAVEL SICKNESS

How to minimize effects of motion	Planes – sit over the wing Ships – sit in the middle, close to the water line Cars – sit in the front Avoid rear-facing seats in any form of transport Focus on stationary objects Avoid alcohol or overeating before journeys Avoid reading or focusing on games Ensure good ventilation; for example, open a window
Dry mouth problems	Many people will complain of a dry mouth with travel sickness medicines. This is easily overcome by sucking on a sweet, which will stimulate saliva production
Matching up length of journey with product	Hyoscine should be recommended for journeys up to 4 hours; cinnarizine for journeys over 4 hours but less than 8 hours and promethazine for journeys longer than 8 hours

Cinnarizine (Stugeron 15)

Adults and children over the age of 12 should take two tablets (30 mg) 2 hours before travel. The dose can be repeated every 8 hours (1 tablet) if needed. For children aged between 5 and 12, the dose is half (15 mg) the adult dose.

Promethazine (Avomine)

Avomine can be given for both prevention and treatment of travel sickness. For prevention, adults and children over the age of 10 should take one tablet (25 mg) at least 1 or 2 hours before travel. For treatment, one tablet should be taken as soon as sickness is felt, followed by a second tablet 6 to 8 hours later. For children over the age of 5, the dose should be half that of the adult dose in both prevention and treatment.

Hyoscine

Hyoscine can be swallowed or chewed (e.g., Joy-Rides and Kwells). Products should be taken 20 to 30 minutes before the time of travel; because they have a short half-life, they have a short duration of action, and the dose might therefore have to be repeated on journeys longer than 4 hours. Anticholinergic side effects are more obvious than with antihistamines, and it does interact with other medicines that have anticholinergic side effects. Because hyoscine hydrobromide crosses the blood–brain barrier, it can cause sedation. It appears to be safe in pregnancy, although the manufacturers state it should be avoided.

Joy-Rides

Joy-Rides can be given from age 3 upwards. Children aged between 3 and 4 years should take half a tablet (75 µg) and no more than one tablet (150 µg) in 24 hours. Children between the age of 4 and 7 should take one tablet (150 µg)

with a maximum of two tablets (300 µg) in 24 hours, and children aged between 7 and 12 should take one to two tablets.

Kwells

Kwells can only be given to children aged 10 and over. Children over the age of 10 should take half to one tablet. For adults the dose is one tablet.

Kwells Kids

Kwells Kids contain half the amount of hyoscine (150 µg) than Kwells and are marketed at children under the age of 10, although older children can take them. Children aged between 4 and 10 should take half to one tablet.

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Emergency hormonal contraception

Background

Emergency hormonal contraception (EHC) is one of only a handful of deregulated products which targets preventative health care. Like other Western countries, the UK has high teenage pregnancy rates and associated high abortion rates. The intention of UK government policy on making EHC available through pharmacies was to improve access for patients requiring EHC at times when other providers might be closed, for example at weekends and evenings. This policy appears to have been effective. Since EHC availability (2001) the percentage of EHC provided through community pharmacies has steadily increased. Community pharmacists are now the main provider of EHC, and studies have consistently demonstrated that women obtain EHC more quickly from community pharmacies than from other providers (NHS Confederation, 2013). This is relevant as EHC is more effective the sooner it is taken after unprotected sex.

Two products are now available OTC in the UK for emergency contraception; levonorgestrel (deregulated in 2001) and ulipristal (deregulated in 2015).

Aetiology

The exact mechanism of action for levonorgestrel is not clear. It appears to have more than one mode of action at more than one site. It is thought to work mainly by preventing ovulation and fertilization if intercourse has taken place in the pre-ovulatory phase. It is also suggested that it causes endometrial changes that discourage egg implantation. Ulipristal works by inhibiting or delaying ovulation via suppression of the luteinizing hormone surge.

Evidence base for over-the-counter medication

The exact effectiveness of EHC is hard to establish, as many people who have been treated with emergency contraception will not have become pregnant even without treatment. Trial data for levonorgestrel have found it to prevent 86% of expected pregnancies when treatment was initiated within 72 hours. Levonorgestrel is more effective the earlier it is taken after unprotected sex; it prevents 95% of pregnancies if taken within 24 hours, 85% between 24 and 48 hours, and 58% if used within 48 to 72 hours (Sandoz 2016). Data from two trials for ulipristal show it to have similar efficacy to levonorgestrel between 0 and 72 hours after unprotected intercourse or contraceptive failure. When these data are pooled, ulipristal shows superior efficacy over levonorgestrel at 24, 72 and 120 hours. Ulipristal is therefore medicine of choice (FRSH Guidance 2017).

Practical prescribing and product selection

Prescribing information relating to EHC is discussed and summarized in [Table 11.2](#).



Table 11.2
Practical prescribing: Summary of medicines for EHC

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in which care is exercised	Pregnancy and breastfeeding
Levonelle One-Step	>16 years	Nausea, headache, disturbed menstrual cycle	Anticonvulsants, rifampicin, griseofulvin, St. John's Wort and ciclosporin	Conditions in which absorption may be impaired, for example, Crohn's disease	Pregnancy – not applicable Breastfeeding – safe to use
EllaOne	any woman of child bearing age	Nausea, headache, dizziness, abdominal pain and disturbed menstrual cycle	Anticonvulsants, rifampicin, St. John's Wort and ritonavir	None	Pregnancy – not applicable Breastfeeding – avoid for 1 week

Assessing patient suitability

Before any sale or supply of EHC the pharmacist has to be in a position to determine whether the patient is suitable to take the medicine. To do this an assessment has to be made on the likelihood that the patient is pregnant:

- First, has the patient had unprotected sex, contraceptive failure or missed taking contraceptive pills in the last 120 hours? If more than 120 hours have elapsed the patient needs to be referred to her doctor for further assessment.
- Is the patient already pregnant? Details about the patient's last period should be sought. Is the period late, and if so, how many days late? Was the nature of the period different or unusual? If pregnancy is suspected a pregnancy test could be offered.
- What method of contraception is normally used? Patients might not need EHC. Guidelines from the Faculty of Sexual and Reproductive Healthcare (2017) state:

If 2 or more active pills are missed when taking a COC (monophasic containing ethinylestradiol) EHC is indicated if these are missed in WEEK ONE and there has been unprotected sex during the pill-free interval or week one.

For progestogen-only pills if pill taking is late or missed (> 27 hours for traditional POP or 36 hours if POP contains desogestrel) EHC is indicated.

Levonorgestrel (Levonelle One Step)

Levonelle should be taken as soon as possible and within 72 hours after unprotected sex or contraceptive failure. The dose consists of a single tablet (levonorgestrel 1500 µg). About one in five patients experience nausea but only 1 in 20 go on to vomit. If the patient vomits within 3 hours of taking the dose, she should be advised that a further supply of EHC would be needed. A number of medicines do, theoretically, interact with Levonelle, most notably those that are enzyme inducers and include anticonvulsants, rifampicin, griseofulvin and St. John's Wort; the clinical significance of the interactions appears low as only a handful of drug interaction reports have been received by the manufacturers. It seems prudent, until such time that more substantial evidence is available, that patients taking these medicines are best referred to the doctor. In such circumstances, increasing the dose of Levonelle is commonly practised (although not licensed).

Advanced sale of levonorgestrel is also permitted. However, pharmacists must consider the clinical appropriateness of a supply, and should consider declining repeated requests for advance supply and advise patients to use more reliable methods of contraception. See 'Hints and Tips' in [Box 11.2](#).

Ulipristal acetate (EllaOne)

The treatment consists of one tablet to be taken as soon as possible but no later than 120 hours (5 days) after

HINTS AND TIPS BOX 11.2: EMERGENCY HORMONAL CONTRACEPTION

Consumer awareness	Studies have shown that most women have heard of EHC (>90%), although their knowledge on when it can be taken and its effectiveness is lower; for example, less than half of women are aware of how long EHC remains effective and less than two-thirds are aware it was most effective the sooner it was taken after intercourse. It is likely that lower levels of awareness surround ulipristal and that it is effective for up to 5 days after unprotected sex compared with 72 hours for levonorgestrel.
Potential for misuse?	Some concerns have been raised about women misusing EHC because of its greater accessibility. However, a review of international experience with pharmacy supply of EHC found only a small proportion of women use EHC repeatedly (6.8% using it twice in 6 months, and 4.1% using it three times) (Anderson & Blenkinsopp, 2006).
EHC failure?	Taking EHC can affect the timing of the next menstrual period and patients should be told that their period might be earlier or later than usual. However, if the period is different than normal or more than 5 days late, then she should be advised to have a pregnancy test.
Do you have to supply EHC?	The supply of EHC is at the discretion of each pharmacist and some, for religious beliefs, might choose not to supply EHC. However, the patient should be advised on other local sources of supply.

unprotected sex or contraceptive failure. If vomiting occurs within 3 hours another tablet should be taken. Common side effects (affecting up to 10% of women) are listed in Table 11.2. Like levonorgestrel, it can interact with a number of medicines including antiepileptics (carbamazepine, fosphenytoin, oxcarbazepine, phenobarbital, phenytoin, primidone), rifampicin, ritonavir and St. John's wort. Ulipristal passes into breast milk and women should not breastfeed for 1 week after use. Patients with severe asthma managed with corticosteroids should not use this product. The manufacturers of EllaOne provide online help for patients to assess their suitability for supply (<https://www.ellaone.co.uk/suitability-checker/>).

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Further reading

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Websites

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Nicotine replacement therapy

Background

Smoking represents the single greatest cause of preventable illness and premature death worldwide. In 2016 nearly 80 000 people in the UK died as a result of smoking; putting this in context, 37% of all deaths from respiratory diseases and 26% of all deaths from cancers were estimated to be attributable to smoking.

Prevalence and epidemiology

The number of smokers over the age of 18 in the UK is falling—from a high of 45% in 1974 to now just 15% in 2017. Recent

decreases in the UK (in 2013, 19% of people were smokers) may be attributable to increases in e-cigarette use (5.5% of people now use them) and reportedly 53% of electronic cigarette users are using them as an aid to stop smoking.

Manual occupations have higher levels of smoking (26%) compared to managerial and professional occupations (10%). Smoking is most common in those under the age of 35; adults aged 25 to 34 were most likely to be current smokers (20%). It is least common (8%) in people over 65.

Aetiology

Hundreds of compounds have been identified in tobacco smoke; however, only three compounds are of real clinical importance:

- tar-based products, which have carcinogenic properties
- carbon monoxide, which reduces the oxygen-carrying capacity of the red blood cells,
- nicotine, which produces dependence by activation of dopaminergic systems.

Tolerance to the effects of nicotine is rapid. Once plasma nicotine levels fall below a threshold, patients begin to suffer nicotine withdrawal symptoms and will crave another cigarette. Treatment is therefore based on maintaining plasma nicotine just above this threshold.

Evidence base for over-the-counter medication

Nicotine replacement therapy (NRT) has established itself as an effective treatment. A 2018 Cochrane review (Hartmann-Boyce et al., 2018) found 136 trials ($N > 64\ 000$) comparing NRT to placebo or non-NRT treatments, and the results indicated that NRT increases rates of quitting smoking by 50% to 60%. The review found that all forms of NRT are effective and there are insufficient data to suggest that one form is superior to another. Therefore personal choice will be the determining factor in which is chosen as being most suitable.

In addition, the effectiveness of NRT is also affected by the level of additional support provided to the smoker. Numerous intervention strategies have been used involving NRT. These include nurse-led services, workplace interventions, and doctor and pharmacy-based services. A 2012 review reported good levels of evidence that community pharmacists can deliver effective smoking cessation programmes and that structured interventions and counselling were better than opportunistic intervention (Brown et al., 2012).

It should be noted that relapse is a normal part of the quitting process and occurs on average three to four times. If a smoker has made repeated attempts to stop and has failed, experienced severe withdrawal or has requested more intensive help, then referral to a specialist smoking cessation service should be considered.

Practical prescribing and product selection

Prescribing information relating to medicines for NRT reviewed in the section 'Evidence base for over-the-counter medication' is discussed and summarized in Table 11.3.

Before instigation of any treatment it is important that the patient does want to stop smoking. Work has shown that motivation is a major determinant for successful smoking cessation, and interventions based on the transtheoretical model of change put forward by Prochaska and colleagues have proved effective (Fig. 11.1). The model identifies six stages, progress through which is cyclical, and patients need varying types of support and advice at each stage.

Most patients who ask directly for NRT will be at the preparation stage of the model and ready to enter the action stage. However, a small number of patients may well be buying NRT to please others and are actually in the precontemplation stage and do not want to stop smoking.

NRT is formulated as gum, lozenges, patches, nasal spray, inhalator, mouth spray, sublingual and orodispersible tablets; therefore there should be a treatment option to suit all patients.

A number of approaches to NRT regimens are advocated. In general, the strength of the formulation is tailored to the number of cigarettes smoked, and one form of NRT is tried at a time. However, it is possible for patients to use more than one form of NRT together, and there is evidence that this produces better results in patients with a high level of dependence. Additionally, patients can use NRT to 'cut down' on the number of cigarettes smoked or as a nicotine substitute.

Most products can be used from age 12 years onwards. If recommending products for adolescents (12–18 years old), the dose is the same as for adults, but if treatment is needed beyond 12 weeks the person should be referred in to a formal structured programme.

Side effects with NRT are rare and are either normally limited to gastrointestinal (GI) problems associated with accidental ingestion of nicotine when chewing gum, or local skin irritation and vivid dreams associated with patches.

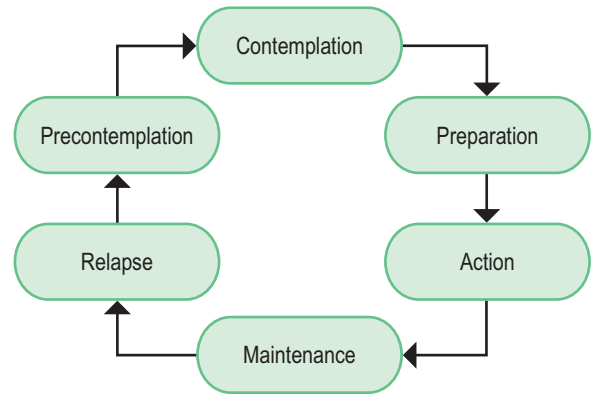


Fig. 11.1 The Prochaska and Diclemente stages of change model.

Headache, nausea and diarrhoea have also been reported. NRT appears to have no significant interactions with other medicines.

Nicorette

Nicorette is available as a gum (2 and 4 mg), inhalation cartridge (15 mg), microtab (2 mg), nasal spray (10 mg/mL) patches (10, 15 and 25 mg), mouth spray (1 mg/spray) and lozenge (2 mg).

Gum

Nicorette gum is available as either fruit or mint flavours (unflavoured gum leaves a bitter taste in the mouth). The strength of gum used will depend on how many cigarettes are smoked each day. In general, if the patient smokes fewer than 20 cigarettes a day, then the 2-mg gum should be used. If more than 20 cigarettes a day, then the 4-mg strength may be needed. A maximum of 15 pieces of gum can be chewed in any 24-hour period.

Inhalation cartridge

The inhalator can be particularly helpful to those smokers who still feel they need to continue the hand-to-mouth



Table 11.3

Practical prescribing: Summary of medicines used as nicotine replacement therapy

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in which care is exercised	Pregnancy and breastfeeding
Nicorette	>12 years	Gastrointestinal disturbances, headache, dizziness	None	Patients with heart disease and diabetes	OK
Nicotinell					OK but manufacturers of Nicotinell liquorice gum advise it not to be used in pregnancy
NiQuitin					

movement. Each cartridge is inserted into the inhalator and air is drawn into the mouth through the mouthpiece. A maximum of six cartridges can be used in 24 hours. Each cartridge can be used for approximately eight 5-minute sessions, with each cartridge lasting approximately 40 minutes of intense use.

The amount of nicotine from a puff is less than that from a cigarette. To compensate for this, it is necessary to inhale more often than when smoking a cigarette.

Microtabs (2 mg)

Microtabs are licensed for either smoking cessation or smoking reduction. For smoking cessation, the standard dosage is one tablet per hour in patients who smoke fewer than 20 cigarettes a day (doubled for heavy smokers). This can be increased to two tablets per hour if the patient fails to stop smoking with the one tablet per hour regimen, or for those whose nicotine withdrawal symptoms remain so strong they believe they will relapse. Most patients require between 8 and 24 tablets a day, although the maximum is 40 tablets in 24 hours. Treatment should be stopped when daily consumption is down to one or two tablets a day.

For those reducing the number of cigarettes smoked, the tablets should be used between cigarettes to try and prolong the smoke-free period.

Nasal spray (each spray delivers 0.5 mg nicotine)

At the start of treatment one spray should be put into each nostril twice an hour to treat cravings. The maximum daily limit is 64 sprays, equivalent to two sprays in each nostril every hour for 16 hours.

Patches

The patches are usually applied in the morning and removed at bedtime (a 16-hour patch). Patients who want to stop smoking should start on the highest strength patch (25 mg – known as Step One) for 8 weeks before stepping down to the middle strength (15 mg – Step Two) for a further 2 weeks. The lowest strength patch (10 mg – Step Three) should be finally worn for another 2 weeks.

Mouth spray (each spray delivers 1 mg nicotine)

The mouth spray can be used for either smoking cessation or smoking reduction. Smokers wanting to reduce the number of cigarettes smoked should use the mouth spray, as needed, between smoking episodes to prolong smoke-free intervals. For smoking cessation, one spray should be used when cravings emerge. If this first spray fails to control cravings a second spray can be used. Most smokers will require one to two sprays every 30 minutes to 1 hour. The maximum number of sprays in a 24-hour period is 64.

Lozenge (2 and 4 mg)

Lozenges, like other dose forms, can be used for either smoking cessation or smoking reduction. The 2-mg lozenge is used for those who smoke 20 cigarettes or less a day. Most smokers require 8 to 12 lozenges per day (maximum 15 lozenges per day). Reduction strategies are the same as other dose forms in that the lozenges are used when needed between smoking cigarettes to prolong smoke-free intervals.

Nicotinell

Nicotinell is available as gum (2 or 4 mg), patches (7, 14 and 21 mg) and lozenges (1 and 2 mg).

Nicotinell gum

Nicotinell gum is flavoured and available as fruit, mint or liquorice. The dosage and administration of Nicotinell gum is the same as that for Nicorette gum.

Patches

The patches are worn continuously and changed every 24 hours, thus Nicotinell patches are suitable for those smokers who must have a cigarette as soon as they wake up, as nicotine levels will be above the threshold of nicotine withdrawal. Treatment, like Nicorette, is based on a stepwise reduction over a maximum period of 3 months. People who smoke more than 20 cigarettes a day should use the highest strength patch (TTS 30 patch, 21 mg) for 3 to 4 weeks, after which the strength of the patch should be reduced to the middle strength (TTS 20 patch, 14 mg) for a further 3 to 4 weeks before finally using the lowest patch (TTS 10 patch, 7 mg). If the patient smokes fewer than 20 cigarettes a day, then he or she should start on the middle-strength patch.

Lozenge

The strength of lozenge used will depend on the number of cigarettes smoked. For those smoking fewer than 20 cigarettes a day the 1-mg lozenge should be used and for those smoking 30 or more cigarettes a day, the 2-mg strength is recommended. For those smoking between 20 and 30 cigarettes a day, then 1- or 2-mg lozenges can be used depending on patient response. Patients should be instructed to suck one lozenge every 1 to 2 hours when they have the urge to smoke. The usual dosage is 8 to 12 lozenges per day, with a maximum of 30 lozenges in 24 hours. Patients should be advised to gradually reduce the number of lozenges needed until they are only using one to two lozenges per day. At this point they should stop treatment.

Lozenges are mint flavoured and should be sucked until the taste becomes strong and then placed between gum and cheek (similar to the gum) until the taste fades, when sucking can recommence. Each lozenge takes approximately 30 minutes to dissolve completely.

NiQuitin

NiQuitin is available as gum (2 or 4 mg), patches (7, 14 and 21 mg), lozenge (2 and 4 mg, or NiQuitin minis: 1.5 and 4 mg) and orodispersible tablets (NiQuitin Strips 2.5 mg).

Patches

Like Nicotinell, patches are designed to be worn continuously (24-hour patch) and dosing is based on a sequential reduction of nicotine over time. Patients who smoke more than 10 cigarettes a day should use the 21-mg patch (Step 1) for 6 weeks, followed by the 14-mg patch (Step 2) for 2 weeks and finally the 7-mg patch (Step 3) for the last 2 weeks. If the person smokes fewer than 10 cigarettes each day the patient should start on Step 2 for 6 weeks, followed by Step 3 for a final 2 weeks.

NiQuitin lozenge

The low-strength lozenge (2 mg) is aimed at smokers who have their first cigarette of the day more than 30 minutes after waking up and the higher strength (4 mg) for those who smoke within 30 minutes of awakening. Like patches the dose of lozenges are marketed as Steps. For smoking cessation the dosing schedule is:

- Step 1 × 6 weeks One lozenge every 1–2 hours
- Step 2 × 3 weeks One lozenge every 2–4 hours
- Step 3 × 3 weeks One lozenge every 4–8 hours

After this programme patients can use one to two lozenges a day over the next 12 weeks when strongly tempted to smoke.

For smoking reduction, as with other products, the lozenges should be used in between cigarettes to try and prolong the smoke-free period.

NiQuitin Minis lozenge

Dosing of this version of the lozenge does vary from NiQuitin lozenges. The low strength (1.5 mg) is marketed for people who smoke fewer than 20 cigarettes a day and the high strength (4 mg) for those who smoke more than 20 cigarettes a day. For smoking cessation, it is recommended in either strength that the person should use between 8 and 12 lozenges per day (up to a maximum of 15 per day) and stop altogether when only using one or two lozenges per day.

For smoking reduction, as with NiQuitin lozenges, the lozenges should be used in between cigarettes to try and prolong the smoke-free period.

Gum

Gum can be used for smoking cessation or smoking reduction. Like lozenges, the lower strength (2 mg) is aimed at smokers who have their first cigarette of the day more than 30 minutes after waking up and the higher strength (4 mg) for those who smoke within 30 minutes of awakening. The 'chew and rest' technique, as with Nicorette and Nicotinell, is used. For smoking cessation, it is recommended in either strength that the person should use between 8 and 12 pieces of gum per day (up to a maximum of 15 per day) and stop altogether when only using one or two pieces of gum per day.

For smoking reduction, as with NiQuitin lozenges, the gum should be used in between cigarettes to try and prolong the smoke-free period.

See 'Hints and Tips' in [Box 11.3](#) for tips on nicotine replacement therapy.

HINTS AND TIPS BOX 11.3: NICOTINE REPLACEMENT THERAPY

Application of patches	Patches should be applied to non-hairy skin on the hip, chest or upper arm. The next patch should be placed on a different site to avoid skin irritation.
16- or 24-hour patches?	A 16-hour patch will be suitable for most patients; however, if a patient requires a cigarette within the first 20–30 minutes after waking, then a 24-hour patch should be given. If sleep disturbances are experienced with the 24-hour patches, the patient can switch to a 16-hour patch or alternatively remove the 24-hour patch when they go to bed.
Diabetics	Should monitor their blood sugar levels more closely than usual when nicotine replacement therapy is started as carbohydrate metabolism can be affected.
Gum chewing technique – 'chew and rest' technique	The gum should be chewed slowly until the taste becomes strong, it should then be rested between the cheek and gum until the taste fades. The gum can then be re-chewed. Each piece of gum lasts approximately 30 minutes.

References

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Further reading

- NHS Digital. Statistics on smoking – England 2018: <https://digital.nhs.uk/data-and-information/publications/statistical/statistics-on-smoking/statistics-on-smoking-england-2018>.
- Office for National Statistics. E cigarette use in Great Britain 2019. <https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/drugusealcoholandsmoking/datasets/ecigaretteuseingreatbritain>.
- Sinclair, H. K., Bond, C. M., & Stead, L. F. (2004). Community pharmacy personnel interventions for smoking cessation. *Cochrane Database System Review*, 1:CD003698. <https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD003698.pub2/full>.

Websites

- Action on Smoking and Health (ASH): <https://ash.org>
- QUIT: <http://www.quit.org.uk/>

Malaria prophylaxis

Background

Malaria is a parasitic disease spread by the female *Anopheles* mosquito. Five species of the protozoan *Plasmodium* produce malaria in humans: *P. vivax*, *P. ovale*, *P. malariae*, *P. knowlesi* and *P. falciparum*. *P. falciparum* is the most virulent form of malaria and is responsible for the majority of cases and associated deaths.

Prevalence and epidemiology

Malaria is a leading cause of death in areas of the world where the infection is endemic. In 2017, 435 000 people died from malaria, with the WHO African Region accounting for 93% of all malaria deaths. However, since 2010 there has been a 25% reduction in malaria mortality. This reduction has been predominantly through increased malaria control and elimination efforts by governments of malaria-endemic countries and international partners.

In the UK, there are between 1500 and 2000 imported cases each year, resulting in, on average, six deaths per year.

In 2018 there were 1683 cases; 1098 cases were contracted by UK residents travelling abroad, with the remaining cases either being new entrants to the UK or foreign visitors to the UK. Figures for that year show that *P. falciparum* accounted for 82% of cases (1375), *P. vivax* 9% (143), *P. ovale* 7% (117), with just 2% (36) for *P. malariae*.

For people travelling to countries where malaria is present, the risk of contracting malaria varies greatly. It depends on the area visited, the time of year, altitude (parasite maturation cannot take place above 2000 metres) and how many infectious bites are received. In general, risk tends to increase in more remote areas than in urban/tourist areas, after rainy or monsoon seasons, and at low altitude. It is therefore possible to have a different risk of contracting malaria within the same country, for example, visiting the southern lowlands of Ethiopia after the rainy season would pose a very high risk, whereas trekking in the Simien mountains in the north of the country during the dry season would pose minimal risk.

Aetiology

Malarial parasites are transmitted to humans when an infected female *Anopheles* mosquito bites its host. Once in the human host, the parasites (which at this stage of their life cycle are known as sporozoites) are transported via the bloodstream to the liver. In the liver they divide and multiply (they are now known as merozoites). After 5 to 16 days the liver cells rupture to release up to 400 000 merozoites, which invade the human host's erythrocytes. The merozoites reproduce asexually in the erythrocytes before causing them to rupture and release yet more merozoites into the bloodstream to invade yet more erythrocytes. Any mosquito that bites an infected person at this stage will ingest the parasites and the cycle will begin again.

Clinical signs and symptoms are observed during the cycle of the parasites in the erythrocytes and not whilst the parasites are developing in the liver. This explains why malarial symptoms can manifest months after return from an infected region as the parasite (especially *P. vivax* and *P. ovale*) can remain dormant in the liver.

Clinical symptoms

The most common symptom is fever, although it may initially present with chills, general malaise, nausea, vomiting and headache. Malaria should be considered as a differential diagnosis in anyone who presents with a febrile illness while in or having recently left a malarious area. *P. falciparum* is unlikely to present more than 3 months after exposure but symptoms associated with *P. vivax* malaria can take up to a year to manifest.

Evidence base for over-the-counter medication

Effective bite prevention should be the first line of defence against malarial infection. Total avoidance of being bitten is not practical and patients must ensure that protective measures from being bitten are always taken.

Insect repellents containing *N,N*-diethyl-*m*-toluamide (DEET) in high concentrations are recommended (see 'Hints and Tips' in Box 11.4). In controlled laboratory studies, DEET provides the longest protection compared with other products. Evidence for other insect repellents suggest they have comparable efficacy to low concentrations of DEET but have shorter duration of protection than DEET (Fradin & Day, 2002).

Besides applying DEET, other preventative measures to reduce the chance of being bitten include wearing long, loose-fitting, sleeved shirts and trousers, especially at dawn and dusk. Protection of ankles appears to be particularly important. Hotel windows should be checked to make sure they have adequate screening, windows and doors should remain closed and, ideally, the bed should have a mosquito net. Mosquito nets do reduce the incidence of being bitten. Ideally they should be impregnated with insecticide, as these are more effective than nonimpregnated nets (Price et al., 2018). If the person is travelling to more remote areas they should purchase their own mosquito net that has been impregnated with an insecticide. There are a number of travel centres and specialty outdoor shops where such

products, including insecticidal impregnated clothes, can be bought.

Chemoprophylaxis

In addition to taking precautions to avoid being bitten, travellers should also take antimalarial medication. The importance of this must be stressed to would-be travellers. Where data were available for malaria cases in 2018, 88% had not taken chemoprophylaxis (https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/812824/Malaria_imported_into_the_United_Kingdom_2018.pdf).

Chloroquine and proguanil have long been available OTC in the UK. Unfortunately, resistance to these two medicines (e.g., chloroquine-resistant *P. falciparum*) is now widespread and limits their usefulness. In 2017, atovaquone was deregulated in combination with proguanil (Maloff Protect) and now provides an alternative option to community pharmacists.

It is important to check current guidelines for the destination the person is travelling to or through. Two easily available UK reference sources in which recommendations can be found are the *British National Formulary* and *MIMS* (subscription required). In addition, a number of organizations produce reference material (e.g., the National Pharmacy Association's vaccination updates).

HINTS AND TIPS BOX 11.4: MALARIA

Application of DEET	<p>The concentration of DEET in commercial products varies widely. Products with concentrations in excess of 50% can cause skin irritation and occasionally skin blistering. It is advisable that these are patch tested first before widespread application</p> <ul style="list-style-type: none"> • The higher the concentration of DEET, the greater the length of protection: • 50% DEET provides protection for up to 12 hours • 30% DEET provides protection for up to 6 hours • 20% DEET provides protection for 1–3 hours <p>Note: reapplication is necessary after swimming or sweating DEET can damage certain plastics, for example, sunglasses. It is important to emphasize to the patient that they wash their hands after applying DEET Make sure exposed areas, such as feet and ankles, are adequately protected DEET reduces the effectiveness of sunblock but sunblock does not affect the effectiveness of DEET</p>
Electronic mosquito repellents	<p>These products are designed to repel female mosquitoes by emitting high-pitched sounds almost inaudible to the human ear. There is no evidence in field studies to support any repelling effects</p>
Alternative remedies	<p>There is currently insufficient evidence supporting the use of vitamin B₁, garlic, tea tree oil, herbal remedies, Marmite or repellents containing lemon eucalyptus (e.g., Mosi-guard), or picaridin They should not be routinely recommended</p>

For people who are travelling to very-high-risk areas (usually sub-Saharan Africa) or for long periods of time, it might be better to refer the person to a specialist centre (see listed websites).

Practical prescribing and product selection

Prescribing information relating to medicines for malaria reviewed in the section 'Evidence base for over-the-counter medication' is discussed and summarized in [Table 11.4](#); useful tips relating to patients travelling to regions where malaria is endemic are given in 'Hints and Tips' in [Box 11.4](#).

Medicine regimens

Antimalarials need to be taken prior to departure, during the stay in the malaria endemic region and after leaving the area. Taking the medication before departure allows the patient to know whether they are going to experience side effects and, if they do, to have enough time to obtain a different antimalarial before departure. It also helps establish a medicine-taking routine that will, hopefully, help with adherence. Medicine taking after leaving an endemic area is to ensure that any possible infection that could have been contracted during the final days of the stay does not develop into malaria. The length of time medication has to be taken varies depending on which antimalarial was taken.

Chloroquine (e.g., Avloclor)

Chloroquine, as a single agent, is now almost obsolete against *P. falciparum* but still remains effective against the

other forms of malaria. Adults should take 300 mg of chloroquine base each week; this is equivalent to two tablets. For children ideally dosing is 5 mg chloroquine base/kg per week but practically this equates to half a tablet for children aged 1 to 4 years old; one tablet for those aged 5 to 8 years old and children 9 to 14 years old should take one and a half tablets.

Chloroquine is associated with a number of side effects, including nausea, vomiting, headaches and visual disturbances, although their exact incidence is unknown. Most patient groups, including pregnant women, can take chloroquine, although it is contraindicated in epilepsy because it might lower the seizure threshold and tonic-clonic seizures have been reported with prophylactic doses. Patients with psoriasis might notice a worsening of their condition. Chloroquine should be avoided in patients taking amiodarone because there is a risk of QT prolongation and ventricular arrhythmia. It should also be avoided with ciclosporin (increased ciclosporin levels), cimetidine (increased chloroquine levels) and possibly digoxin (increased digoxin levels).

Proguanil (Paludrine)

Adults and children over the age of 14 should take 200 mg (two tablets) daily. Like chloroquine, it can be given to children of all ages and the dose ideally should be on a milligram per kilogram basis, but practically the dosing schedule is: under 1 year, quarter tablet daily; 1 to 4 years, half tablet daily; 5 to 8 years, one tablet daily; 9 to 14 years, one and a half tablets daily.

Side effects associated with proguanil are usually mild and include diarrhoea. Patients with renal impairment may



Table 11.4

Practical prescribing: Summary of medicines for malaria prophylaxis

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in which care is exercised	Pregnancy and breastfeeding
Chloroquine	All ages	Gastrointestinal disturbances and visual problems	Amiodarone, ciclosporin, cimetidine, digoxin	Avoid in epilepsy	OK
Proguanil		Diarrhoea	None	Renal impairment	
Atovaquone/proguanil		Common – anaemia, allergic reactions, anorexia, abnormal dreams, depression, insomnia, dizziness, pruritus, rash, fever, cough	Etoposide, rifampicin, warfarin, metoclopramide, tetracycline, indinavir, efavirenz and zidovudine		

require dosage adjustments based on their creatinine clearance (see emc, <https://www.medicines.org.uk/emc/product/5493/smpc> for full details)

A travel pack suitable for adults on a 2-week holiday is available and combines 14 chloroquine tablets with 98 proguanil tablets.

Atovaquone/proguanil (Maloff Protect)

Each Maloff Protect tablet contains 250 mg atovaquone and 100 mg proguanil hydrochloride. The dose (for adults only) is one tablet daily taken with food or a milky drink. It has a number of licence restrictions, including any person with liver or renal impairment, those with a history of depression and seizures, patients with tuberculosis and during pregnancy. Interactions of note include etoposide, rifampicin, warfarin, metoclopramide, tetracycline, indinavir, efavirenz and zidovudine. Side effects are wide ranging but those reported as very common are headache, nausea, vomiting, diarrhoea and abdominal pain. Other common side effects are listed in [Table 11.4](#).

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Further reading

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- World Malaria Report 2018. <https://www.who.int/malaria/publications/world-malaria-report-2018/en/>.

Websites

- Fit for travel <https://www.fitfortravel.nhs.uk/home.aspx>
- Liverpool School of Tropical Medicine: <https://www.lstmed.ac.uk/>
- Malaria Reference Laboratory: <https://www.gov.uk/government/collections/malaria-reference-laboratory-mrl>
- Travel Health Pro: <https://travelhealthpro.org.uk/>

Bites and stings

Background

A whole host of animals (and plants) have the capacity to cause injury to the skin and, depending on the severity, this

can result in systemic symptoms. The majority of cases in the UK are caused by insects and are of nuisance value.

Prevalence and epidemiology

The prevalence of bites and stings is largely unknown. Most people self-treat and never seek advice. Biting and stinging insects are generally more common in warmer climates and during warmer months.

Aetiology

Stinging insects are broadly defined as those that use some sort of venom as a defence mechanism or to immobilize their prey. Examples include bees, wasps and ants. The venom is usually 'injected' using a stinger and includes proteins and substances that help break down cells and increase the penetration of the venom (e.g., phospholipase A and hyaluronidase). People can develop allergic reactions to these substances and, unlike with most biting insects, can occasionally suffer significant reactions, including anaphylaxis. The severity of the reaction depends on the quantity of the venom injected and the person's predisposition to hypersensitivity.

Biting insects are those that feed off the blood supply of humans and other creatures. They include mosquitoes, ticks, and fleas. Apart from having some sort of apparatus to draw the blood, these insects usually secrete anticoagulant-like substances to facilitate feeding. It is these anticoagulant substances that people will react to. However, it is only after repeated bites that sensitivity occurs. Some insects (e.g., horseflies, midges) do not have specialized mouthparts and take blood by biting a hole through the skin. These bites are typically more painful.

In the UK, the most common plant that causes skin reactions is the stinging nettle. An urticarial-type reaction occurs as hairs on the leaf pierce the skin, releasing histamine, acetylcholine and serotonin (see [Fig. 8.29](#)).

Clinical features of bites and stings

Itching papules, which can be intense, is the hallmark symptom of insect bites. Weals, bullae and pain can occur, especially in sensitized individuals. Lesions are often localized and grouped together, and occur on exposed areas, for example hands, ankles and face ([Fig. 11.2](#)). Scratching can cause excoriation, which might lead to secondary infection. In contrast, stings are associated with intense burning pain. Erythema and oedema follow but usually subside within a few hours. If systemic symptoms are experienced, they occur within minutes of the sting.



Fig. 11.2 Insect bites. Grouped red, crusted papules with red flare. Reproduced with permission from Marks, J. G., & Miller, J. J. (2019). *Lookingbill and Marks' principles of dermatology* (6th ed.). Elsevier.

Ticks and Lyme disease

Ticks can be picked up when walking in open grassy areas and feed on the human host. A small proportion of ticks carry a spirochete bacterium that can lead to the person developing Lyme disease. A person with a history of a tick bite (even months previously) who develops an erythematous spreading rash needs to be referred. Other symptoms can also include flu-like symptoms (e.g., fatigue, fever, headache).

Lyme disease most commonly occurs on the south coast of England, the Lake District and the Scottish highlands. If a tick is found on the body, it will need removal. Ticks should be removed with fine tweezers by gripping the insect close to the skin and pulling straight up. Twisting movements should be avoided as these increase the chance that mouthparts will be left in the skin.

Evidence base for over-the-counter medication

Avoiding bites and stings in the first place is obviously important. This means using an effective insect repellent and avoiding times and places when insects are about. DEET is the most effective insect repellent and found in most commercial preparations. For avoidance measures and more information on DEET, see page 363.

Topical OTC treatments for bites and stings include local anaesthetics, corticosteroids and antihistamines. However, there is a lack of evidence for the efficacy of these treatments and, in general, recommendations for treatment are based on expert opinion and clinical experience.

Antihistamines (both topical and systemic) have been used for their antipruritic properties. Some studies, with systemic antihistamines, have shown efficacy of the less sedating antihistamines for mosquito bites (Foëx & Lee, 2006). Sedating antihistamines are probably most useful to combat itching that can disturb sleep.

Practical prescribing and product selection

Prescribing information relating to products for bites and stings is reviewed in the section 'Evidence base for over-the-counter medication' and summarized in Table 11.5.

Before OTC treatment is offered, the severity of symptoms should be assessed because small local reactions can be managed primarily with topical products, whereas large local reactions will generally require systemic treatment. Patients with systemic symptoms should be referred.

If the person has been stung and the stinger is still in situ, then this should be removed. The best way of removal is to scrape the stinger away with a sharp edge (e.g., card or knife blade) or alternatively a fingernail.

Small local reactions

Local pain and swelling is best treated with cold compresses/ice and, if needed, oral pain killers (ibuprofen or paracetamol). Local itching can be treated with topical crotamiton or low-potency corticosteroids (hydrocortisone 1%). If itching interferes with sleep, then an oral sedating antihistamine might be helpful at night.

Large local reactions

Occasionally, severe pain and swelling can extend beyond the immediate surroundings of the lesion. They should be managed with oral pain killers and antihistamines.

Local anaesthetics (e.g., benzocaine [Lanacane], lidocaine [Savlon Bites and Stings Pain Relief Gel])

Local anaesthetics can be used in adults and children over the age of 12 years and are in general applied three times a day. They are safe to use in pregnancy and are generally well tolerated. Local anaesthetics are known to be skin sensitizers and can produce contact dermatitis.

Hydrocortisone

Hydrocortisone is applied once or twice a day to the affected areas. It can be used in adults and children over 10 years of age. It can be used for a maximum of 7 days.

Sedating antihistamines (e.g., chlorphenamine)

As well as causing sedation they also possess anticholinergic side effects, which commonly result in dry mouth and



Table 11.5
Practical prescribing: Summary of medicines used for insect bites and stings

Name of medicine	Use in children	Very common ($\geq 1/10$) or common ($\geq 1/100$) side effects	Drug interactions of note	Patients in which care is exercised	Pregnancy and breastfeeding
Benzocaine Lanacane	> 12 years	Can cause sensitization reactions	None	None	OK
Lidocaine Savlon Bites and Stings Pain Relief Gel	> 12 years				
Hydrocortisone	> 10 years	None	None	None	OK
Crotamiton	> 3 years	None	None	None	OK
Chlorphenamine	> 1 year	Dry mouth, sedation and constipation	Increased sedation with alcohol, opioid analgesics, anxiolytics, hypnotics and antidepressants	Glaucoma, prostate enlargement	Pregnancy OK. Standard references state OK, although some manufacturers advise avoidance. This is presumably because it has the potential to cause drowsiness and may lead to poor feeding

possibly constipation. It is these anticholinergic properties that mean patients with glaucoma and prostate enlargement should ideally avoid their use because it could lead to increased intraocular pressure and precipitation of urinary retention. They interact with other sedating medication, resulting in potentiation of the sedative properties of the interacting medicines.

Chlorphenamine (e.g., Piriton)

Chlorphenamine can be given from the age of 1 year. Children up to the age 2 should take 2.5 mL of syrup (1 mg) twice a day. For children aged between 2 and 5, the dosage is 2.5 mL (1 mg) three or four times a day, and for those over the age of 6, the dosage is 5 mL (2 mg) three or four times a day. Adults should take 4 mg (one tablet) three or four times a day.

Crotamiton (Eurax)

Adults and children over 3 years of age should apply crotamiton two or three times a day. A combination product containing hydrocortisone is available (Eurax HC) but is best

avoided if possible. This is to decrease the exposure of patients to unnecessary corticosteroids and their potential adverse effects.

References

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Further reading

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Website

Lyme Disease Action: <https://www.lymediseaseaction.org.uk/>

Weight loss

Background

Obesity is a growing epidemic, particularly in developed countries. As a consequence, the risk of diseases such as diabetes and cardiovascular disease are also increasing, resulting in a situation where the current and future generations could have a shorter life span than their parents. Although a number of measures of obesity have been proposed, the internationally accepted measure is the body mass index (BMI). This is calculated as weight (kg) divided by height squared (m²). A BMI of over 25 is classified as overweight and for obesity the value is 30.

Prevalence and epidemiology

In 2018, more than a quarter of adults in England were classified as obese. This represents a doubling in values since 1993, and projected figures for 2030 are 35% of the population will be obese. Figures are even higher for those classed as overweight – 42% of men and 32% of women. This equates to 63% of adults being overweight or obese. Figures for Wales and Scotland are similar.

Aetiology

Although a number of causes of obesity have been proposed, and genetics may play an important role, for a significant proportion of the population it results from an imbalance between energy intake (food and beverages) and energy expenditure (exercise). Other factors associated with obesity include cultural norms, socioeconomic status, gender and ethnicity. In addition certain medical conditions (e.g., hypothyroidism) and medicines (e.g., corticosteroids, beta-blockers, anticonvulsants) can cause weight gain.

Evidence base for over-the-counter medication

Orlistat inhibits pancreatic and gastric lipase, which reduces the absorption of fat from the gut. There is a

significant body of evidence demonstrating the benefits of modest weight loss (about 5%–10% of initial body weight) and lifestyle modification, ranging from lipid profile modification to reduction in blood pressure. Clinical trials have shown that orlistat can produce these modest levels of weight loss (Hill et al., 1999). A 2014 systematic review and metaanalysis identified five trials that used orlistat at the approved dose (120 mg three times a day) and found the average weight loss after 12 months was 2.34 kg (Dombrowski et al., 2014). The best results with orlistat are seen in the short term (6–12 months); long-term results rely heavily on lifestyle changes (Hints and Tips Box 11.5).

Practical prescribing and product selection

Orlistat (Alli)

Orlistat is indicated for weight loss in adults (18 or over) who are overweight (BMI \geq 28 kg/m²) and should be taken in conjunction with a mildly hypocaloric, lower-fat diet.

The recommended dose of orlistat is one 60-mg capsule three times daily. The capsule should be taken immediately before, during or up to 1 hour after each main meal. If a meal is missed or contains no fat, the dose of orlistat should not be taken. If weight loss has not been achieved after 12 weeks, then the patient should stop taking orlistat.

Very common or common side effects relate to GI disturbances such as faecal urgency and incontinence, oily evacuation and spotting, flatus and abdominal pain. These can be minimized by restricting fat intake to less than 20 g per meal. Supplementation with fat-soluble vitamins (A, D, E and K) is recommended and can be achieved by taking a multivitamin. Because of the effect on vitamin K levels, patients on warfarin should avoid using orlistat. Orlistat may decrease ciclosporin levels and requires monitoring. There are limited data of orlistat being used in pregnant and breastfeeding women, and it is therefore not recommended.

HINTS AND TIPS BOX 11.5: WEIGHT LOSS

Realistic weight loss goals	Recommended goals are 1–4 kg/month in the short term, and 10%–20% of body weight in the medium to long term.
Exercise	People should be encouraged to start with regular, moderate exercise (e.g., brisk walking) three times a week, with the aim of increasing exercise to a minimum of 80 minutes/day to maintain weight loss.

References

- Dombrowski, S. U., Knittle, K., Avenell, A., Araujo-Soares, V., & Sniehotta, F. F. (2014). Long-term maintenance of weight loss with nonsurgical interventions in obese adults: Systematic review and meta-analyses of randomised controlled trials. *BMJ*, 348. <https://doi.org/10.1136/bmj.g2646>.
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Erectile dysfunction

Background

Sildenafil (Viagra Connect) was deregulated in November 2017. It is a potent and selective inhibitor of cGMP specific phosphodiesterase type 5 (PDE5) in the corpus cavernosum, which enhances the relaxant effect of nitric oxide allowing inflow of blood. For an erection to occur, sexual stimulation is required.

Prevalence and epidemiology

Erectile dysfunction is a common disorder. It can occur at any age, with studies involving men over the age of 40 reporting rates between 19% and 50%. Prevalence also increases with increasing age and is due to chronic disease, co-morbid conditions and age-related changes.

Aetiology

Erectile dysfunction is a symptom and not a disease. It tends to have an organic or psychological cause. Organic causes broadly fall in to blood flow problems, conditions affecting nerve impulses and hormone regulation or structural abnormalities. Psychological causes range from depression to performance anxiety.

Evidence base for over-the-counter medication

Trials involving the 50-mg dose compared with placebo have shown clinically and statistically significant improvements in causing penile erection. Data show that over 40% of patients respond after the first dose, but some men only reported improvements after several doses.

Table 11.6

Medicines known to cause erectile dysfunction

Cardiovascular	Beta-blockers, verapamil, methyldopa, and clonidine, diuretics (e.g., spironolactone and thiazides), digoxin, amiodarone
Psychotropic	Anti-depressants, e.g., selective serotonin reuptake inhibitors, tricyclics, monoamine oxidase inhibitors, lithium, chlorpromazine, haloperidol
Anti-epileptics	Carbamazepine, phenytoin, barbiturates
Endocrine	Hormones and hormone-modifying drugs – antiandrogens (flutamide, cyproterone acetate), luteinizing hormone releasing hormone agonists (leuprorelin, goserelin), corticosteroids,
Others	5-Alpha reductase inhibitors (e.g., finasteride), H ₂ antagonists, recreational drugs

Practical prescribing and product selection

Before sildenafil can be supplied a number of considerations need to be taken into account. Firstly, erectile dysfunction associated with medicines needs to be eliminated. Many medicines are associated with causing erectile dysfunction. Table 11.6 highlights those most commonly implicated.

Secondly, there are a number of restrictions on its sale and the manufacturer provide useful information and checklists to help in supplying the product appropriately (<https://hcp.viagraconnect.co.uk/>). Fundamentally, men with cardiovascular disease or who are in poor physical health (i.e., those men who with light or moderate physical activity, such as walking briskly for 20 minutes or climbing two flights of stairs, feel very breathless or experience chest pain) should not take sildenafil.

Sildenafil (Viagra connect)

Men over the age of 18 should take one tablet with or after food approximately 1 hour before sexual intercourse. If a patient needs to take it a number of times on different occasions before achieving a satisfactory penile erection for sexual activity they should be advised to see a doctor. The most common side effect seen is headache (very common), with dizziness, flushing, nausea, dyspepsia, nasal congestion and visual disturbances reported as common. Sildenafil levels can be affected by concomitant treatment with CYP3A4 inhibitors and may require lower dosing (e.g., 25 mg). Likewise patients may require lower

doses of sildenafil if taking alpha-blocker medicines (e.g., alfuzosin, doxazosin or tamsulosin) but ritonavir and sildenafil should not be given together should be avoided.

Future deregulations

The number of POM to P deregulations in the last few years has slowed, while P to GSL switches have increased. This wider availability of medicines fits with current UK government policy that promotes self-care. It has resulted in the number of medicines sold only through pharmacies shrinking. The lack of POM to P switches over the last 5 to 10 years is partially a result of burdensome regulatory processes. Fewer than a dozen switches were seen between 2010 and 2019 (most being from classifications already available OTC, e.g., proton pump inhibitors, nasal corticosteroids, and four from new therapeutic classes – orlistat, tranexamic

acid, sildenafil and tamsulosin). Over the same time, two products were switched back to POM (domperidone and oral diclofenac) and a number of recent deregulated products have unfortunately been discontinued or are not being actively marketed by the manufacturer; for example, simvastatin, tamsulosin and calcipotriol.

The future for further switches therefore appears relatively poor in the short term. It is likely that future deregulation may be a combination of:

- Product license extensions
- 'Me too' products – i.e., medicines from therapeutic classes already available OTC
- Products that have been deregulated already in other countries

Table 11.7 highlights some future candidates that are potential POM to P switches.

Table 11.7
Possible future deregulated medicines from POM to P

Product license extensions	
Hydrocortisone	Available from 2 years of age in Australia and in different strengths
Products available over-the-counter in other countries	
Salbutamol	Available in Singapore, New Zealand
Nonsteroidal anti-inflammatory drugs	Mefenamic acid available in Australia, New Zealand
Trimethoprim	Available in New Zealand
Metoclopramide	Available in Australia, New Zealand
Non-sedating antihistamines	Desloratadine and fexofenadine available over-the-counter in Australia
Medicines supplied under protocols	
Oral contraception	Evidence of successful patient group directions in operation
Topical antibiotics for impetigo (e.g., fusidic acid, mupirocin)	
Anti-retrovirals for influenza	

Self-assessment questions

The following questions are intended to supplement the text. Two levels of questions are provided: multiple choice questions and case studies. The multiple choice questions are designed to test knowledge and application of knowledge, and the case studies allow this knowledge to be put in context in patient scenarios.

Multiple-choice questions

- 11.1** Which species of plasmodium is associated with most malarial deaths?
- P. falciparum*
 - P. knowlesi*
 - P. malariae*
 - P. ovale*
 - P. vivax*
- 11.2** Which of the listed side effects is least commonly associated with EllaOne?
- Abdominal pain
 - Dizziness
 - Headache
 - Nausea
 - Urticaria
- 11.3** What medicine is most appropriate for an adult travelling to the Gambia from the UK on a 6-hour flight in terms of minimizing doses and side effects?
- Cinnarizine 15 mg
 - Chlorphenamine 2 mg
 - Cyclizine 50 mg
 - Hyoscine 150 µg
 - Promethazine 25 mg
- 11.4** What would be the best differentiating feature between an insect bite and scabies in a person with lesions on the wrist?
- Development of papules and vesicles
 - Intensity of itching
 - Occupational history
 - Severity of redness
 - Symptom improvement after taking antihistamines
- 11.5** Lyme disease should be suspected in a patient after experiencing a tick bite who presents with rash and what other symptom?
- Abdominal pain
 - Fever
 - Nausea
 - Rash
 - Tinnitus
- 11.6** What is the maximum length of time after unprotected sex in which levonorgestrel can be given?
- 24 hours
 - 48 hours
 - 72 hours
 - 96 hours
 - 120 hours
- 11.7** What medicine is most appropriate for an 8-year-old child travelling to Calais from Dover on a 3-hour ferry crossing?
- Chlorphenamine 2 mg
 - Cinnarizine 15 mg
 - Cyclizine 50 mg
 - Hyoscine 150 µg
 - Promethazine 25 mg
- 11.8** Which 'stage of change' do patients ideally need to demonstrate before starting NRT?
- Action
 - Contemplation
 - Maintenance
 - Precontemplation
 - Preparation
- 11.9** Which ONE of the following patients should be referred to the GP?
- 15-year-old female asking for naproxen
 - 17-year-old female asking for levonorgestrel
 - 18-year-old male asking for orlistat
 - 21-year-old male asking for sildenafil
 - Parent of 11-year-old male asking for clobetasone for the child
- 11.10** Mrs LC, 25 years old, visits your pharmacy and wants to have a word in private. You take her to the consultation room and she explains that she has missed one pill of her

combined oral contraceptive. You ascertain that she is currently in the middle part of her cycle, and she has not missed any pills until this incident. What would be the most appropriate course of action?

- Advise additional precautions such as using condoms are required for next 7 days
- No action needed. Reassure the patient to continue taking her pill as normal from tomorrow
- Omit the pill free period in the current pack and start the new pack immediately
- Recommend taking emergency hormonal contraceptive
- Take the missed pill and continue to take the rest of the pack as usual

11.11 Mr BN is going on holiday to Ecuador for 2 weeks and requires antimalarial medication. You recommend that he buys chloroquine and proguanil tablets as a combination pack. What would be the most appropriate dosage regimen advice for Mr BN?

- Take 1 week before departure, whilst in Ecuador and for 4 weeks after returning
- Take when they arrive in Ecuador, for the duration of the holiday and for 4 weeks after returning
- Take 1 week before departure, whilst in Ecuador and for 2 weeks after returning
- Take 1 week before departure, and for the duration of your holiday only
- Take 2 weeks before departure, whilst in Ecuador and for 4 weeks after returning

11.12 Miss ZB, 29 years old, comes into your pharmacy wanting to buy Alli (orlistat 60 mg capsules) over the counter. She has a BMI of 35 and a very sedentary lifestyle and takes no exercise. Her diet consists mostly of takeaways but she tells you that she is keen to lose weight for her holiday in 6 months. Which one of the statements is correct regarding the sale of Alli?

- Alli can be sold to any individuals with BMI over 25
- Before starting Alli the patient should have a diet and exercise programme in place
- The maximum dose of Alli in 24 hours is 120 mg
- The minimum age Alli can be purchased is 16 years
- Treatment with Alli should not exceed 9 months

11.13 Which is the most common side effect associated with sildenafil?

- Dizziness
- Dyspepsia
- Flushing
- Headache
- Nasal congestion

11.14 What is the recommended dose for OTC sildenafil in a 70-year-old male with mild renal impairment?

- 25 mg od
- 25 mg bd
- 50 mg od
- 50 mg bd
- Not advised

11.15 Which is the most common side effect associated with MaloffProtect?

- Cough
- Dizziness
- Fever
- Headache
- Rash

Questions 11.16 to 11.21 concern the following medicines:

- Chloroquine
- Proguanil
- Hyoscine
- NRT
- Levonorgestrel
- Sildenafil
- Ulipristal
- Orlistat

Select, from A to H, which of the above medicines:

11.16 Should be avoided in epilepsy?

11.17 Should be avoided in patients taking nitrates?

11.18 Needs to be used with caution in patients with renal impairment

11.19 Needs to be used with caution in patients with glaucoma

11.20 Affects absorption of vitamin A

11.21 May worsen psoriasis

Questions 11.22 to 11.25 concern the following medicines:

- A. *Benzocaine cream*
- B. *Chlorphenamine syrup*
- C. *Crotamiton cream*
- D. *DEET lotion*
- E. *Hydrocortisone ointment*

Select, from A to E, which of the above treatments:

- 11.22 Can be given to a 12-month-old child suffering from an insect bite?
- 11.23 Is least suitable in pregnancy?
- 11.24 Is restricted to a maximum of 7 days use for insect bites?
- 11.25 Is most likely to cause skin irritation?

Answers

11.1 Answer: a

Rationale: Most deaths are seen from sub-saharan Africa where Falciparum is most prevalent and therefore the species associated with most deaths.

11.2 Answer: e

Rationale: All side effects listed have been reported with EllaOne. Options a–d are listed in the SmPc as common, whereas urticaria (e) is rare.

11.3 Answer: a

Rationale: Promethazine (a) and cinnarizine (c) have sufficiently long duration of actions that only one dose would be needed to 'cover' the length of the flight but promethazine is more likely to cause sedation.

11.4 Answer: c

Rationale: Both conditions will present with similar signs and symptoms – fundamentally intense itchy (b) red rash (a). Severity of redness (d) is a poor differentiator and itch is likely to be reduced in both after taking antihistamines (e). An occupational history is often seen in scabies and is therefore a good way of deciding the cause.

11.5 Answer: b

Rationale: Flu-like symptoms can be experienced, so from the listed symptoms only fever (b) would be likely.

11.6 Answer: c

Rationale: Levonorgestrel remains effective up to 72 hours post unprotected sex although its effectiveness decreases with time. Note Ulipristal can be given up to 120 hours after unprotected sex.

11.7 Answer: d

Rationale: All medicines would provide anti-emetic cover for a 3-hour journey. Given it is good practice to match treatment with length of journey then those medicines that have an effect for a prolonged period (cinnarizine (b), promethazine (e)) are best avoided. Chlorphenamine (a) and cyclizine (c) are associated with sedation more than hyoscine, and on this basis hyoscine would be a more suitable choice.

11.8 Answer: e

Rationale: Precontemplation (d) is where the person is not thinking seriously about making a change; Contemplation (b) is where people are thinking about

change; Action (a) is where people have determined what they are going to do and set themselves 'goals'; and maintenance (c) is the goal of change.

11.9 Answer: e

Rationale: This question is purely based on the age at which each product is licensed for. Clobetasone can only be given to those 12 years and above.

11.10 Answer: e

Rationale: No additional or emergency contraception is usually necessary. The patient should take the missed pill and continue to take the rest of the pack as usual. EHC may be considered if pills have been missed earlier in the packet or in the last week of the previous packet.

11.11 Answer: a

Rationale: Taking medication prior to departure allows the patient to know if they are going to experience any side effects, and if they do still have time to obtain a different antimalarial. This rules out option (b). It also rules out option (e) as there is no need for medicine taking to begin so early. This combination product needs to be taken for 4 weeks after returning to ensure that any possible infection that could have been contracted during the last few days of the holiday does not develop into malaria – eliminating options (c) and (d).

11.12 Answer: b

Rationale: Treatment with Alli is to individuals with BMI over 28, not 25 (a); the maximum dose is 180 mg not 120 mg (c); the minimum age is 18 not 16 (d); and treatment should not exceed 6 months, not 9 months (e).

11.13 Answer: d

Rationale: All listed side effects are reported, although only headache recorded as occurring very commonly – all others are 'common'.

11.14 Answer: c

Rationale: No dose adjustments needed in this older male with mild renal disease so therefore the standard dose can be given.

11.15 Answer: d

Rationale: Cough (a), dizziness (b), fever (c) and rash (e) are listed as common, whereas headache (d) is very common.

11.16 Answer: A

Rationale: All OTC medicines have associated risk in use, whether this be their side effect or interaction profiles or use in certain patient groups. Vigilance should always be exercised when dealing with requests from patients with conditions that are treated with higher risk medicines. Such a condition is epilepsy as the medicines used tend to have many side effects and the ability to interact with multiple other medicines. Chloroquine may lower the convulsive threshold and thus antagonize the actions of antiepileptics and lead to loss of seizure control.

11.17 Answer: F

Rationale: Consistent with its known effects on the nitric oxide/cyclic guanosine monophosphate (cGMP) pathway sildenafil potentiates the hypotensive effects of nitrates.

11.18 Answer: B

Rationale: Many medicines require dose adjustment in renal failure to accommodate renal clearance. From the list proguanil is most likely to require dosage adjustment, especially in severe renal impairment.

11.19 Answer: C

Rationale: Any medicine that can exert anti-cholinergic action has the potential to cause glaucoma in individuals with narrow anterior chamber angles by dilating the pupil and causing pupillary block.

11.20 Answer: H

Rationale: As orlistat works by inhibiting gastrointestinal lipases the body is unavailable to hydrolyse dietary fat,

which may also potentially impair the absorption of fat soluble vitamins.

11.21 Answer: A

Rationale: Many adverse events are not predictable and are only observed after repeated use in clinical practice – the precipitation of worsening psoriasis with chloroquine is such an example.

11.22 Answer: B

Rationale: Only chlorphenamine could be given for this age child from the options listed. Benzocaine is 12 years; crotamiton is 3 years; the lowest age in which DEET can be given is difficult to establish and UK commercial products have differing ages. A product made by Boots the Chemist (Boots Repel Maximum) states over 2 years of age; hydrocortisone is 10 years.

11.23 Answer: B

Rationale: Only chlorphenamine listed is orally taken and therefore most likely to cause systemic side effects.

11.24 Answer: E

Rationale: Product licence restriction on all forms of hydrocortisone for any indication limit use to a maximum of 7 days.

11.25 Answer: D

Rationale: Whilst any topically applied product has the potential to cause skin irritation through sensitization it is well documented that DEET, even at low concentrations, is prone to causing skin reactions.

Self-assessment questions

The following questions are intended to supplement the text. Two levels of questions are provided: multiple choice questions and case studies. The multiple choice questions are designed to test knowledge and application of knowledge, and the case studies allow this knowledge to be put in context in patient scenarios.

Multiple choice questions

- 11.1** Which medicine used for motion sickness is subject to abuse?
- Chlorphenamine
 - Cinnarizine
 - Cyclizine
 - Hyoscine
 - Promethazine
- 11.2** What side effect of Levonelle[®] One Step is the commonest?
- Diarrhoea
 - Dizziness
 - Headache
 - Irregular menstruation
 - Vomiting
- 11.3** In which group of the population is smoking the least prevalent?
- Elderly men
 - Middle-aged males
 - Middle-aged females
 - Teenage females
 - Teenage males
- 11.4** Which patients should use 24-hour patches?
- People who need a cigarette before they go to sleep
 - People who smoke more than 20 cigarettes a day
 - People who smoke more than 40 cigarettes a day
 - People who need a cigarette within 20 minutes of waking up
 - People who smoke cigars
- 11.5** Which dermatological condition can be worsened by taking chloroquine?
- Acne vulgaris
 - Atopic dermatitis
 - Eczema
 - Psoriasis
 - Rosacea
- 11.6** How long after unprotected sex can oral forms of EHC be given?
- 24 hours
 - 48 hours
 - 72 hours
 - 96 hours
 - 120 hours
- 11.7** What is the commonest smoking-related disease?
- Lung cancer
 - Chronic obstructive pulmonary disease
 - Throat cancer
 - Motor neurone disease
 - Type II diabetes
- 11.8** Care should be taken when recommending promethazine to which patient group?
- Diabetes mellitus
 - Glaucoma
 - Hypertension
 - Parkinson's disease
 - Peptic ulceration
- Questions 11.9 to 11.11 concern the following NRT products:
- Gum
 - Inhalator
 - Lozenge
 - Microtab
 - Patch
- Select, from A to E, which of the above products:
- 11.9** Is most suitable for patients in which adherence may be an issue?
- 11.10** Delivers constant levels of plasma nicotine
- 11.11** Is useful for those people who need to have their hands occupied?

Questions 11.12 to 11.14 concern the following medicines:

- A. Chloroquine
- B. Hyoscine
- C. Levonorgestrel
- D. NRT
- E. Proguanil

Select, from A to E, which of the above medicines:

11.12 Most commonly causes diarrhoea

11.13 Most commonly causes visual disturbances

11.14 Most commonly causes dry mouth

Questions 11.15 to 11.17: for each of these questions *one or more* of the responses is (are) correct. Decide which of the responses is (are) correct. Then choose:

- A. If 1, 2 and 3 are correct
- B. If 1 and 2 only are correct
- C. If 2 and 3 only are correct
- D. If 1 only is correct
- E. If 3 only is correct

Directions summarized

A	B	C	D	E
a, b and c	a and b only	b and c only	a only	c only

11.15 When using DEET, the following rule(s) should be followed:

- a. It should be applied regularly
- b. It should be kept away from plastic
- c. It should never be applied to the face

11.16 *Plasmodium falciparum* is associated with:

- a. High levels of drug resistance
- b. The highest incidence of death compared to other forms of malaria
- c. Widespread distribution on the African continent

11.17 What side effects can be seen in patients chewing nicotine gum?

- a. Taste disturbance
- b. Sweating
- c. GI disturbances

Questions 11.18 to 11.20: these questions consist of a statement in the left-hand column followed by a statement in the right-hand column. You need to:

- Decide whether the first statement is true or false
- Decide whether the second statement is true or false

Then choose:

- A. If both statements are true and the second statement is a correct explanation of the first statement
- B. If both statements are true but the second statement is NOT a correct explanation of the first statement
- C. If the first statement is true but the second statement is false
- D. If the first statement is false but the second statement is true
- E. If both statements are false

Directions summarized

	1st statement	2nd statement	
A	True	True	2nd explanation is a correct explanation of the 1st
B	True	True	2nd statement is not a correct explanation of the 1st
C	True	False	
D	False	True	
E	False	False	
	First statement	Second statement	
11.18	Antimalarials have to be taken before travel	Side effects may preclude patients from taking antimalarials	
11.19	Malaria can be contracted months after return from an endemic area	The liver holds a reservoir of parasites that are hard to eradicate	
11.20	Pregnancy is a contraindication for malaria prophylaxis	Infants cannot take antimalarials	

Answers

11.1 Answer: c

Rationale: There are reports of cyclizine abuse amongst people addicted to opioids who are receiving methadone. It is said to produce strong psychoactive effects.

11.2 Answer: c

Rationale: Data from the SmPc shows that all listed side effects do occur. Headache is listed as very common (> 10%), where as all others are common (1%–10%).

11.3 Answer: a

Rationale: Smoking in the general population is decreasing across all groups; however, statistics show that smoking in the elderly is the lowest (ONS data 2018).

11.4 Answer: d

Rationale: 24-hour patches are useful when constant plasma nicotine levels are advantageous; for example, in those people where they crave cigarettes as soon as they awake.

11.5 Answer: d

Rationale: Chloroquine has been associated with inducing certain skin disorders including urticaria in black-skinned Africans and case reports of vitiligo. From the list shown, there have been reports of psoriasis flare-ups within the first few weeks of taking chloroquine.

11.6 Answer: e

Rationale: Two forms of EHC can be sold OTC; Levonelle One Step can be used up to 72 hours after unprotected sex and EllaOne can be used up to 120 hours.

11.7 Answer: b

Rationale: Despite smoking rates being at an all time low in 2019 (14.4%) it still remains the nation's biggest killer. All conditions listed can be caused by smoking, and the majority of lung cancers are attributable to smoking. However, in terms of total numbers, it is in COPD that smoking accounts for the most deaths.

11.8 Answer: b

Rationale: Promethazine is a sedating antihistamine and has anticholinergic properties, and because of this it has the potential to worsen symptoms of glaucoma.

11.9 Answer: E

Rationale: Most NRT is designed to try and mimic the cravings for cigarettes and used on a 'when needed' basis but for some people there is a need to eliminate cravings completely. This is best achieved through patches.

11.10 Answer: E

Rationale: See answer to 11.4.

11.11 Answer: B

Rationale: Some people find they need to mimic the physical act of smoking and therefore NRT (inhalators), which replicate this action, can be useful.

11.12 Answer: E

Rationale: From SmPc data only chloroquine and proguanil have diarrhoea listed as a side effect, although the incidence is stated as not known. However, it appears from the literature/case reports that diarrhoea with proguanil is more commonly reported than chloroquine when used as chemoprophylaxis.

11.13 Answer: A

Rationale: Only chloroquine is associated with visual disturbance and, although the incidence is unknown, there are multiple eye-related side effects listed in the SmPc.

11.14 Answer: B

Rationale: Hyoscine causes dry mouth most frequently but is listed as uncommon in the SmPc.

11.15 Answer: B

Rationale: DEET can be applied to any skin surface and depending on the concentration used will require regular re-application; for example, on the 'fitfortravel' website the recommendation is '20% DEET between 1 and 3 hours, 30% DEET up to 6 hours, 50% DEET up to 12 hours.' DEET is also water soluble and should be reapplied after washing/swimming or sweating. It is also well recognized that DEET does damage synthetic materials.

11.16 Answer: A

Rationale: P. falciparum is the form of malaria that is most associated with causing deaths especially from sub-Saharan Africa and has high levels of drug resistance.

11.17 Answer: E

Rationale: NRT is not usually associated with side effects; transdermal delivery using a 24-hour patch can cause dreams/nightmares and using oral forms [gum, lozenges, etc.] means the patient can swallow nicotine, which leads to GI problems.

11.18 Answer: a (True/True - statement 2 is a correct explanation of statement 1)

Rationale: Ideally they should be taken before travel as it not only allows a tablet-taking regimen to be established but also to see if side effects are experienced and the chance to swap to an alternative.

11.19 Answer: c (True/False)

Rationale: The parasite causing malaria can lie dormant in the liver for a long time.

11.20 Answer: e (False/False)

Rationale: Pregnancy is not an absolute contraindication for all OTC antimalarials and, likewise, children can take them (but not MaloffProtect; however, age restrictions apply and mg/kg dosing is advocated.

Case studies

CASE STUDY 11.1

Mr and Mrs J and their two children, Sammy, aged 5, and Jessica, aged 12, are going on their summer holidays. They want to know what travel sickness tablets they should take.

- a. What information do you need to know before recommending a suitable product? For each question state your rationale.

You need to know:

- *Who is affected by travel sickness: this may influence recommendation, especially if it affects one of the parents who might be driving.*
- *The length of the trip: this will influence which product will be the most appropriate. It is sensible to match up the length of journey with a medicine that has the same duration of action as the trip.*
- *Medication history: patients who are taking medication for glaucoma or prostate enlargement should avoid taking OTC medicines. Additionally, medicines with anticholinergic action will potentiate the side effects of OTC travel medication.*
- *Past medication for similar journeys: it is likely that the family have had to purchase such products in the past. It is worth finding out what they were and how well tolerated they were before potentially recommending the same product.*

You find out they are going to northern France by ferry. This is a 2-hour boat journey followed by a further 2-hour

drive. Mr J gets seasick and neither of the children likes boat or car journeys. Jessica also suffers from narcolepsy.

- b. What would be the best drug regimen for the family? State your rationale.

It appears that the total journey time is relatively short and a hyoscine-based product would be the most suitable product for the two children and their father. Kwells Kids could be used by everyone; Mr J would have to take 2 tablets, Jessica 1 tablet and Sammy ½ a tablet. As Jessica has narcolepsy it is necessary to see if she takes any medication to help with the condition. If she does, then checks would have to be made to ensure that Jessica could still take hyoscine.

- c. What practical advice would you also offer the family?

Hyoscine will cause dry mouth and potential sedation. Sucking on sweets can compensate for a dry mouth. Sedation might be a problem for Mr J because he has to drive after the ferry crossing. He should be told about the possible effects of hyoscine. He might choose not to take the medication, although no alternative is available that does not cause possible sedation.

The two children might experience less nausea if they are kept occupied by playing games.

CASE STUDY 11.2

Ms HS walks into the pharmacy on Saturday morning and asks to buy the morning-after pill.

a. What key questions do you need to ask?

- Her age
- How long ago did she have unprotected sex or contraceptive failure?
- The date of her last period and was it different than normal.

You find out she is 18 and had sex last night. She normally takes Microgynon. Her period was about 3 weeks ago and was the same as previous periods.

b. What else do you need to know?

You also need to know about her pill-taking compliance.

She says that she has not taken her last 2 days of tablets (Thursday and Friday) and does not know whether she should take today's tablet. She has three tablets left before the end of the packet.

c. What advice are you going to give her?

There is no need for EHC as she has forgotten to take her tablets at the end of the cycle. She should be told to continue taking the rest of her tablets but when the last tablet is taken, she should not have a 7-day pill-free period but go straight on to the next packet.

CASE STUDY 11.3

Mr Heaney asks the counter assistant for advice on stopping smoking. The counter assistant refers him to the pharmacist.

- a. Outline what factors should be taken into account to determine whether Mr Heaney is a suitable candidate to be given a smoking-cessation product.

Before instigation of any treatment it is important that the patient does want to stop smoking. Studies has shown that motivation is a major determinant for successful smoking cessation, and interventions based on the transtheoretical model of change put forward by Prochaska and colleagues have proved effective. Most patients who ask directly for NRT will be at the preparation stage of the model and ready to enter the action stage.

Mr Heaney smokes 20 cigarettes a day and craves a cigarette when he gets up in the morning.

- b. Outline the treatment option/s that will be most suitable for Mr Heaney.

A 24-hour patch might be the formulation of choice for Mr Heaney to combat early-morning cravings. Alternatively, he could use a 16-hour patch and then use a short-acting type of NRT first thing in the morning to get over any cravings (e.g., inhalator).

- c. What general advice will you give Mr Heaney in addition to any NRT product supplied?

Set a quit date; remove temptations; avoid environments where smoking happens. Promote healthy lifestyle advice – exercise, diet, weight control, alcohol intake.

You supply him with a week's worth of NRT and make an appointment for him to see you for further supply. On his return, you use a carbon monoxide (CO) monitor to check his adherence.

- d. Outline the principles behind CO monitoring.

The best cut-off breath CO level for the determination of smoking status is 5 ppm as it gives the best sensitivity and specificity. As there is a clustering of CO levels in individuals who smoked within the last 5 hours, this cut-off level may be a useful adjunct in detecting smoking status in individuals who have smoked within the last 5 hours. However, it is lower than the usual 6 to 10 ppm, as recommended by some studies. A cut-off breath CO level of greater than 8 ppm is strongly associated with self-reports on smoking. Charts produced by CO monitor manufacturers are useful visual aids to show acceptable levels: <http://www.camquit.nhs.uk/uploads/Carbon%20Monoxide%20Chart.pdf>.

Evidence-based pharmacy practice

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What is evidence-based practice?

Evidence-based medicine (EBM) and evidence-based practice (EBP) are not new concepts, with some authors tracing the history back to the Hippocratic oath (Goodman, 2003). There are numerous definitions of EBM, but the most accepted comes from David Sackett and colleagues, who described EBM as ‘...the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients...integrating individual clinical expertise with the best available external clinical evidence from systematic research’ (Sackett et al., 1996). This definition encapsulates the important aspects of practising in an evidence-based fashion. First, we need to be conscientious and explicit in the use of evidence, meaning that we need to seek out, and keep up to date with, the current evidence for the efficacy and safety of a medicine. Therefore EBM does require some effort. Second, EBM involves integrating clinical knowledge with evidence, meaning that neither should dominate decision making. We should not make decisions based on our clinical experience alone, as our experiences may be biased. For example, we may get the impression that a treatment works because people return to tell us how ‘wonderful’ the treatment that we recommended was, without knowing how many people found the treatment useless and vowed never to return to the pharmacy. However, evidence from clinical trials should not be the sole basis for decision making either, as they may not be applicable to the patient you have before you. Therefore incorporating both clinical experience and evidence is required. Finally, we should seek out the ‘best’ evidence,

meaning that we need to understand which types of evidence are more robust, and which evidence is less reliable.

Myths about evidence-based practice

Not surprisingly there has been some resistance to the concept of EBP. In this section we will look at some of the myths that have been promulgated about practicing in an evidence-based manner.

Evidence-based practice is ‘cookbook’ medicine

Some critics have accused EBP as being too ‘standardized’, with all clinicians practicing the same way. However, this in fact ignores the important fundamental principle that each clinician must use their clinical experience, in addition to good external evidence, to reach a decision. Therefore by definition, each decision making process using EBP will be different.

There is no evidence for non-prescription medicines and complementary and alternative medicines (CAM)

Many argue that we cannot use an evidence-based approach with respect to non-prescription medicines and CAM because there is no published evidence about them. Although there is a paucity of data for many older non-prescription medicines, there are an ever-increasing number of non-prescription

products for which there is good evidence. This is largely due to the trend to reclassifying prescription-only to non-prescription medicines. Examples include the histamine-2 antagonists, azole anti-fungal preparations, and proton-pump inhibitors.

The situation for CAM is more complicated. Advocates of complementary medicine claim that it is not possible to apply typical EBM principles to CAM as it takes a more 'holistic' approach to treatment compared with Western medicine, and that it encompasses other influences, including emotional and spiritual factors (Hunter & Grant, 2005). However, there are a number of CAMs that have stood the EBM test such as St John's Wort for depression (Linde et al., 2008). Therefore it is difficult to sustain the argument that we should not continue to look for evidence of efficacy of CAMs.

However, as the saying goes, 'a lack of evidence of efficacy is not evidence of a lack of efficacy'. What it does mean is that we should be more cautious when embracing or recommending products for which there is limited or no evidence. This is particularly important when the product has limited or no evidence of efficacy but evidence of harm; for example, cough and cold preparations in children. In these situations the benefit to risk ratio makes it difficult to recommend a treatment. However, a pharmacist promoting something that lacks evidence of efficacy but has little or no harm; for example, homeopathic medicine, also runs the risk of having their reputation as a healthcare professional questioned by the public and other healthcare professionals (Dwyer, 2011).

It is too hard to find the evidence

In the pre-Internet era it was certainly true that finding the evidence was extremely labour intensive, requiring hours of searching using paper-based indexes. However, the World Wide Web along with the advent of the portable document format (PDF) has made searching and obtaining evidence much easier. Although there is still the issue of locating the 'best' evidence and the time taken to search and read all the evidence on a particular topic, there are resources that we will discuss in this chapter that assimilate the evidence and present it in a concise manner, thus saving a considerable amount of time.

What is good evidence?

As outlined previously, practising in an evidence-based way means using the *best* available evidence. As a guide, a hierarchy of evidence has been developed. This grading is based on the level of potential bias in the study design, with those with lowest potential for bias given the highest ranking. The abbreviated ranking, from highest to lowest is:

- Systematic reviews of randomized controlled trials (RCTs)
- Well-conducted RCTs
- Observational studies (e.g., cohort and case-control)
- Case series and case studies.

Thus ideally, decisions should be based on systematic reviews followed by RCTs. It is important to note that 'expert opinion' is no longer considered a reliable source of evidence.

What is 'bias'?

There are a number of definitions of what is meant by the term 'bias'. In terms of clinical trials, bias is a *systematic* deviation from the truth. Thus something has to occur routinely in one arm of a study that does not occur in the other. Examples of biases that happen in studies include:

- Selection bias – e.g., where individuals who are allocated to one treatment are systematically different from the other treatment, and these differences have an influence on the outcome
- Reporting/measurement bias – e.g., where patients report the outcome differently in one arm than the other
- Survival bias – e.g., patients who make it to the end of the study are systematically different from those who drop out

In assessing the quality of a study we are focused on looking at how the study attempted to minimize any potential biases. This is discussed later under *Evaluating the evidence*.

Locating the evidence

The first step in practising in an evidence-based manner involves finding the evidence. This can be done in a systematic way as follows:

- Formulate your question
- Identify appropriate sources
- Search the appropriate sources

Formulating your question

Searching for an answer will be more productive if you start with a well-formulated question. A common way of doing this is to arrange your question in the PICO format, with the letters standing for:

- P – Patient population
- I – Intervention
- C – Comparator
- O – Outcome

For example, if you decide to find the evidence for the efficacy of omega-3 supplements in treating Alzheimer's dementia, your questions would look like:

- P – People with dementia
- I – Omega-3 supplementation
- C – Nothing
- O – Improvement in symptoms of dementia

By doing this you will know which key words and phrases to use in your searching strategy.

Identifying appropriate sources

The question you are trying to answer, and the time you have to get the answer, often determine which sources you use. The common types of questions that pharmacists are interested in answering are usually either disease focused (e.g., what is the best treatment for condition Y?) or drug focused (e.g., how well does drug X work in condition Y?). For disease-focused questions, evidence-based guidelines are usually the best source of summarized information. An example of this in a UK context is the National Institute for Health and Care Excellence (NICE): www.nice.org.uk/guidance

In trying to answer a question about the efficacy of a particular drug for a condition, the types of sources can be divided into summaries or reviews, and original research. Evidence-based reviews of medicines can be found in a number of sources. Probably the best source of systematic reviews is the Cochrane library (www.cochranelibrary.com/). There are two drawbacks of the Cochrane library. First, although there are over 6000 systematic reviews in the database, not all topics have been covered. Therefore you may not find a systematic review to answer your question. Second, reviews take years to compile and are only updated every few years. Therefore a Cochrane review may not reflect the most up-to-date information, and it is important to look at when the review was last updated when interpreting the results.

Sourcing original research has its challenges. The largest free database is Medline, which can be searched using PubMed search engine (www.ncbi.nlm.nih.gov/pubmed/). PubMed allows you to access over 20 million citations dating back over 50 years. The current PubMed interface is reasonably sophisticated, allowing you to search in certain fields (e.g., search for an author's name in the author field) and limit your searches to certain types of journal articles (e.g., RCTs and systematic reviews). However, once you have found a relevant citation, you need to be able to access it. PubMed will provide you with links to full-text articles. Please note, although many journals are now 'open access' (i.e., free), a large number still remain subscription only.

Other sources of information

If you only have a limited amount of time, you will need to 'filter' the information quickly. To help you do this there are a number of websites that help quickly identify evidence-based resources. These include:

- Evidence Updates from BMJ – plus.mcmaster.ca/EvidenceUpdates/
- TRIP database – www.tripdatabase.com/
- SUMSearch 2 – sumsearch.org/
- NPS – www.nps.org.au/health_professionals/guide_to_medicines_information_resources.

Another good source of information is UK Medicines Information (UKMi). UKMi is an NHS pharmacy-based service provided by a network of over 200 medicine information centres that are based in the pharmacy departments of most hospitals. The centres are mainly staffed by pharmacists with particular skills in locating, assessing and interpreting information about medicines. Contact details can be found at the end of this chapter of the 12 regional centres.

Searching appropriate sources

Searching most information resources is usually done using free-text terms. For example, if you were interested in the use of fish oil for dementia, you would simply enter the terms 'fish oil' and 'dementia' into the search engine. It is important to note that using free-text terms can be limiting as it relies on these terms being used usually somewhere in the title or abstract of the article. Therefore you may also need to consider what other terms could mean the same thing. For example, with 'fish oil', alternatives could include 'omega-3 fatty acids', 'DHA', 'EPA', 'krill oil' and so on. Both the Cochrane Library and PubMed offer advanced search options that allow you to look for terms in specific fields, and the use of Boolean logic (i.e., AND, OR and NOT). More information on searching these resources can be found on their sites.

Evaluating the quality of the evidence

Evaluating the quality of a study involves examining for potential bias (see *What is good evidence?*). In this section we will look at how to do this for systematic reviews and RCTs.

Judging the quality of a systematic review

There are published guidelines regarding assessment of systematic reviews. The most widely accepted is PRISMA (Preferred Reporting Items for Systematic Reviews and

Table 1
Assessing the quality of a systematic review

Question to ask	Rationale	What to look for
Did the authors have an <i>a priori</i> protocol?	Authors should have stated up front, before they start the review, what their study question was and how they would approach the review. This prevents the authors from 'changing the goal posts' later and doing something different.	Check if a protocol was published first. For a Cochrane review this is always reported in the database as a 'protocol'.
Did they use multiple sources of data?	Authors should undertake a comprehensive search of the literature to try and find ALL evidence available.	The use of multiple databases (at least Medline and Embase) and attempts to get unpublished data from authors and pharmaceutical manufacturers.
How did they select the studies?	Authors need to have clear criteria for including or excluding studies.	Clearly stated eligibility criteria and more than one person selecting the included studies. A list of included and excluded studies should be provided.
Was the quality of the included studies assessed and used in combining the results?	It may not be appropriate to combine the results of studies of different quality or design (e.g., combining poor quality studies with high quality studies).	For RCTs features including randomization, the method of blinding and the follow-up of participants should be assessed.
Was potential publication bias examined?	Published studies tend to be 'positive' and may give an overly optimistic view of the results.	The use of funnel plots or Egger's regression test to examine for publication bias.
Were the results presented graphically?	Graphing of the results of the individual studies allows for easy examination of potential heterogeneity in the results.	The presentation of a forest plot (Fig. 1) of the results of the individual studies included in a meta-analysis.
Was heterogeneity examined?	If studies have results that are significantly different from each other (heterogeneous), then the reasons for the heterogeneity should be investigated and/or the results pooled using a random effects model.	A test for heterogeneity is included which could be the Q statistic or the I ² statistic. If the Q statistic has a p value of <0.1 or if the I ² is >50%, then this suggests the studies are heterogeneous.

Meta-Analyses – www.prisma-statement.org). The key features of what to look for in a systematic review are summarized in Table 1.

Judging the quality of a randomized controlled trial

The quality of an RCT can be judged by four key characteristics:

- The methods used to randomize patients
- The methods used to blind treatments
- The follow-up of participants
- Registration or publication of the trial protocol.

It is important to note that publishing in prestigious international journals does not automatically make it a good quality RCT. Therefore it is important that the reader assesses the quality of every trial.

Method of randomization

Randomization is used to minimize selection or allocation bias. If performed properly, it should enable potential confounders to be distributed evenly across the groups. Confounders are patient characteristics that might influence the outcome. For example, if you were conducting a weight-loss trial and all the people who exercised regularly ended up in one arm of the study, you would bias the results.

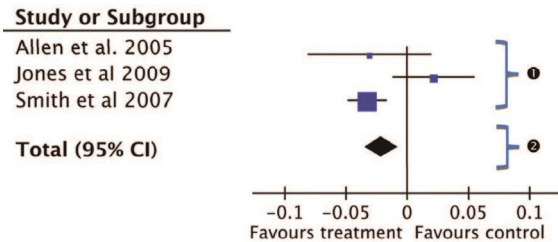


Fig. 1 Example of a forest plot based on hypothetical studies.

- ❶ These are the results of the individual trials in the meta-analysis. They show the point value (the box) and the 95% confidence interval around the outcome (the line). The size of the box usually indicates the weight the trial was given in the meta-analysis. The weighting is related to the variability in the trial, with trials with the least variability (i.e., that have the most precise estimate of the outcome) having the greatest weighting.
- ❷ This is the pooled estimate from all the studies. The width of the diamond represents the 95% confidence interval for the pooled estimate. In this example the pooled result is statistically significant because the 95% confidence interval does not include 0 (the null value).

Therefore we would randomize participants so that we would obtain similar numbers of patients who exercise regularly in each arm.

The best methods of randomization use computer-generated randomization lists. However, tossing a coin or rolling dice is also acceptable, provided you are certain the dice were not loaded! Methods that are not considered to be truly random include using the patient's birth month, medical record number or week day he or she turns up to a clinic, to allocate to treatments. These are known as quasi- or pseudo-randomization methods.

It is also important that the random allocation is done 'off site' or away from the investigators. This is called concealment of allocation, and prevents the investigators from perverting the randomization. To do this usually involves the investigator contacting an external organization that randomly allocates the patient to the appropriate arm in the study. Evidence has shown that failing to conceal the allocation sequence can lead to significant overestimation of the true efficacy of a treatment (Schulz et al., 1995).

To explore if randomization was done properly, you should also look at the table of baseline characteristics/ demographics of the participants (usually Table 1 of any trial

report). You would expect to see a similar distribution of characteristics among the groups.

Method of blinding

Blinding is used in a trial to help overcome measurement or ascertainment bias. Measurement/ascertainment bias occurs when a patient reports an outcome differently, or the outcome is measured differently, because the patient or the investigators know what treatment they are receiving. For example, in a trial of a new analgesic, a patient may be more likely to report lower levels of pain if they know they are using the new treatment compared with if they know they are taking the old treatment or placebo. The greater the subjectivity in the outcome, the more open to measurement bias it is. In reality, only 'all-cause mortality' can be considered free of measurement bias; any other types of mortality (e.g., cardiovascular mortality) are still open to bias as there is subjectivity as to what caused the death.

Blinding can be described as single, double or even triple. In single-blinded trials only either the patient or the investigators are usually blinded to the treatment allocation. The most common type of blinding is double-blinding where both the patient and investigator are blinded. Triple-blinding includes not only the patient and investigators, but also blinding other parties that might be involved in measuring the outcome (e.g., a research nurse or a laboratory technician). The most common way to blind oral medicines is to make each preparation identical in terms of appearance and taste. This can be achieved by a number of methods, including encapsulating tablets in identical capsules. If you are comparing two treatments that are given by different routes of administration—for example, a patch and a tablet—it becomes more difficult. However, this can be overcome using what is called a double-dummy approach where everyone would have to use/take both preparations. For example, if you were comparing a patch and a tablet, one group would receive an active patch and a placebo tablet, and the other group would receive a placebo patch and an active tablet.

Follow-up of participants

Whenever a trial is conducted it is nearly impossible to retain all the participants to the end of the study. Along the way some people will drop out for a variety of reasons. If the drop-outs are not accounted for in some way, there is potential for what is called 'survival' or 'follow-up bias'. This means that those who make it to the end of a study (i.e., do not drop out) are systematically different to those who drop out. When we conduct an RCT, we hope that at the beginning of the trial the participants in each arm only differ by two things: the

treatments they received and the random chance they were allocated to that group. As we will discuss later, at the end of a study we perform statistical tests to eliminate the 'chance' component, leaving us to conclude that any difference seen is due to the treatment. However, if we do not account for dropouts, then at the end of the study we will have three potential differences: the treatment they received, the random chance they were allocated to the group and the fact that they made it to the end of the study. Statistical tests can only eliminate one of these three potential differences.

There are two things about the follow-up that must be examined. First, it is important to assess how many people dropped out and whether it differed between the groups. If a large number of participants fail to complete the trial, or if more people drop out in one arm compared with another, it raises concerns about the validity of the outcomes reported. Unfortunately there are no rules on how many dropouts are too many, but as a guide, a dropout rate of over 20% should be viewed cautiously. The second aspect is how the investigators dealt with the dropouts. One method used to deal with dropouts is to perform what is called an intention-to-treat (ITT) analysis. An ITT involves analyzing patients who drop out, or who cross over into the alternative arm (s), in the arm they were randomized to. The question that arises is what 'outcome' do you attribute to those who drop out? In most trials where the outcome is something we think will improve over time with treatment (e.g., cures, pain levels), the last observation or measurement that they had is used as the final outcome. This is referred to as the 'last observation carried forward' and abbreviated to LOCF. In trials where the outcome being measured is something we are trying to avoid (e.g., death, stroke), then those who drop out can be assumed to have had the outcome. The effect of doing this is that it will make finding a difference between the two treatments more difficult. Thus it is a more conservative approach to the analysis, and therefore not likely to overestimate the effectiveness of a new treatment. However, it is important to note that ITT analysis cannot compensate for large losses to follow-up, and as a rule if more than 10% are lost then even the ITT results should be viewed with caution.

Registration or publication of the trial protocol

When evaluating a trial it is important to ensure that the investigators have not 'moved the goal posts' and reported on outcomes that were different from what the trial was intended to examine. For example, given the preference for journals to publish 'positive' trials, it could be tempting that if a study failed to find a significant difference in the primary outcome, that the investigators go 'searching' for an

outcome that was significant and report that instead. This is sometimes called 'data dredging'.

To overcome this problem there are a number of trial registries where investigators can lodge the protocol of their trial before they start their investigations. For example, the World Health Organization coordinates an international trial registry (www.who.int/ictrp/en/). Although some journals require trials to be registered before they will accept them for publishing, this is not universal. Therefore the reader should look for either a trial registry number being quoted, usually in the Methods section, or look for reference to the protocol being published previously in a journal somewhere.

Interpreting the evidence

Once you have located relevant information, and assessed its quality, you need to interpret the findings in the paper. To do this you should ask two questions:

- How big was the effect seen?
- Can I apply these results to my situation/patients?

Size of the effect in the study

When examining the outcome of a study two things need to be considered: was the effect seen *statistically* significant; and, was the effect seen *clinically* significant? To do this we need to first look at the metrics used to measure outcomes in studies.

Surrogate, clinical and patient-relevant outcomes

The outcomes that are measured in clinical trials can range from surrogate outcomes through to patient-relevant outcomes. Surrogate outcomes are generally biomedical markers and examples include blood pressure, white blood cell counts and bone mineral density. An important feature of a surrogate outcome is that the patient generally cannot feel or report what the outcome is. At the other end of the spectrum we have patient-relevant outcomes. Arguably these are the things that we ultimately want to change for a person and include outcomes such as improved quality of life, relief of pain and the ability to undertake normal daily activities. In between are what are called clinical outcomes. These are outcomes directly related to an underlying condition, such as fracture rates in osteoporosis and myocardial infarctions in cardiovascular disease. Examples of surrogate, clinical and patient-relevant outcomes can be found in [Table 2](#).

The advantages of surrogate outcomes are that they are usually easy to measure and can be quantified with

Table 2
Examples of surrogate, clinical and patient-relevant outcomes

Condition	Surrogate outcome	Clinical outcome	Patient-relevant outcome
Osteoporosis	Bone mineral density	Spinal fractures	Pain relief, ability to do normal daily activities
Respiratory tract infection	Viral count/load	Sore throat, fever	Ability to work or go to school
Asthma	FEV ₁ or Peak flow	Wheeze, use of rescue medication	Ability to play sport

reasonable amount of objectivity. By contrast, patient-relevant outcomes are the most subjective and are often difficult to measure reliably. However, interpreting changes in a surrogate outcome can be difficult unless we know what a change in a surrogate outcome does to, say a clinical or patient-relevant outcome. For example, what improvement in FEV₁ do you need before a person can function normally? Thus only changes in validated surrogate outcomes can be easily interpreted.

Continuous versus dichotomous outcomes

Most surrogate outcomes are continuous variables and are usually reported as *means*. When comparing results of two arms you may report the mean levels at the end of the study in each arm (e.g., the mean diastolic blood pressure at the end of the study with Drug A was 90 mm Hg and with Drug B it was 85 mm Hg) or the mean change from baseline in the outcome (e.g., patients on Drug A lowered their diastolic blood pressure in the study by a mean of 10 mm Hg, while those on Drug B reduced their diastolic blood pressure by 8 mm Hg). When comparing continuous outcomes we are interested in either the differences in the means, or the mean difference.

Most clinical outcomes are examples of dichotomous outcomes such as death, cure, achieving a 10% reduction in body weight and so on. These results are usually expressed as proportions or percentages in each arm. When comparing two arms in a study the results can be stated in a number of ways, including the risk difference (RD) or absolute risk

difference (ARD), the number needed to treat (NNT), the relative risk (RR) or the odds ratio (OR). The relationship between these four ways of expressing the differences in dichotomous outcomes is demonstrated in Fig. 2.

In the example in Fig. 2 the difference (ARD or RD) in the chance of healing is 0.1 or 10% in favour of Rambovir, but the RR of healing is 1.21, meaning that you have 1.21 times the chance of healing on Rambovir compared with placebo at 5 days. This can also be expressed as a 21% relative increase in the chance of being healed at 5 days with Rambovir. The OR is a difficult metric to interpret, as it is not related to the chance of the event as such, but the odds. Odds are a gambling-like concept, comparing the likelihood that the event will occur to the likelihood that it will not occur. For example, in horse racing, if a horse has odds of 4:1 it means that it loses 4 in 5 races, and wins 1 in 5 races. The OR is the ratio of the odds of the event occurring in one arm compared with the other. In the example in Fig. 2, the OR was 1.49. This means that people using Rambovir had 1.49 greater odds of being healed at 5 days compared with placebo; it does NOT mean that they had 1.49 greater chance of being healed at 5 days (they actually had 1.21 times greater chance of being healed as measured by the RR). Odds and OR have mathematical properties that make them attractive to statisticians, but from a clinical perspective they are virtually impossible to interpret most of the time and therefore we focus on ARD and RR.

When we are looking at how effective a new treatment is, we are interested in the absolute benefit with the new treatment (ARD or RD), not the relative benefit (RR or OR). This is because a range of different 'absolute' differences can give the same relative benefit. For example, if with drug A 10% of patients are cured but with placebo 5% of patients are cured, then the absolute difference is 5% (i.e., 10% – 5%), but the relative benefit is 2 (i.e., 10% ÷ 5%). Put another way, you are twice as likely to be cured with drug A compared with placebo. However, we could have the situation where 0.1% of people are cured with Drug A compared with 0.05% cured with placebo. In this case the relative benefit is still 2 (i.e., 0.1%–0.05%) or you are still twice as likely to be cured; however, the absolute benefit now is only 0.05% (i.e., 0.1%–0.05%). Thus in this second example the drug has a much smaller effect and yet can still claim a doubling in the rate of cure.

Another metric that is increasingly reported for dichotomous outcomes is the NNT, which is the reciprocal of the risk difference. For the example in Fig. 2, the NNT = 10 (i.e., 1 ÷ 0.1). This means that for every 10 people who we treat with Rambovir instead of placebo, we will get one additional person who is healed at 5 days. Another way of thinking of this is that 9 out of 10 people treated with Rambovir[®] will get the same benefit as they would have had if they had taken placebo, but one of them will be healed at 5 days who would

A trial with 100 people in each arm was run comparing a new (hypothetical) antiviral Rambovir® with placebo to treat cold sores. The main outcome is patients healed at 5 days. The results were as follows:

	Healed at five days	Not healed at five days	Total
Rambovir®	57	43	100
Placebo	47	53	100

$$\text{Risk difference} = \frac{57}{100} - \frac{47}{100} = 0.1 \text{ or } 10\%$$

$$\text{Number needed to treat} = \frac{1}{0.1} = 10$$

$$\text{Relative risk} = \frac{57/100}{47/100} = 1.21$$

$$\text{Odds ratio} = \frac{57/43}{47/53} = 1.49$$

Fig. 2 Example of the results of a hypothetical clinical trial of a new topical antiviral for cold sores.

not have been healed had a placebo been taken. The NNT gives us a quick way of quantifying the benefits of a new treatment that can be understood by patients and clinicians.

Statistical versus clinical significance

If a study claims a difference in an outcome for a treatment, we want to know if the observed difference is a true difference (statistical significance) and something that the patient would detect or feel (clinical significance). Statistical significance tells us whether any observed difference could have occurred by chance. Traditionally this has been tested using statistical methods that produce what is called a 'P value'. The 'P value' tells us what the probability of any observed difference is due to chance. The customary cut off used is 0.05. This means that if you get a P value of less than 0.05, there is less than 5% probability, or a 1-in-20 probability, that the difference you are seeing is by chance alone. The cut off of 0.05 is arbitrary, and in some trials the authors may set the level lower (e.g., 0.01, which means that there is less than a 1% probability that the difference is due to chance alone). Thus if a result for the P value is less than the cut off, we say that the result is statistically significant. An alternative way of testing the statistical significance is using confidence intervals. The confidence interval gives a range of plausible values for the outcome. The most commonly used is the 95% confidence interval. One way of interpreting this is that we are 95% certain that the true difference lies

somewhere between the two stated values. For example, the result in Fig. 2 for the risk difference gives a value of 0.1 with a 95% confidence interval from -0.04 to $+0.23$ (or 10% with a 95% confidence interval from -4% to $+23\%$). What this means is that the most likely difference is 0.1, but it could be -0.04 (the negative sign meaning that the difference actually favours placebo) or as high as $+0.23$. To interpret whether the result is statistically significant you need to see if the 'null value' is within the 95% confidence interval. The 'null value' is the value you would get if there were no difference. So for a risk difference (or ARD), the null is 0. For a relative risk or odds ratio, the value of null would be 1. Thus in the example above, the value 0 lies between -0.04 and $+0.23$. This means the result is not statistically significant, as 'no difference' is also a plausible value. Confidence intervals are becoming popular, as they provide us with two pieces of information. First, they let us test for statistical significance like the P value does. Second, they give us a sense of the spread or the precision of the results. Thus if the 95% confidence interval is very narrow (i.e., close around the central value) the estimates are very precise, whereas if the 95% is wide, there is a lot of uncertainty in the true result.

Being statistically significant does not make the difference a clinically significant difference. Statistical testing is dependent on the variability in the outcome, which is often related to the sample size used in the study. The larger the sample size, the more precise your results usually are (i.e., the narrower the confidence intervals) and thus the greater

the ability to detect even very small differences as being statistically significant. As an example, a trial examining finasteride for benign prostatic hypertrophy (Lowe et al., 2003), involving 725 patients, found an improvement in the urine flow rate of 2.9 mL/s, which was statistically significant ($P < .001$) compared with placebo. This equated to patients taking finasteride having a urine flow rate of about 14 mL/s compared with 11 mL/s for placebo. Assuming the average male voids 1500 mL per day, this means finasteride saves approximately 30 seconds each day in the restroom. This would not be seen as having much impact on the average person despite being statistically significant. Unfortunately, unlike statistical significance, there are no 'rules' about what makes the difference clinically significant. Each outcome has to be interpreted in the context of the disease being treated using your clinical judgement. The question that has to be asked is 'Would the patient notice this difference?' or 'Am I going to notice a difference in my patients?'

Can I apply the results to my patients?

Once you have assessed that the study is not fundamentally biased and that the results are statistically and clinically significant, the final question to ask is whether you can apply the results in your setting. This is referred to as the 'external validity' of the trial. To do this you need to look at several aspects of the trial and answer the following questions:

- Did they use this in the same type of patients that I intend to use it in?
- Did they compare the drug to what I am currently using or best practice?
- Did they use the drug the way I will use it?

What were the patients like in the study?

To apply the results, the patients should be similar to those in whom you plan to use the drug. This could be with respect to age, possibly ethnicity, or disease severity. For example, you may not be able to expect the same outcome if the study used patients with mild or moderate disease, but you plan to use the medicine in severe cases of the disease. However, the absence of the patient population you are interested in being involved in the study does not necessarily mean the results are not applicable. For example, many studies exclude women of childbearing age because of concerns regarding potential birth defects. However, you would need to ask the question as to whether the drug would not act the same in females of this age. In most cases the answer will be yes, it would act similarly.

The best place to find this information will be in the inclusion and exclusion criteria, usually described in the 'Methods'

section. You should always check the table of demographics to see what the actual population looked like.

What did they compare the drug to?

When a new medicine becomes available the question we want to answer is how it compares to what we currently do. However, trials that are conducted to get a product onto the market generally compare the treatment to placebo. This is because regulators, such as the Therapeutic Goods Administration, want to establish that a new drug does something and is better than doing nothing at all. This makes the use of studies designed for regulatory agencies difficult to use for EBM.

One way that placebo-controlled trials can be used is to compare the results of the new and the existing treatment each against placebo (i.e., new vs placebo and existing treatment vs placebo). This is referred to as using a common comparator approach. Therefore if the new drug produces a bigger improvement compared with placebo than the existing therapy does, then the inference is that the new therapy is better than the existing therapy. However, you should be cautious about drawing conclusions about comparative efficacy through common comparators, particularly when claiming better efficacy. These are two completely different studies, conducted usually at different times and in different places, and there may have been differences in the populations that influence the outcome. At best a common comparator may indicate that a new therapy is no worse than the existing therapy, but should not be used to establish better efficacy.

Another issue with the comparator is whether or not the proper dose of the comparator was used. The easy way to make a new drug look better than a comparator is to 'under-dose' the comparator. Therefore it is important that in a clinical trial they not only use the current best therapy, but also that they have used the correct dosing of the current best therapy.

How was the new drug used?

It is just as important that the new drug has been used in the way that you intend to use it. For example, trials of the antiviral drugs for influenza involved giving the study drug within hours of the onset of symptoms. The results showed a modest reduction in influenza symptoms of about 1 day. However, in countries where this drug is prescription only it may take several days after the onset of symptoms for a patient to get an appointment with a GP and then a prescription for the agents. Therefore patients are not likely to see the same benefits in these settings. Thus the new treatment must be given by the same route, dose and duration in the trial as it will be when you use it.

Developing an evidence-based personal formulary

For many common conditions there is a plethora of non-prescription medicines to choose from. Although you may keep an almost complete range of these products in a pharmacy to satisfy 'product-based' requests, when you are asked to help a patient choose an appropriate therapy it is better that you do so from a limited range of products that you know well, and that you have confidence in them being evidence based. This is referred to as your 'personal formulary'. In many ways the choice of non-prescription medicines is to the pharmacist what prescribing is to the physician.

The concept of a 'personal formulary' and the selection of a personal formulary drug ('p-drug') is based on the World Health Organization's (WHO) Guide to Good Prescribing, which is used to teach medical students to prescribe. Selecting a 'p-drug' involves a systematic, evidence-driven approach to selecting the best medicine to manage a particular condition. The approach described in the next section has been adapted from the WHO Guide to Good Prescribing (apps.who.int/medicinedocs/pdf/whozip23e/whozip23e.pdf).

Selecting a 'p-drug'

The process of selecting a 'p-drug' involves a number of steps:

- Defining the patient's problem
- Specifying the therapeutic objective
- Making an inventory of possible treatments
- Selecting your p-drug based on efficacy, safety, suitability and cost.

Defining the patient problem and specifying the therapeutic objective

To start you must define clearly what you are planning to treat, and what outcome you wish to achieve. This will help when deciding what outcomes we are interested in when looking at the efficacy of the treatments. For example, if we are considering what our 'p-drug' should be for treating threadworm, then the patient problem is pinworm infection and the therapeutic objective is pinworm eradication.

Making an inventory of possible treatments

The next step is to list all possible treatment options that are available. These should, of course, include pharmaceutical and non-pharmaceutical options. In the case of the threadworm

examples there are two pharmaceutical options to consider: pyrantel and mebendazole.

Selecting your p-drug based on criteria

The WHO approach to select between the possible therapies uses four criteria:

- Efficacy
- Safety
- Patient suitability
- Cost.

In general these are considered in this order. The first thing you look at is comparative efficacy. If there is nothing to differentiate the treatments based on efficacy, we then consider safety. Again, if there are no significant differences in terms of safety, we would then consider patient suitability and so on. When considering patient suitability, we are looking at things such as ease of use, better adherence and so forth. The issue of cost is an interesting one in a community pharmacy setting. Some would argue that this should not be a consideration by the pharmacist and should be left to the consumer who ultimately pays. However, if you have two or more products that are considered equivalent in terms of efficacy, safety and patient acceptability, then it would seem reasonable to offer the patient the less expensive option. In the case of many non-prescription products the efficacy and safety are similar, but there may be differences in patient suitability such as less frequent application or a shorter duration of treatment. An example of this would be comparing the imidazoles (e.g., clotrimazole) with terbinafine cream for tinea pedis. There is no appreciable difference in terms of efficacy and safety. However, imidazoles are usually applied several times a day for several weeks, whereas terbinafine is applied once a day for 1 week. If they were the same cost, you would clearly choose terbinafine. However, terbinafine is generally more costly and therefore it would seem reasonable to offer both products to the patient, explaining the difference in dosing and cost and allowing the patient to choose which they would prefer.

The example of treating threadworm is described in [Table 3](#) with a summary of this in [Table 4](#).

In this case you might consider pyrantal the best choice as it has slightly better efficacy and can be given to all ages.

Having a back-up 'p-drug'

In selecting a 'p-drug' you usually make a choice based on the 'average' patient that you might encounter. However, it is always wise to have an alternative available, if necessary, for certain patient populations such as children, elderly or pregnant women.

Table 3
Example of selecting a p-drug for threadworm

Drug	Efficacy	Safety	Suitability	Approx. Cost
Pyrantel*	~90% eradication	Nausea, vomiting, diarrhoea, abdominal cramps	Dosage based on weight Pregnancy category B2 Used in children of all ages: tablets, liquid, chocolate squares	~\$8.00
Mebendazole	60% to 70% eradication	Infrequent nausea, vomiting and diarrhoea	Flat dosing >6 months Pregnancy category B3 Children >6 months: tablet, liquid, chocolate squares	~\$4.00

*Not available in the UK but used for indicative purposes.

Table 4
Summary of selecting a p-drug for threadworm

Drug	Efficacy	Safety	Suitability	Cost
Pyrantel	++	+	+	+
Mebendazole	+	+	+	++

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- Centre for Evidence-Based Medicine Toronto: ktclearinghouse.ca/cebm/
- Bandolier: www.medicine.ox.ac.uk/bandolier/index.html

Abbreviations

ACE	angiotensin-converting enzyme	mEq	milliequivalent
ADR	adverse drug reaction	mg	milligram
CB	chronic bronchitis	MI	myocardial infarction
CSM	Committee for the Safety of Medicines	mL	millilitre
DEET	diethyl toluamide	mmol	millimole
DPH	diphenhydramine	NRT	nicotine replacement therapy
EHC	emergency hormonal contraception	NSAID	nonsteroidal antiinflammatory drug
FDA	US Food and Drug Administration	ORT	oral rehydration therapy
GORD	gastro-oesophageal reflux disease	OTC	over-the-counter
GP	general practitioner	P	pharmacy
GSL	general sales list	PD	primary dysmenorrhoea
h	hour	PID	pelvic inflammatory disease
HPV	human papilloma virus	PMS	premenstrual syndrome
HSV	herpes simplex virus	POM	prescription-only medicine
IBS	irritable bowel syndrome	PV	per vagina
IgE	immunoglobulin E	SSRI	selective serotonin reuptake inhibitor
IHS	International Headache Society	STD	sexually transmitted disease
INR	international normalized ratio	TB	tuberculosis
IUCD	intrauterine contraceptive device	TCA	tricyclic antidepressant
KCS	keratoconjunctivitis sicca	UTI	urinary tract infection
L	litre	WHO	World Health Organization
MAOI	monoamine oxidase inhibitor	µg	microgram
MAU	minor aphthous ulcer		

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Glossary of terms

Chapter 1

- Agranulocytosis:** Acute deficiency of neutrophil white blood cells leading to neutropenia.
- Atopy:** A form of hypersensitivity characterized by a familial tendency.
- Cervical lymphadenopathy:** Enlargement of the cervical lymph nodes.
- Dyspnoea:** Difficulty in breathing.
- Gastro-oesophageal reflux:** The backflow of gastric contents into the oesophagus.
- Haemoptysis:** Coughing up blood.
- Malaise:** General feeling of being unwell.
- Orthopnoea:** Difficulty in breathing when lying down.
- Otoscope examination:** Examination of the ear drum by means of an apparatus that shines light onto the ear drum.
- Pleurisy:** Inflammation of the pleural membranes caused by the two pleural membranes adhering to one another.
- Purulent:** Refers to a material containing pus.
- Rhinorrhoea:** Watery nasal discharge.
- Vascular engorgement:** An area of tissue that has been excessively perfused with blood.
- Vasodilation:** Increase in the diameter of the blood vessels.

Chapter 2

- Chalazion:** Also referred to as a *meibomian cyst*.
- Conjunctivitis medicamentosa:** Conjunctivitis caused by repeated administration of ocular eye drops, especially sympathomimetic agents. On withdrawal of the medicine, the patient suffers from rebound redness of the eyes.
- Glands of Zeiss and Moll:** Both are located within the eyelid. The gland of Zeiss secretes sebum, and the gland of moll secretes sweat.
- Hordeola:** Commonly known as a sty.
- Limbal area:** Area where the cornea meets the sclera.
- Meibomianitis:** Inflammation of the meibomian gland.
- Photophobia:** A dislike of bright lights.
- Visual acuity:** The ability to read text. For example, distance visual acuity is the person's ability to read

letters across the room, and near visual acuity is the person's ability to read letters close to him or her.

Chapter 3

- Conductive deafness:** Sound waves are hindered from reaching the inner ear (e.g., by ear wax) resulting in distortion of sounds that impairs the understanding of words.
- Effusion:** Escape of fluid, such as exudate from the ear.
- Laceration:** A tear in the skin causing a wound.
- Oedematous:** Abnormal accumulation in intercellular spaces of the body.
- Tinnitus:** A noise in the ears that sounds like ringing or buzzing.

Chapter 4

- Amenorrhoea:** Absence or the stoppage of menstruation.
- Haematoma:** A localized collection of blood, usually clotted, in an organ, space or tissue.
- Myalgia:** Muscular pain.
- Paraesthesia:** An abnormal sensation; for example, a burning or prickling sensation.
- Pericranial:** Area relating to around the skull.
- Purpuric rash:** Rash with a distinctive red-purple colouration caused by haemorrhage of small blood vessels in the skin.

Chapter 5

- Anovulatory:** Term used to describe women who do not ovulate.
- Bacteriuria:** Bacteria in the urine.
- Dyspareunia:** Difficult or painful sexual intercourse.
- Dysuria:** Painful or difficult urination.
- Haematuria:** Blood in the urine.
- Menarche:** Onset of menstruation.
- Nocturia:** Excessive urination at night.
- Perianal:** The area around the anus.
- Perineal:** The area around the perineum. The perineum describes the area between the vulva and anus.

Postmenopausal women: Women who have finished menstruating. The average age for women to be postmenopausal is 51 years.

Prostate gland: The gland that surrounds the neck of the bladder and urethra in men.

Pyelonephritis: Inflammation of the kidney due to bacterial infection.

Suprapubic: Refers to area above the pubic region.

Chapter 6

Annular lesions: Skin lesions that are circular.

Diverticulitis: Inflammation of a diverticulum, which is a pouch or sac. It occurs normally after herniation.

Halitosis: Bad breath.

Suprapubic: Refers to area above the pubis area of the abdomen.

Tenesmus: The feeling of incomplete bowel evacuation.

Ureter: Tube connecting the kidney to the bladder.

Chapter 7

Atopy: Literally means 'strange disease' – the triad of atopic dermatitis, asthma and allergic rhinitis.

Comedone: A plug of oxidized sebaceous material obstructing the surface opening of pilosebaceous follicle, commonly referred to as a *blackhead*.

Crust: Dried exudate.

Erythema: Redness of the skin.

Intertrigo: Dermatitis on areas of the skin in flexural body sites (e.g., groin, axilla).

Wheal: Areas of transient dermal oedema; typically associated with urticaria and following insect bites.

Chapter 8

Ankylosis: Stiff joint or joint fused in a particular position.

Abduction: Refers to movement of a part away from the median plane of the body; for example, moving the leg straight out to the side.

Arthropathy: Pathology in a joint.

Articular cartilage: Cartilage in a joint.

Disc herniation: Abnormal protrusion of the nucleus pulposus of a disc, which may impinge on a nerve root.

Epicondylitis: Inflammation of the epicondyle, which is the protuberance above the condyle. The condyle is the rounded part at the end of the bone used for articulation with another bone.

Chapter 9

Erythematous: Redness of the skin due to capillary vasodilation.

Intertriginous area: Skin eruption on apposed skin surfaces.

Lichenification: Thickening and hardening of the skin.

Chapter 10

Erythrocytes: Alternative name for red blood cells.

Melanocytes: Cells in the skin epidermis responsible for producing melanin.

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