A FOCAL POINT LEARNING PROGRAMME

focal point: ANTIBACTERIALS

BOOK 1
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Learning with CPPE

The Centre for Pharmacy Postgraduate Education (CPPE) offers a wide range of learning opportunities in a variety of formats for pharmacy professionals from all sectors of practice. We are funded through the NHS Multi-professional Education and Training Fund from Health Education England to offer continuing professional development for all pharmacists and pharmacy technicians providing NHS services in England. For further information about our learning portfolio, visit: http://www.cppe.ac.uk

We recognise that people have different levels of knowledge and not every CPPE programme is suitable for every pharmacist or pharmacy technician. We have created three categories of learning to cater for these differing needs:

**CPPE 1** Core learning (limited expectation of prior knowledge)

**CPPE 2** Application of knowledge (assumes prior learning)

**CPPE 3** Supporting specialties (CPPE may not be the provider and will direct you to other appropriate learning providers).

This is a **CPPE 2** learning programme and assumes that you already have some knowledge of the topic area.

**Continuing professional development (CPD)** – You can use this focal point unit to support your CPD. Consider what your learning needs are in this area. Use your CPD record sheets to plan and record your learning.

**Programme guardians** – A programme guardian is a recognised expert in an area relevant to the content of a learning programme. They will review the programme every six months to ensure quality is maintained. We will post any alterations or further supporting materials that are needed as an update on our website. We recommend that you check for these updates if you are using a programme more than six months after its initial publication date.

**Feedback** – We hope you find this learning programme useful for your practice. Please help us to assess its value and effectiveness by visiting the my CPPE record page on our website. Alternatively, please email us at feedback@cppe.ac.uk.
About CPPE focal point programmes

We have developed focal point to give you short, clinically focused learning sessions. It will help you learn with your colleagues and improve the services you offer your patients. Each unit presents information and activities that are relevant for pharmacy professionals working in primary care and in the community. There are two types of learning event for you to choose between when using focal point units – you can either attend a CPPE tutor-led event or you can learn as part of a CPPE learning community. Have a look at the CPPE website: http://www.cppe.ac.uk/ for more information about how to set up a learning community.

Reference sources for all the books, articles, reports and websites mentioned in the text can be found at the end of the programme. References are indicated in the text by a superscript number (like this 3).

A note about web links

Where we think it will be helpful we have provided the web links to take you directly to an article or specific part of a website. However, we are also aware that web links can change. A new website: www.gov.uk/government encompasses the Department of Health website, as well as the new executive agency, Public Health England. To search for any Department of Health publication or information mentioned in this programme either visit the gov.uk home page and enter the title into the search facility, or search via Google or your preferred internet search provider.

If you have difficulty in accessing any other web links, please go to the organisation’s home page and use appropriate key words to search for the relevant item.

This book gets you started. It provides key information to help you meet the learning objectives presented on the following pages, but it also encourages you to identify your own learning needs. It then challenges you to relate what you have learnt to your own area of practice and professional development. We have included practice points and talking points to stimulate your thinking and we will refer to these again at the focal point event. Make sure you have studied these activities before your event.

You will receive Book 2 when you attend the focal point event. It uses case studies and clinical vignettes to help you apply what you have learnt and encourages you to make changes to improve your practice. We also include some suggested answers to the learning activities.
About this focal point unit on antibacterials

In this unit we consider:
- how pharmacy teams can support other health professionals and patients to optimise patient outcomes in antibiotic therapy, while minimising harm
- the application of antimicrobial guidelines to ensure appropriate antibacterial use
- the issues of antimicrobial resistance and healthcare-associated infections and how to reduce their impact
- practical issues relating to antibacterial treatment.

Learning objectives

You can meet the learning objectives that we identify here by reading the information that we provide and refer you to, undertaking the various activities that we suggest and putting what you have learnt into practice. We have split our learning objectives into appropriate sections. This should help you determine how to meet them. We have also linked the learning objectives in this programme to the General Level Framework (GLF) and the NHS Knowledge and Skills Framework (KSF) dimensions. We have suggested some competences, but you may be able to apply your learning to other aspects of these frameworks.

Moving into focus and Reading

<table>
<thead>
<tr>
<th>Objective</th>
<th>KSF</th>
<th>GLF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name the major classes of antibacterials and describe their mode of action.</td>
<td>Quality Level 2</td>
<td>Cluster: Delivery of patient care Competency: Medicines information and patient education</td>
</tr>
<tr>
<td>List five patient factors that should be considered when dispensing antibacterial therapy.</td>
<td>Quality Level 2</td>
<td>Cluster: Delivery of patient care Competency: Selection of drug</td>
</tr>
<tr>
<td>Discuss the issues involved in antimicrobial resistance and healthcare-associated infections and how antimicrobial stewardship can reduce the impact of these.</td>
<td>Service improvement Level 3</td>
<td>Cluster: Management and organisation Competency: Clinical governance</td>
</tr>
</tbody>
</table>
Practice points, talking points, case studies and clinical vignettes

You’ll find these in this book and Book 2, and will work on them during the event.

<table>
<thead>
<tr>
<th>Objective</th>
<th>KSF</th>
<th>GLF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name the empirical therapy for common bacterial infections.</td>
<td>Quality Level 2</td>
<td>Cluster: Delivery of patient care Competency: Selection of drug</td>
</tr>
<tr>
<td>Apply the national and local antibacterial guidelines to management of patients.</td>
<td>Quality Level 2</td>
<td>Cluster: Delivery of patient care Competency: Selection of drug</td>
</tr>
<tr>
<td>Be able to discuss antibacterial medicines optimisation issues with prescribers, including the choice of antibiotic, route of administration, the dose and duration of treatment.</td>
<td>Communication Level 3 Quality Level 3</td>
<td>Cluster: Delivery of patient care Competency: Drug specific issues Cluster: Problem solving Competency: Analysing information</td>
</tr>
<tr>
<td>Explain key messages to help educate patients regarding appropriate use of antibiotics.</td>
<td>Communication Level 3</td>
<td>Cluster: Personal Competency: Effective communication skills</td>
</tr>
</tbody>
</table>

Directing change and follow-up activities

You will achieve practical outcomes after completing this unit, when you apply what you have learnt to your everyday practice. You will find advice in Book 2.

<table>
<thead>
<tr>
<th>Objective</th>
<th>KSF</th>
<th>GLF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apply antimicrobial stewardship in a community setting.</td>
<td>Quality Level 3</td>
<td>Cluster: Management and organisation Competency: Clinical governance</td>
</tr>
</tbody>
</table>
Useful resources

We have selected some resources that you can use when developing improved pharmacy services for people prescribed antimicrobials.

Clinical knowledge and therapeutics support

Royal College of General Practitioners. TARGET antibiotics toolkit - http://www.rcgp.org.uk/TARGETantibiotics/

This toolkit, developed by the Royal College of General Practitioners (RCGP), the Health Protection Agency (HPA*) and the Antimicrobial Stewardship in Primary Care (ASPIC), along with other stakeholders, aims to provide a central resource of information regarding antibiotic prescribing.

The resources include the quick reference guide, Management of infection guidance for primary care for consultation and local adaptation:
http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/PrimaryCareGuidance/

This guidance forms the basis of most local policies and is an invaluable resource. Quick reference guides for a number of specific infections, such as urinary tract infections, are also available.

Other useful resources include Antibiotic information leaflet and the booklet, When should I worry?

*The HPA transferred functions in April 2013 to become part of Public Health England.


This website provides a summary of the current evidence base and practical guidance on best practice for over 300 common and/or significant conditions presented in primary care. You can search for specific conditions, such as otitis media, and there is also a section on infections and infestations.


This report from the chief medical officer, Professor Dame Sally Davies, highlights the threat of antimicrobial resistance. The report suggests that development of new antimicrobial drugs should be encouraged but there is also a need to take measures to preserve existing drugs. These include better hygiene measures to prevent infections, prescribing fewer antibiotics and ensuring that they are only prescribed when needed.

Published in September 2013, this forms part of the response to the challenges outlined in the chief medical officer’s annual report, *Infections and the rise of antimicrobial resistance*. The overarching goal of the strategy is to slow the development and spread of antimicrobial resistance. It focuses activities around three strategic aims:

- improve the knowledge and understanding of antimicrobial resistance
- conserve and steward the effectiveness of existing treatments
- stimulate the development of new antibiotics, diagnostics and novel therapies.


Tables at the beginning of chapter five of the *British National Formulary (BNF)* indicate recommended empirical antibiotics for a wide range of infections.

**Patient support**

NHS Choices – http://www.nhs.uk/

This website has been developed to help patients make positive choices about their health. It provides facts about lifestyle decisions, such as smoking, drinking and exercise, and offers information about the practical aspects of finding and using NHS services. It provides patients with explanations of nearly 800 treatments and conditions. As a pharmacy professional you can direct people to the NHS Choices information on infections.
Checklist for planning

To meet the learning objectives you will need to carry out the activities listed in the table below. We’ve given you this list now so that you can start to plan your learning. Although it will only take you about two hours to work through Book 1, feedback from other users suggests that it is useful to plan your activities over a timescale that suits you - perhaps over several days. Try to set yourself a realistic deadline for each task.

<table>
<thead>
<tr>
<th>You will need to:</th>
<th>This will take about:</th>
<th>I will do this by: (Insert date)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Answer the Moving into focus questions</td>
<td>5 minutes</td>
<td></td>
</tr>
<tr>
<td>List three learning needs</td>
<td>5 minutes</td>
<td></td>
</tr>
<tr>
<td>Read the whole book</td>
<td>60 minutes</td>
<td></td>
</tr>
<tr>
<td>Undertake the practice points</td>
<td>20 minutes</td>
<td></td>
</tr>
<tr>
<td>Make notes for the talking points</td>
<td>10 minutes</td>
<td></td>
</tr>
<tr>
<td>Work through the Directing change exercise.</td>
<td>20 minutes</td>
<td></td>
</tr>
</tbody>
</table>
Moving into focus

Consider the following questions. Use them to focus your thoughts and stimulate your learning. Are you confident you know the answers?

1. Which antibiotics should be used with caution in a patient who says they are allergic to penicillin?

2. What is the TARGET antibiotics toolkit?

3. List five clinical or biochemical indicators of infection.

4. List three common organisms associated with healthcare-associated infections.

5. List five patient factors that could affect the choice of antibacterial.
What do you want to learn?

Write down three things that you would like to gain from this focal point learning unit. These will help you plan your own CPD entry. You will need to tell others about them at the focal point event.

1. 

2. 

3. 

Now you have completed your reflection and planning for this focal point unit, it's time to undertake the background reading.
Reading

1.1 Background

Antibacterials have revolutionised medical care, enabling a wide range of infections to be treated and lives saved. However, the inappropriate and excessive use of antibacterials, together with a reduction in the rate of new antibacterial development, has led to the growth of resistant strains or superbugs, such as meticillin-resistant Staphylococcus aureus (MRSA).

In 2010, in England, infectious diseases accounted for seven percent of all deaths, four percent of all potential years of life lost (to age 75) and were also the primary cause of admission for eight percent of all hospital bed days. They are also responsible for a large proportion of sickness absence from work. The NHS spends an estimated £1 billion annually on antibacterials.

Strategies for preventing and controlling infection, and Europe-wide initiatives, such as European Antibiotic Awareness Day (held annually in November), form the mainstay of public and healthcare-professional education on appropriate use of antibiotics. Further action is needed to preserve the effectiveness of antibacterials for future use and a report from the chief medical officer, Professor Dame Sally Davies, has highlighted the threat of antimicrobial resistance. The report suggests that development of new antimicrobial drugs should be encouraged but there is also a need to take measures to preserve existing drugs, otherwise routine surgical procedures may, in the future, result in a threat to health. The UK five year antimicrobial resistance strategy 2013 to 2018, published in September 2013 forms part of the response to the challenges outlined in the chief medical officer’s report and the overarching goal of the strategy is to slow the development and spread of antimicrobial resistance.

In November 2011, the Department of Health launched updated guidance on antimicrobial use. The guidance, Antimicrobial stewardship: “Start smart - then focus”, encompasses key interventions and audits that support antibiotic stewardship activities in hospitals. A further initiative, the TARGET antibiotic toolkit, aimed at improving antimicrobial stewardship in primary care, has been introduced.
1.2 Mode of action

Antibacterials can be classed by their site of action within the bacterial cell. Most classes of antibacterials act on the cell wall or by inhibiting protein or nucleic acid synthesis. The greater the difference between host and bacterial synthesis pathways, the greater the selectivity an antibacterial will have.

The variety of antibacterial modes and sites of action results in antibacterials targeting bacteria with different degrees of activity. Table 1 illustrates the diversity in action for a selected range of antibacterial agents. Susceptibility data alone should not be used to select an antibacterial therapy. To make a rational antibacterial choice, the patient’s laboratory results should be used, as well as their clinical details.

Table 1: Classes of antibacterial agents and examples of susceptible bacteria

This table lists common bacteria and the antibacterial(s) they are usually susceptible to. The list is not comprehensive and local resistance patterns should be taken into account. Where no antibacterial is indicated for a class of bacteria, different species have different susceptibilities. You should refer to information on individual species for susceptibility data.
### Table 1: Classes of antibacterial agents and examples of susceptible bacteria

<table>
<thead>
<tr>
<th>Mode of action</th>
<th>Class</th>
<th>Antibacterial</th>
<th>Examples of susceptible bacteria</th>
</tr>
</thead>
</table>
| Cell wall synthesis inhibitors | Penicillins | Amoxicillin | *Streptococcus pneumoniae*  
| | | | *Beta-haemolytic streptococci* |
| | | Flucloxacin | *Staphylococcus aureus*  
| | | | *Staphylococcus epidermidis* |
| | | Co-amoxiclav | *Escherichia coli*  
| | | | *Haemophilus influenzae* |
| | | Tazocin (piperacillin with tazobactam) | *Pseudomonas aeruginosa* |
| | Cephalosporins (use widely restricted, use in exceptional circumstances) | - | *Escherichia coli*  
| | | | *Streptococcus pneumoniae*  
| | | | *Neisseria meningitidis* |
| | Monobactams | Aztreonam | *Haemophilus influenzae*  
| | | | *Pseudomonas aeruginosa* |
| | Carbapenems | Imipenem  
| | | Meropenem | *Pseudomonas aeruginosa*  
| | | | *Staphylococcus aureus* |
| | Glycopeptides | Vancomycin | *Clostridium difficile (C. difficile)*  
| | | | *Meticillin-resistant*  
| | | | *Staphylococcus aureus (MRSA)* |
| | Aminoglycosides | - | *Pseudomonas aeruginosa*  
| | | | *Staphylococcus aureus* |
| | Macrolides | - | *Moraxella catarrhalis*  
| | | | *Beta-haemolytic streptococci* |
| | Tetracyclines | Doxycycline | *Chlamydia trachomatis*  
| | | | *Streptococcus pneumoniae* |
| | Others | Clindamycin | *Staphylococcus aureus*  
| | | | *Streptococcus pneumoniae* |
| | Quinolones | Ciprofloxacin | *Escherichia coli*  
| | | | *Pseudomonas aeruginosa* |
| | Others | Metronidazole | *Bacteroides spp*  
| | | | *Clostridium difficile (C. difficile)* |
| | | Trimethoprim | *Escherichia coli* |
1.3 Mechanism for bacterial resistance

Bacterial resistance is increasingly becoming an issue for the management of infection. There are several mechanisms for developing resistance, so previously active antibacterials may have little or no effect on a bacterium. Resistance could develop when one or more of the following situations exist.

- Enzymes inactivate the antibacterial before it binds to the bacteria, for example, beta-lactamase production is the mechanism for *Staphylococcus aureus* resistance to amoxicillin.
- The antibacterial is less able to permeate the bacterial cell wall.
- The antibacterial is actively removed from the bacteria cell.
- There is mutation at the site where the antibacterial binds to the bacteria, for example, a mutation in the penicillin-binding protein is the mechanism for MRSA resistance to flucloxacillin.
- The bacteria develop new synthesis pathways.

Resistant organisms are on the rise and new multi-resistant mechanisms continue to be identified.

We are finding ways to control organisms like MRSA, but others, such as glycopeptide-resistant enterococci (GRE), extended-spectrum beta-lactamase (ESBL) producing organisms and AmpC cephalosporinase producing organisms, are of increasing concern.

The Health Protection Agency has recently identified a new beta-lactamase enzyme, which poses an infection control risk in UK hospitals. The enzyme, called New Delhi metallo-beta-lactamase (NDM-1), confers resistance to all beta-lactam antibiotics, including carbapenems, and is one of many emerging carbapenemases. You can find out more information about this via the following link:

http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/CarbapenemResistance/GeneralInformation/

For further information see section 3.2 Reducing healthcare associated infections later in this book, or access the CPPE programme, *Avoiding antibiotic resistance: the role of the pharmacy team*, available via our website: http://www.cppe.ac.uk
Talking point A

If you were developing a new antibacterial, list the ideal properties you would like it to have.

What ideal properties would a patient want an antibacterial to have?

2. Management of infection

We may see patients who are acutely unwell but do not yet have a diagnosis of infection. In a community setting we may suspect infection, based on a range of clinical signs, but we are unlikely to have access to biochemical tests, which would indicate the likelihood of an infection being present.

2.1 Signs of infection

Signs of infection are often non-specific. Clinical signs and symptoms of infection include:

- fever, aches, pain
- presence of pus, swelling or redness in the potentially infected site
- confusion, of new onset, particularly in older people
- drowsiness, irritability, poor appetite in children
- changes in blood pressure, heart rate or respiratory rate.

Biochemical results indicating infection include:

- raised or depressed white blood cells
- raised neutrophils
- altered platelet levels
- raised C-reactive protein
- raised erythrocyte sedimentation rate
- worsening renal function.

Check local biochemical normal reference ranges for more details.
2.2 Choosing an appropriate antibacterial

Empirical therapy

Empirical, or best guess, therapy describes those occasions where therapy is started before the causative organism is known and before sensitivities can be provided. In urgent cases it is reasonable to begin treatment before these results are available. It is important to be able to make a reasonable assessment of a patient’s presenting complaint and identify which antimicrobial is likely to be the most appropriate treatment to start. It is possible that returned cultures will not always confirm the presence of bacteria, even when clinical signs of infection have been correctly interpreted.

National and local guidelines

Local policies and guidelines include local patterns of resistance and the most likely pathogens, so these should be your first consideration when making decisions in the absence of sensitivity data. Most local guidelines are based on the Health Protection Agency guidance, Management of infection guidance for primary care for consultation and local adaptation, so if local policies are not available, you can use these to guide your recommendations.

Tables at the beginning of chapter five of the British National Formulary (BNF) recommend empirical antibiotics for a wide range of infections.

The National Institute for Health and Care Excellence (NICE) website hosts clinical knowledge summaries, which provide a summary of the diagnosis and treatment of a number of conditions, including infections (see resources).
Practice point 2

Access the Health Protection Agency guideline, *Management of infection guidance for primary care for consultation and local adaptation*: http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/PrimaryCareGuidance/

What would be recommended for an acute exacerbation of chronic obstructive pulmonary disease (COPD)?

If possible, obtain your local guideline and see if the recommendation would be any different. Local guidelines are most likely to be available from medicines management teams within clinical commissioning groups.

Bring a copy of the HPA guideline and your local guideline to your focal point event.
Combination therapy

Combination therapy is used for the following reasons:

- to provide broad spectrum activity (e.g., cephalosporins and metronidazole for mixed or unknown infections)
- to prevent the emergence of resistant strains (e.g., tuberculosis treatment)
- to provide synergistic action - when the agents used in combination have a greater effect than when used alone (e.g., penicillin and gentamicin used in the treatment of infective endocarditis).

Treating patients with combination therapy has the disadvantage of increasing the cost and the potential for adverse effects (e.g., increased nephrotoxicity when gentamicin is combined with a cephalosporin). 1

The combination of two or more antibacterials may provide a broader spectrum of activity but the risk of superinfection with fungi, such as Candida albicans, and bacteria, such as Clostridium difficile, is increased.

2.3 Patient factors

When choosing an appropriate antibacterial a number of patient factors need to be taken into consideration.
### Age

| Children | ■ Most antibacterials are licensed for use in children.  
|          | ■ Children differ from adults in the way they respond to infections and antibacterials.  
|          | ■ Tetracycline is contraindicated in children, as it causes deformity of growing bones and discolouration of teeth.  
|          | ■ Ciprofloxacin can cause arthropathy, so it should be used with caution.  
|          | ■ The doses of some antibacterial medicines will be based on weight.  
| Older people | ■ Older patients are more likely to have renal and hepatic impairment.  
|            | ■ They are more likely to be on a high number of medicines, increasing the chances of drug interactions.  
|            | ■ Older patients are more prone to the adverse effects of antibacterial drugs, such as *Clostridium difficile* infection.1 |

### Allergies

Between one and ten percent of exposed individuals will report a hypersensitivity reaction to penicillin. Wherever possible, the nature of the allergy should be investigated, as well as the timeframe, the severity of the reaction and whether it was a first or second-hand recollection.

The allergic reaction is commonly due to the basic structure of the beta-lactam ring or the side chain within penicillin. Patients who report an allergic reaction to one type of penicillin may therefore be allergic to all of them. This includes penicillins found in co-formulations, for example, co-amoxiclav, co-fluampicil, Tazocin and Timentin.

Cross-reactivity between penicillins and cephalosporins was believed to be approximately ten percent. Pegler and Healy12 contested this figure as an overestimate, suggesting the risk is closer to 0.5 percent for first generation cephalosporins in patients with true penicillin allergy. While due care must be taken when using cephalosporins in those with known allergy to penicillins, second and third generation cephalosporins (which have a different side chain in their structure) can be considered in those where alternative antibiotics would be suboptimal, so long as adequate supervision is provided.10
Renal function

Patients with renal impairment may require a reduced dose or frequency of many antibacterials (eg, aminoglycosides, carbapenems, penicillins, ciprofloxacin). Information on dose adjustment can be found in the BNF, the manufacturer’s summary of product characteristics or The renal drug handbook, which also recommends suitable doses for patients who are undergoing haemodialysis and peritoneal dialysis.

Hepatic function

Some antibacterials should be avoided or used with caution in patients with hepatic impairment or cardiac disease (due to reduced blood flow to the liver). The metabolism of rifampicin may be impaired in liver disease, so it should be avoided or the dose reduced and hepatic function monitored.

Some antibiotics may cause adverse effects to the liver. A common example is co-amoxiclav, which may cause cholestatic jaundice. The BNF states that co-amoxiclav is contraindicated in co-amoxiclav or penicillin-associated jaundice or hepatic dysfunction. The BNF should be checked for information about individual antibacterials for patients with significant hepatic impairment. Antibacterials to use with caution in hepatic impairment include fluclouxacin, antituberculosis drugs, macrolides, tetracyclines, metronidazole, nitrofurantoin and sodium fusidate. Liver function tests and full blood counts should be monitored. Patients and carers should be counselled on how to recognise signs of liver disorder, such as nausea, vomiting, itching and jaundice.

Pregnancy and breastfeeding

Some antibiotics are harmful when taken by women who are pregnant or breastfeeding. Where possible, antibiotics that are known to be unharmsful should be used. If this is not possible, the potential risks and benefits to mother and child must be carefully considered before initiating an alternative. The BNF contains information about drugs in pregnancy and breastfeeding. For more information contact your local medicines information centre.

Patient history

Previous antibacterial treatment may affect the choice of antibiotic, for example, if a recent course has failed or the infection has recurred. Recent travel abroad or known contact with other infected patients is also important information.

Consider two patients presenting in the community with the same symptoms of pneumonia. If one has recently been discharged from hospital and the other has had no recent inpatient admissions, it is likely that different organisms are responsible for their infections. If either of them had received an antimicrobial recently, this would need to be taken into account, since the infecting organism might be resistant to it.
2.4 Drug interactions

Many antibacterials have drug interactions that may lead to antibacterial therapy failure or increase the risk of an adverse event. Appendix 1 in the *BNF,¹⁰* or *Stockley’s drug interactions¹¹⁴* are useful resources to help assess the significance of interactions identified during the clinical checking of prescriptions.

**Practice point 3**

Write down four common drug interactions you see with antibacterials. What action would you take for each?

1. 

2. 

3. 

4. 

It is important to consider interactions between drug and disease state, such as fluoroquinolones in epilepsy.
2.5 Route, dose, frequency and duration of treatment

The chosen antibacterial must be able to reach the site of infection in sufficient concentration to have an effect.

**Route of administration**

Topical products are appropriate if the infection is localised and of a minor nature (e.g., bacterial conjunctivitis). Where topical administration is not sufficient to reach all infected sites, systemic treatment will be needed, for example, cellulitis needs to be treated orally or parenterally.

Parenteral therapy is preferred for serious infections, as high therapeutic concentrations can be achieved reliably and rapidly. However, long-term use is associated with risks of line-infection, phlebitis, extravasation and embolism. Medication errors are also more likely with the intravenous route. In some cases, such as for cellulitis treatment, home intravenous therapy may be an option. Outpatient parenteral antimicrobial therapy (OPAT) provides an alternative to inpatient care by allowing suitable patients to receive intravenous antimicrobials in the community.\(^{15}\) Switching from intravenous to oral antibacterials should be considered within 48 hours if possible.\(^7\)

Oral therapy is more convenient for the patient and avoids some of the risks associated with intravenous use. Some oral antibacterials (e.g., ciprofloxacin) have very high oral bioavailability and therapeutic blood levels are comparable to intravenous administration. The intravenous route for these antibacterials is restricted to patients who cannot take or absorb oral therapy, or for those who have severe sepsis.

Intramuscular therapy is less reliable than other routes and is painful, so it should be avoided where possible. However, the intramuscular route is sometimes used for patients with negligible venous access, generally off-licence, e.g., gentamicin in intravenous drug users.

**Dose and frequency**

The dose and frequency of an antibacterial needs to be sufficient to bring drug levels into the therapeutic range. For some antibacterials drug monitoring will be required. The appropriate dose will depend on a number of factors, including severity of illness, patient’s age, weight, renal and hepatic function, immune status and previous antibiotic regimen. The \(BNF\)\(^ {10}\) and the \(BNF for children\)\(^ {16}\) are good
reference sources for checking the appropriate dose and frequency. Inadequate dosing can lead to the emergence of resistant strains and treatment failure, while high dosing increases the likelihood of drug-related adverse effects.

**Duration of treatment**

In hospital the need for antibiotic therapy should be reviewed on a daily basis but in primary care the course of treatment is generally decided when the prescription is written. For most infections five to seven days is currently recommended in national guidance. Uncomplicated urinary tract infections can be treated with three days of antibiotics. Tuberculosis requires six months, while treatment for HIV is life-long.

To prevent the emergence of resistant strains, prudent prescribing and use of antibiotics is essential. It is important to follow the recommended duration for treatment and avoid prolonged use of antibiotics. This will also prevent the emergence of superinfections and lower the risk of toxicity.

**Reasons for treatment failure**

- Incorrect diagnosis
- Suboptimal dose (including lack of adherence)
- Wrong route of administration (including inability to absorb orally)
- Bacterial resistance to the drug or development of resistance during treatment
- Abscesses requiring drainage
- Foreign bodies in a wound
- Drug interactions

**2.6 Drug monitoring**

Some antibacterial agents have a narrow therapeutic index and monitoring is essential to manage the treatment of the infection and avoid toxicity to the patient. Gentamicin and vancomycin are two examples, although generally not used in primary care.
When a prescription for an antimicrobial is clinically checked, consider whether the patient has an infection that needs treating, if the prescribed drug is the most appropriate and if the route, dose, frequency and duration are appropriate. Ensure patient factors have been taken into account and consider if there are any clinically significant drug interactions.

3. Antimicrobial stewardship

The World Health Organisation (WHO) defines the appropriate use of antimicrobials as ‘the cost effective use of antimicrobials which maximises clinical therapeutic effect while minimising both drug-related toxicity and the development of antimicrobial resistance’.17

In the chief medical officer’s report, the following description is used: antimicrobial stewardship ‘embodies an organisational or healthcare-system-wide approach to promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness’.2 It has three major goals.

1. Optimise therapy for individual patients.
2. Prevent overuse, misuse and abuse.
3. Minimise development of resistance at patient and community levels.

Pharmacy professionals can support these aims through dialogue with prescribers about appropriate choice of antibacterial and by ensuring patients are referred to prescribers appropriately, counselled about how and when to take their antibiotic and possible side-effects to expect, so that treatment is not stopped prematurely.
**Talking point B**

*Clostridium difficile* and MRSA have become major infections because of inappropriate antibacterial use.

Discuss this statement.

---

3.1 Reducing resistance

The chief medical officer’s report highlights concerns that the increasing levels of organisms’ resistance to antimicrobial agents and the decreasing number of new agents in development will lead to a health threat. The report highlights the need to preserve existing antimicrobial agents by good stewardship and encourages development of new agents.2

Areas for action include prioritising antimicrobial resistance as a major area of concern, educating healthcare professionals and the public to encourage responsible use of antibacterials, and improving prevention, diagnostic technology and surveillance.2

The *UK five year antimicrobial resistance strategy 2013 to 2018*6 was published in September 2013 and forms part of
The response to the challenges outlined in the chief medical officer’s report. The overarching goal of the strategy is to slow the development and spread of antimicrobial resistance. The strategy identifies seven key areas for future action.

1. Improving infection prevention and control practices.
2. Optimising prescribing practice.
3. Improving professional education, training and public engagement.
4. Developing new drugs, treatments and diagnostics.
5. Better access to and use of surveillance data.
7. Strengthened international collaboration.

The contribution that pharmacy teams can make to the strategy will be discussed in section 3.3.

3.2 Reducing healthcare-associated infections

A healthcare-associated infection (HCAI) is any infection that results from a healthcare intervention, whether in primary or secondary care. In 2011, approximately 6.4 percent of patients in UK hospitals contracted an HCAI. The prevalence of HCAIs in primary and community care settings in the UK is not known.

A variety of organisms are implicated, leading to a wide variety of diseases. Since April 2011, NHS acute trusts have been required to report cases of meticillin-sensitive *Staphylococcus aureus* (MSSA) and *Escherichia coli* bacteraemias, as well as cases of MRSA and *Clostridium difficile*. HCAIs lead to longer hospital stays, higher costs, an increase in the severity of the illness and poorer outcomes for the patient. MRSA, *Clostridium difficile* and ESBLs are the most common and problematic HCAIs at present.

**Meticillin-resistant *Staphylococcus aureus***

*Staphylococcus aureus* frequently colonises human skin and mucosa and is found in around 30 percent of the population. Colonisation does not cause a problem but the infection can enter the bloodstream and cause bacteraemia. MRSA is a major cause of HCAI. Most strains are treatable as they are sensitive to a number of antibacterial agents. These antibacterials may be used in combination, depending on the site of infection. Infection is easily spread from person to person but can be reduced by observing hygiene procedures and other infection prevention and control strategies.
The cases of MRSA bacteraemias have fallen over the past few years. Cases from April to June 2012 had decreased by 30 percent, compared to the same period in 2011.23

**Clostridium difficile**

*Clostridium difficile* is found in the lower bowel of around five percent of the population. Normally other commensal organisms that colonise the intestine prevent overgrowth of *Clostridium difficile*. However, when antibacterial therapy is given to patients it can upset the normal gastrointestinal flora, which allows *Clostridium difficile* to multiply.

The toxins produced by *Clostridium difficile* damage the lining of the gastrointestinal tract and cause symptoms ranging from mild diarrhoea to severe pseudomembranous colitis. Elderly patients, immunocompromised patients and patients with severe underlying disease are at increased risk of developing *Clostridium difficile* infection. *Clostridium difficile* produces spores that are shed in the diarrhoea and can persist in the environment. This causes infection to spread to other vulnerable patients.

There continues to be a significant decline in the number of *Clostridium difficile* cases in the UK. During the period of 2011/2012, 18,005 cases were reported in patients aged two years and over. This represents a 17 percent reduction from the previous year and 50 percent reduction on the 36,095 cases reported in the 2008/2009 period.24

Prudent antibacterial prescribing, isolating infected patients, good infection prevention and control and improved cleaning of the environment can all help to prevent the spread of *Clostridium difficile*. Fluoroquinolones, third generation cephalosporins and other broad spectrum antibacterials have been associated with an increased incidence of *Clostridium difficile*.25

The majority of *Clostridium difficile* strains are susceptible to oral metronidazole and oral vancomycin. Fidaxomicin is a newer antibiotic for the treatment of *Clostridium difficile* infection and shows similar efficacy to vancomycin but reduces the relapse rate for subsequent *Clostridium difficile* infections.26
When a patient is infected with *Clostridium difficile* any causative antibiotics should be stopped when possible.

**Extended-spectrum beta-lactamases**

The extended-spectrum beta-lactamase-producing organisms are usually resistant to penicillins, cephalosporins, quinolones and monobactams and are treated with carbapenems, aminoglycosides or sometimes nitrofurantoin. Patients with these infections are often admitted to hospital for treatment. These organisms include *Escherichia coli* and *Klebsiella*, which are commonly associated with urinary tract infections. These infections can sometimes progress to more serious bacteraemia.

**Glycopeptide-resistant enterococci**

Enterococci are found in the bowels of humans and many animals. They are a common cause of urinary tract infections, wound infections and bacteraemia. Glycopeptide-resistant enterococci and particularly vancomycin-resistant enterococci have emerged as major causes of HCAIs and treatment is difficult.

**Catheter-associated urinary tract infections**

Urinary tract infections caused by catheter insertion are one of the most common types of healthcare-associated infection, which can result in overprescribing of antibacterials. Pharmacy professionals have a role to play in ensuring treatment is restricted to managing symptomatic urinary tract infections.

### 3.3 Role of the pharmacy team

The pharmacy team can contribute to antimicrobial stewardship in primary care in a number of ways.

**Help to ensure that antibiotics are only prescribed when they are needed**

In community pharmacy, promoting symptomatic relief of infections and referring patients to the GP only when necessary is an important part of stewardship. The NICE clinical guideline 69, *Respiratory tract infections – antibiotic prescribing*, suggests that patients should be given advice on the natural history of an infection and the average illness duration (for example three weeks for acute cough). Pharmacy
teams should be aware of the normal history of such conditions and be able to explain the lack of benefit of antibiotics in these cases. This will help to manage patient expectations and reduce referral to GPs.28, 29

**Managing patient expectations**

Patient expectation plays a big role in the decision of a patient to consult their GP and also affects the doctor’s decision to prescribe. As described above, pharmacy teams have a role in discussing with patients whether they should be referred to the GP practice. Prescribers frequently assume a patient with an acute respiratory infection will not be satisfied unless they receive a prescription for an antimicrobial; whereas studies show that patients are often happier if they receive accurate explanations and reassurance, rather than inappropriate antimicrobial therapy.30 Once an antimicrobial has been prescribed for a patient, they are more likely to return for another antimicrobial prescription for the same condition in the future.31

There are a number of leaflets available for patients that can help explain the decision not to prescribe, such as the *Antibiotic information leaflet* and the *When should I worry?* booklet, both available from the TARGET toolkit.8

Patient education is important and pharmacy teams should support national initiatives, such as European Antibiotic Awareness Day (18 November), and use materials made centrally available by the Department of Health for health promotion activities in their pharmacies.

Providing a delayed prescription is an approach that can be used by prescribers to reduce antimicrobial use. The patient is given a prescription and told to only have it dispensed if symptoms persist or get worse. Often they are given a set time frame for this. Pharmacy professionals can support patients in making a decision as to when the prescription may be needed and can advise patients of other self-management strategies that can be employed.
Check that antibiotics are prescribed appropriately
You should consider the following questions when dispensing antibiotic prescriptions.

Does the patient have an infection that needs to be treated?

Is the prescribed agent the most appropriate antibacterial?

Is this an appropriate route, dose, frequency and duration for the patient?

Take steps to ensure people use their antibiotics properly
Counselling patients when dispensing antibiotic prescriptions is key.

Patients should be advised:

■ to take the antibiotic regularly, as directed
■ to finish the course even if they feel better or symptoms resolve
■ to discard unused antibiotics by returning them to the pharmacy (if they need to change medicines, following side-effects or sensitivity reports)
■ not to use out-of-date antibiotics
■ not to take antibiotics prescribed for someone else.

Practice point 4
For the next ten patients who present with a prescription for antibiotics, note down the counselling points that you make.

Key point
The pharmacy team has a key role in antimicrobial stewardship by managing patient expectations and referring appropriately, advising prescribers and counselling patients on the optimal use of antibiotics.
**Summary of background reading**

- Antibacterials allow a wide range of infections to be successfully treated and lives saved.
- Antibacterials have different modes of action and will be active against different bacteria.
- Empirical therapy is often started in the absence of confirmation of infection and sensitivity. Guidelines are available to support prescribers to decide whether to treat and to select a suitable therapy.
- A number of patient factors, such as allergies, age, renal and hepatic function and other drugs being taken, need to be considered when choosing antibacterial treatment.
- Antimicrobial stewardship aims to support appropriate use of antibiotics and reduce the impact of antimicrobial resistance and healthcare-associated infections.
- The pharmacy team has a key role to play in contributing to the appropriate use of antibacterials by managing expectations of patients and referring appropriately, advising prescribers and counselling patients on the optimal use of antibiotics.

You should now complete the Directing change exercise on the next page to prepare for the workshop, where this will be discussed.
Directing change

Here we give you the opportunity to reflect and consider how you could improve your practice in this area.

At the focal point event we would like you to share with your colleagues an experience that you have had regarding an intervention you have made on a prescription for an antibacterial agent. Take some time to make notes to support you on the evening.

You should include the following information:

- the age of the patient
- the infection being treated
- the antibacterial agent prescribed
- pre-existing conditions and other medications, including prescribed and over-the-counter medicines
- issues that you encountered and how you resolved them.
# Checklist for action

At this point in the learning programme you will have carried out the following.

<table>
<thead>
<tr>
<th>Task</th>
<th>Completed on:</th>
</tr>
</thead>
<tbody>
<tr>
<td>I have answered the Moving into focus questions</td>
<td></td>
</tr>
<tr>
<td>I have listed three learning needs</td>
<td></td>
</tr>
<tr>
<td>I have read the whole book</td>
<td></td>
</tr>
<tr>
<td>I have undertaken the practice points</td>
<td></td>
</tr>
<tr>
<td>I have made notes for the talking points ready to share at the event</td>
<td></td>
</tr>
<tr>
<td>I have worked through the Directing change exercise</td>
<td></td>
</tr>
</tbody>
</table>

Signed: ........................................................................................................

Date: ........................................................................................................

Take this book with you to your *focal point* event. Make sure that you know when and where it is and what time it starts. Enjoy your learning.
References


   http://www.pjonline.com/Hospital/Editorial/200801/special/p7/acquiredinfection.html

   http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1317138914904


   http://www.pjonline.com/news/apocalypse_now_we_can%E2%80%99t_afford_to_wait_to_take_action_on_antibiotic_resistance

   http://www.chemistanddruggist.co.uk/feature-content/-/article_display_list/4422680/8-ways-you-can-help-reduce-antibiotic-resistance


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Do you have any comments on your focal point learning experience? Email: feedback@cppe.ac.uk

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