Antibiotics

Why this subject matters...

Antibiotic resistance is a serious, global problem. Every decision you make about antibiotics matters not just for your patient but for everyone. You need to be able to guide antibiotic prescribing with confidence, considering the patient, the causative organism and the site of infection.

It's a huge topic and this section cannot cover everything you will ever need to know, but it will give you a framework for reviewing an antibiotic prescription. It will guide you through some of the more common infections you are likely to encounter, and how to tailor therapy to your individual patient.

Prescribing responsibly

Resistance

Resistance occurs naturally over time, but inappropriate antibiotic use means that this problem has increased significantly over the last 40 years. That, together with fewer new antibiotics being developed, means quite simply that we may struggle to treat patients effectively in the future. It's a worldwide issue but you have the potential to make a difference with every antibiotic prescription you review.

Public Health England have produced a strategy to tackle antimicrobial resistance and they recommend a "Start Smart – Then Focus" approach for every antibiotic prescription.

Start Smart means

• do not start antimicrobial therapy unless there is clear evidence of infection
• take a thorough drug allergy history
• initiate prompt effective antibiotic treatment within one hour of diagnosis (or as soon as possible) in patients with severe sepsis or life-threatening infections. Avoid inappropriate use of broad-spectrum antibiotics
• comply with local antimicrobial prescribing guidance
• document clinical indication (and disease severity if appropriate), drug name, dose and route on drug chart and in clinical notes
• include review/stop date or duration
• obtain cultures prior to commencing therapy where possible (but do not delay therapy)
• prescribe single dose antibiotics for surgical prophylaxis where antibiotics have been shown to be effective
• document the exact indication on the drug chart (rather than stating long-term prophylaxis) for clinical prophylaxis

Then Focus means

- reviewing the clinical diagnosis and the continuing need for antibiotics at 48-72 hours and documenting a clear plan of action - the 'antimicrobial prescribing decision'.
- the five 'antimicrobial prescribing decision' options are:

  1. Stop antibiotics if there is no evidence of infection
  2. Switch antibiotics from intravenous to oral
  3. Change antibiotics – ideally to a narrower spectrum – or broader if required
  4. Continue and document next review date or stop date
  5. Outpatient Parenteral Antibiotic Therapy (OPAT)

- it is essential that the review and subsequent decision is clearly documented in the clinical notes and on the drug chart where possible e.g. stop antibiotic.

Before choosing an antibiotic, 2 factors need to be considered – the patient and the causative organism. The next few pages will walk you through the key considerations in making this decision.

Managing infections

About a third of patients in hospital will be given an antibiotic, and so it is important that you know how common infections are treated. Specifically, you need to know how different organisms are classified, which bacteria are most likely to infect different parts of the body, and which antibiotics are effective.

Check out your knowledge on bugs and drugs using this quiz. Please select 'practice' as your game mode then click Start Game. There is also a 'click and drag' quiz here. Depending upon how you do, you might like to read on. Alternatively, you can skip to the next page.

Organising bacteria

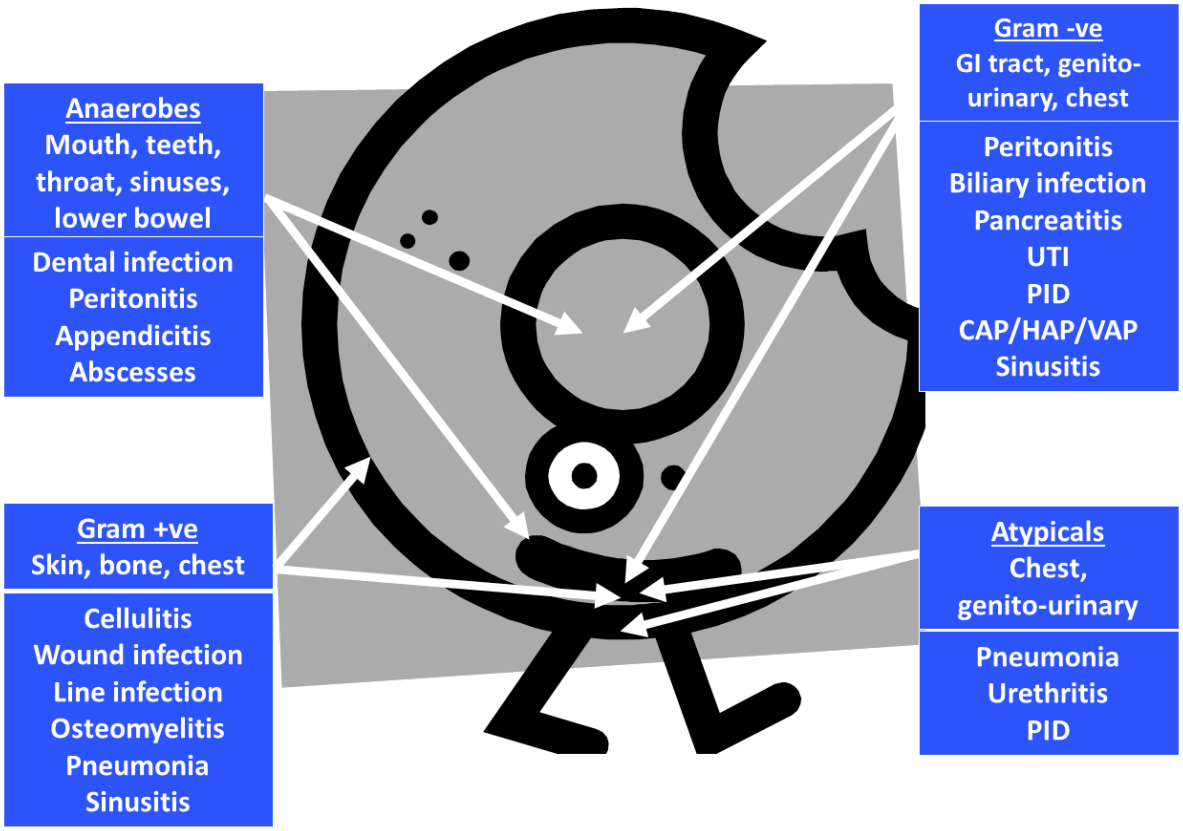
There are several different ways to **broadly** classify bacteria. In a clinical setting they are grouped as Gram positive, Gram negative and atypical according to the structure of their cell walls or where they live. They are also distinguished according to their oxygen requirements as anaerobes or aerobes.

Gram positive	Staphylococci Streptococcus Enterococci Listeria Bacillus
Gram negative	Pseudomonas Haemophilus *E.coli* Enterobacter Klebsiella Proteus Salmonella Shigella Helicobacter
Anaerobes	Clostridia – also mostly gram positive Bacteroides – also gram negative
Atypical	Mycoplasma Chlamydia Legionella – also gram negative

There are some exceptions such as *Mycobacterium tuberbulosis* which is Gram positive but it doesn't take up a Gram stain. This is because its cell wall contains lots of mycolic acid.

What bugs are where?

Remembering what bacteria are likely to infect different body systems is important, especially when making decisions about antibiotic therapy empirically ('blind') or before laboratory sensitivities are available. There is no easy way to remember this, but the picture below illustrates **in general** what bacteria are found where.



What is the most common infection you see on your ward? What is the causative organism and what body system does it affect?

Bugs and drugs

As a pharmacist you need to have a working knowledge of the spectrum of commonly used antibiotics. It is difficult to group drugs according to their activity against different pathogens; some only cover Gram positive or Gram negative organisms, but others may cover mostly Gram negative organisms but have some Gram positive cover (e.g. ciprofloxacin, gentamicin), or vice versa (e.g. rifampicin). Therefore the following table lists antibiotics according the groups of pathogens against which they show most activity.

Used only or mainly for Gram positive (Staphylococcus and/or Streptococcus)	Phenoxymethylpenicillin and benzylpenicillin Flucloxacillin Clindamycin Fusidic acid Rifampicin Vancomycin Teicoplanin Linezolid
Used only or mainly for Gram negative	Ciprofloxacin Gentamicin, tobramycin, amikacin Ceftazidime Aztreonam Colistin
Anaerobes	Metronidazole Clindamycin Co-amoxiclav (infections above the diaphragm) Piperacillin-tazobactam Etrapenem, imipenem, meropenem
Atypicals	Azithromycin, clarithromycin, erythromycin Doxycycline, minocycline , oxytetracycline Ciprofloxacin, levofloxacin, ofloxacin
Broad spectrum	Azithromycin, clarithromycin, erythromycin Trimethoprim, nitrofurantoin Amoxicillin, co-amoxiclav Doxycycline, minocycline, oxytetracycline Ceftriaxone, cefotaxime cephalexin Levofloxacin, moxifloxacin Piperacillin-tazobactam, ticarcillin-clavulanic acid Ertapenem, imipenem, meropenem Chloramphenicol

Again this is difficult to memorise – you may like to keep the table to hand, but don't use it isolation; **ALWAYS** check your local guidelines.

Broad versus narrow spectrum antibiotics

Inappropriate use of broad-spectrum antibiotics is associated with the selection of resistant bacteria and the induction of *Clostridium difficile* infection (CDI). Their use can also cause long-lasting harmful changes to the body's protective microbial flora. Cephalosporins, ciprofloxacin, clindamycin and co-amoxiclav ('the 4Cs'), and piperacillin-tazobactam and the carbapenems have been most strongly associated with CDI, but all antibiotics should be avoided unless there are clear clinical indications for their use. Indications for using broad spectrum agents include life-threatening infection (e.g. neutropenic sepsis), significant risk of a resistant pathogen (e.g. recent hospital admission, care home resident, recent exposure to antibiotics), or on advice from a microbiology doctor. Antibiotics should always be used for the shortest duration possible that gives an appropriate clinical outcome.

Tailoring treatment

As well as considering the organism, and the site and severity of the infection, you need to make sure that antibiotics are safe and effective for the individual patient concerned. Guidelines are useful in helping us to choose the most appropriate antibiotic for most patients, but you need to ensure that it is right for **your** patient taking into account any other medicines they may take, their medical history including their renal and liver function, their age, weight and allergy status and so on.

Read through the following real-life examples of patients with special considerations with respect to their antibiotic therapy. Think about how you would have managed the question and what decision would you have made.

Patients with kidney disease

Question

You're asked by a doctor on your general medical ward about a patient with cellulitis. She has been advised to use oral clarithromycin as the patient is penicillin-allergic. However the patient has chronic, stable kidney disease and the doctor wants to know the correct dose to prescribe. The hospital guidelines advise that 500mg twice daily should be used but she is concerned that this is too high. The doctor tells you that the patient has an eGFR of 24ml/min.

Outcome

After checking your patient has no contraindications to clarithromycin, the first step you take is to calculate the creatinine clearance (CrCl) as you know that drug dosing is more reliably based upon this measure of renal function rather than eGFR. You establish that the patient is male, weighs 94kg, is 68 years old, their creatinine is 230 micromols/L and that they are approximately 6 feet tall. Using the Cockcroft Gault formula you establish that their CrCl is 29.9 ml/min and so their drug clearance may be better than their eGFR would suggest.

You decide to check the SPC for clarithromycin first and this states that the dose should be reduced by half when the CrCl is less than 30ml/min. However the Renal Drug Database states that for patients with a CrCl between 10 and 30 ml/min 250 to 500mg may be given twice daily.

Therefore since your patient's CrCl is at the 'cut-off' for dose adjustment according to the SPC, you advise the doctor to use 500mg twice daily orally. However if the patient's renal function deteriorates then she should consider reducing the dose.

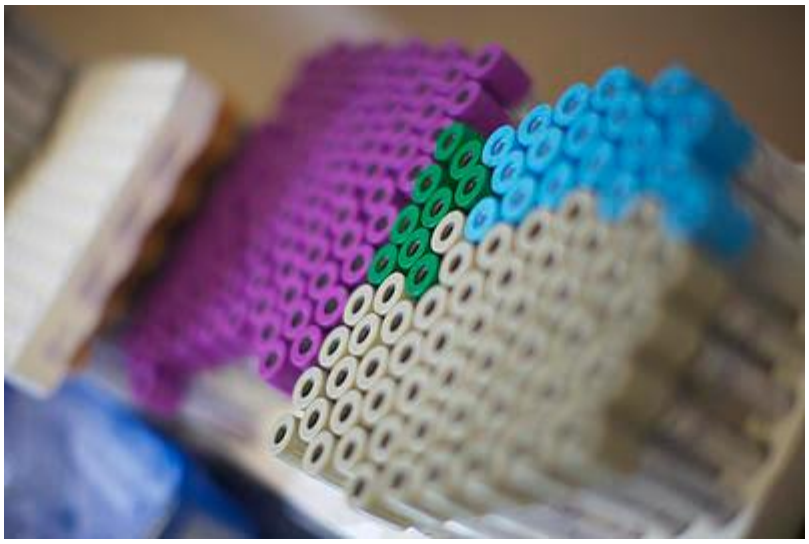
Obese patients

Question

You are covering the acute medical admissions unit and you're asked by a registrar about the dose of chloramphenicol in a patient with severe community acquired pneumonia. He would normally prescribe 1 gram four times a day according to the hospital guidelines but the patient is 178 kg. Does the dose need to be adjusted in view of the patient's weight?

Outcome

After a quick check of your hospital guidelines and the patient's medical history you are reassured that chloramphenicol is a suitable antibiotic. You then search your general and specialist resources but they have no guidance specifically for dosing chloramphenicol in patients who are obese. You turn to your medicines information pharmacist who points you towards some theoretical considerations around antibiotic dosing in obesity.



You look at the pharmacokinetic profile of chloramphenicol and establish that it might be expected to have a higher volume of distribution compared to a patient of a healthy weight, but that it's not an exact science. Discussing your findings with your microbiology pharmacist, you conclude that this ultimately is a balance of risk versus benefit. If you use 1 gram four times a day as per the hospital policy there is a risk that the patient will be under-dosed and not respond to treatment. If you use a higher dose the patient's pneumonia may be treated effectively but they may be at an increased risk of side effects. In the absence of any guidance, together you decide that since the dose of chloramphenicol may be doubled in severe infections that it would be reasonable to use 2 grams four times a day for this specific patient, reviewing and reducing the dose as they improve. Your hospital pathology department is also able to process chloramphenicol blood samples and so you advise the registrar that therapeutic drug monitoring may be prudent.

Interacting medicines

Question

It's the last day of your medicines information rotation and you receive an urgent call from the pharmacist covering the orthopaedic unit. She is trying to establish if there is an interaction between rifampicin and apixaban. Upon questioning you find out that the patient usually takes apixaban for atrial fibrillation. He was switched to enoxaparin after surgery on his knee for osteomyelitis. He has been taking rifampicin post-operatively as per the hospital guidelines and requires a further 6 weeks' treatment. The team would like to discharge him today and so want to restart his apixaban.

Outcome

It quickly becomes apparent that apixaban and all the direct oral anticoagulants interact unpredictably and significantly with rifampicin. Warfarin interacts with rifampicin too, but the patient's INR could be monitored and the dose adjusted accordingly. Enoxaparin at home might be an option while the patient is taking rifampicin, and then swapping back to apixaban when the antibiotic course is complete. A further solution might be to use a different antibiotic depending upon the sensitivities of the causative bacteria.

You present all these options to your colleague and discuss the relative merits and disadvantages for the individual patient concerned, taking into account the support he has at home managing his medicines. She takes these potential solutions to the medical team and rings you back an hour later to let you know that they have changed the antibiotic to clindamycin and restarted the apixaban. You document this outcome as evidence of your impact, and for the next time this scenario occurs.

Children

Question

You take a call through your patient helpline from a mother whose child has been prescribed flucloxacillin by the paediatric assessment unit. The child is 2 years old and has been prescribed a 7 day course of the antibiotic for cellulitis. The mother has just tried to give the first 5ml dose but the child has spat the medicine out and is now refusing any further doses. Can the antibiotic be mixed with food and if not what should the mother do?

Outcome

You know that flucloxacillin is very bitter and that ideally it should be given on an empty stomach, but you can't find any specific guidance to help the mother administer the antibiotic to her child. However your paediatric pharmacist directs you to some general advice about administering liquids to children. It suggests offering the child milk or fruit juice after giving the medicine. If this fails then it advises that some medicines may be mixed with milk or fruit juice if appropriate. Your paediatric pharmacist explains that the evidence to support this practice will be based on expert consensus rather than formal clinical studies.

You need to weigh up the benefits of the child being able to take the antibiotic versus the potential risks of trying to disguise the taste.

Applying this guidance to flucloxacillin, you rule out using milk. However the child could be offered fruit juice after taking the antibiotic. If this fails then mixing the flucloxacillin with juice prior to administration would also seem acceptable.

You ring the mother back and advise her that the flucloxacillin should not be mixed with food but that fruit juice may be used. If this doesn't work and her child is not able to tolerate the medicine, then an alternative antibiotic may be required. You reassure her that flucloxacillin does have an unpleasant taste and that it is not unusual for children to refuse to take it.

Breastfeeding

Question

You're overrunning on your ward visit and as you try to leave the ward Sister asks you about a patient who is exclusively breastfeeding her 3-month-old child but who has been started on ciprofloxacin. The patient has been advised to stop breastfeeding whilst taking the antibiotic and the Sister wants to know when she can restart. The patient has an intra-abdominal infection and has been prescribed ciprofloxacin 500mg twice daily for 7 days. Upon questioning you establish that the child is healthy and was born term.

Outcome

Whilst you are on the ward you check the manufacturer's prescribing information. It confirms that ciprofloxacin should not be used whilst breastfeeding. This is because of the potential risk of joint damage to the child. However the SPC does not give any advice about resuming feeding once the drug has been stopped.

You drop into the medicines information office on your way back from the ward to consult some specialist lactation resources. These advise that the amount of ciprofloxacin that passes into the breast milk is actually quite low, and that quinolones are generally considered safe to use in mothers who are breastfeeding. Waiting 3-4 hours after each dose before feeding can minimise infant exposure to the drug. Joint damage has only been reported in children taking quinolones themselves and not those exposed via the breast milk. Gastrointestinal side effects and oral candida might be expected in the child, especially with higher doses.

Armed with your findings you go back to the ward and establish that the patient decided to

stop breastfeeding herself after reading a parenting forum online. You explain that the risks posed to her child are actually quite low and are probably outweighed by the benefits of continuing to breastfeed. Reassured by your advice, the patient decides that she wants to resume breastfeeding. She is currently feeding her child every 4 hours, and so you advise her to take the antibiotic immediately after finishing a feed. You also counsel her on the side effects that her child might experience. Finally you document your advice in the patient's medical and nursing notes and speak to the ward Sister.

Pregnancy

Question

It's 6pm and you're on the late shift in the dispensary. A nurse calls in requesting some gentamicin injection for a patient who is 10 weeks pregnant and has suspected sepsis. The patient has already received the first dose and the next is due in 2 hours' time. You review the prescription and the dose prescribed is 1.5 mg/kg three times daily. You know that your hospital policy is usually to use extended interval gentamicin for sepsis rather than conventional dosing and you question this with the nurse. She is unsure and so you agree to look into this and give her a call in the next 30 minutes. You also want to check the appropriateness of using gentamicin in pregnancy.

Outcome

A scan of the manufacturer's prescribing information reveals that if gentamicin is clearly indicated during pregnancy then it may be given. Other sources agree that for maternal sepsis, gentamicin is appropriate in combination with other antibiotics.

Reassured by this information, you try to establish whether it should be given as a single daily dose or as conventional dosing. Your hospital sepsis guidelines aren't helpful and your pregnancy resources don't cover dose and administration. However you do discover that gentamicin kinetics are altered in pregnancy due to the increase in glomerular filtration rate and plasma volume, and that therapeutic levels can sometimes be difficult to achieve.

An internet search reveals a Royal College of Obstetrics and Gynaecology guideline which advises giving gentamicin as a single daily dose, but you also find multiple sepsis protocols from NHS hospitals across the UK which recommended conventional dosing for pregnant

women.

Faced with this conflicting information and an approaching deadline you discuss this with your senior pharmacist in the dispensary. She helps to provide some perspective in that before extended interval regimes were introduced, all patients would have received multiple daily dose regimes. Therefore this patient's prescription is not unsafe, but may not represent current practice. Since the patient has already received a dose and is due a further dose soon you decide to supply the gentamicin with a view to following it up with your obstetrics pharmacist in the morning.

Allergy

Question

You pick up a request to supply clindamycin on your ward. The patient concerned has severe tonsillitis and laryngitis. This seems a little usual and so you investigate further.

Outcome

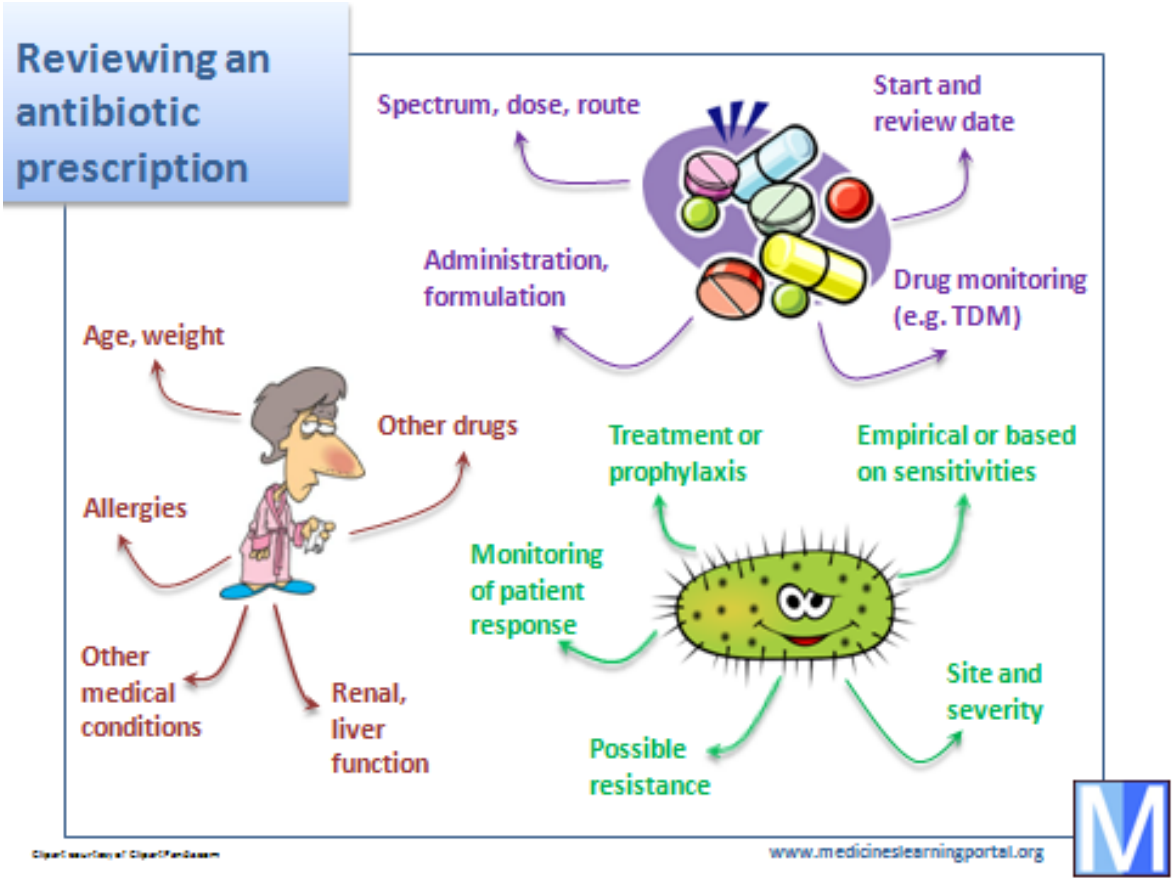
Your local guidelines suggest phenoxymethylpenicillin or clarithromycin as first line options. However you note that the patient has a documented allergy to both penicillins and macrolides. The prescribing doctor is off the ward but the medical notes indicate that a microbiologist has reviewed the patient and recommended clindamycin.

You review the spectrum of activity of clindamycin and remember that it covers a range of Gram positive organisms including *Streptococci*. The dose prescribed is 300mg every six hours which is within the usual range. You check the patient's medical history and he does not have any renal or liver impairment or other significant co-morbidities. He is currently taking some soluble analgesia but does not normally take any regular medicines.

Speaking to the patient, you discover that he will not be able to swallow clindamycin capsules and you quickly need to find out whether a liquid exists or if the capsules can be opened. Fortunately your pharmacy logistics team help you to track down an oral suspension but it will take 24 hours to arrive. In the meantime you establish that clindamycin capsules may be opened and the contents mixed with water, although this is unlicensed practice. You check with the prescriber that they are happy to give the medicine in this way, and then speak to the nursing team and the patient about administration and the potential side effects to expect.

Reviewing a prescription

When faced with a new prescription for an antibiotic it can be helpful to consider the patient, the infection and the drug in turn.



The Patient

- Check the patient's age.
  If this is a child, then you'll need to think about whether the antibiotic prescribed is suitable. Extra care is needed with some agents such as tetracyclines and quinolones for example.
- Check the patient's weight.
  A dose adjustment may be needed for an adult that is either underweight or overweight. Children's doses are sometimes based upon their weight. For older or overweight children take care not to exceed the recommended adult dose for patients.
- Does the patient have any relevant medical history? Do they have any kidney or liver impairment? Are they pregnant or breastfeeding?
  An alternative antibiotic, extra monitoring, or dose adjustment may be required.
- Does the patient take any other medicines that may interact with the antibiotic?
  Some combinations may be contraindicated in which case, an alternative antibiotic may be required, or sometimes it's clinically acceptable to temporarily suspend the other medicine (such as simvastatin with erythromycin or fusidic acid). Maybe the interacting

medicine could be swapped to an alternative that doesn't interact if appropriate. Think about where the patient is if any extra monitoring is required and who will do this. If you need a refresher, visit the Interactions topic.

- Does the patient have any confirmed allergies?
  Take care to distinguish between allergy and intolerance. What is the nature and severity of the allergy?

The Infection

- Check whether the indication for the antibiotic is for treatment of an infection or prophylaxis.
- Is the antibiotic being used empirically ('blind') or is treatment being guided by sensitivities?
  Check your local guidelines. If the antibiotic choice seems a little unusual, establish who has recommended this.
- Check the site and severity of infection.
  Does the antibiotic reach adequate levels at the site of infection? The severity of the infection will guide the route of the antibiotic.
- Are there risk factors for resistance?
  Has the patient been in a hospital recently or have they been admitted from a care home? Know how to find out whether a particular organism demonstrates antibiotic resistance locally.
- Ensure that there is a plan to monitor the patient's response to treatment.
  Response may be monitored subjectively - how the patient tells you they feel if they are able - or objectively through lab tests etc.

The Antibiotic

- What is the spectrum of the antibiotic?
  An obvious point perhaps, but make sure it covers the necessary organism(s).
- Are the dose and route of the antibiotic appropriate?
- How is the antibiotic administered? Is there an appropriate formulation?
  If treatment is oral, can the patient swallow tablets or capsules? Maybe a liquid will be required – how does this taste, especially if the patient is a child. If the antibiotic is to be given intravenously, ensure there are clear instructions on how it should be prepared and administered.
- What monitoring is required?
  Is TDM indicated? What are the significant side effects?
- When was the antibiotic started? Is there a review date?
  What is the usual recommended duration of treatment? If the antibiotics are being given IV, there should be a plan to switch to oral treatment.

Treatment of common infections

In practice, you will encounter many different types of bacterial infection, but some are more common than others. The following pages focus on the specific infections that you are most likely to see on a general medical ward. Throughout we will stress the importance of checking your local guidelines, so make sure you know how to find them.

Chronic obstructive pulmonary disease (COPD) (acute infective exacerbation)

Case definition

An acute infective exacerbation of COPD presents as a rapid, sustained worsening of the patient's symptoms that is beyond their normal day-to-day variations. Common symptoms include worsening breathlessness, cough, increased sputum production and change in sputum colour.

More than one third of COPD exacerbations that result in admission are not related to infection.

Exclusions: severe sepsis, immunocompromised, pneumonia or predominant bronchiectasis.

Typical pathogen profile

Gram positive *Streptococcus pneumoniae* (10-15%)	**Gram negative** *Haemophilus influenzae* (20-30%) *Moraxella catarrhalis* (10-15%) *Pseudomonas aeruginosa* (5-10%)
Anaerobes N/A	**Atypicals** *Chlamydophila pneumoniae* (3-5%) *Mycoplasma pneumoniae* (1-2%)

Microbiology investigations

Blood and sputum samples may be required.

- If sputum is purulent, send sample for microscopy, culture and sensitivities (M,C&S).
- Consider nasopharyngeal aspirate or combined nose and throat swap for virus detection if the patient's presentation suggests a viral infection
- Take blood cultures if patient pyrexial. If patient afebrile but has signs of severe sepsis, then consider blood cultures before starting intravenous antibiotics.

Evidence of infection

Sputum purulence may be used to guide treatment.

- Patients reporting a change in sputum colour from uncoloured to yellow-green over the past 72 hours should receive antibiotics.
- Uncomplicated* patients who report no changes in sputum colour over the past 72 hours may be managed without antibiotics.
  (*None of: pneumonia/ immunocompromised/ on critical care/ non-invasive ventilation/ heart failure/ neoplasm/ recent hospitalisation).

Risk of antibiotic resistance

P. aeruginosa is a less common infecting pathogen but is resistant to many antibiotics. Risk factors for colonisation or infection with *P. aeruginosa* include:

- Bronchiectasis
- *Pseudomonas* isolated from sputum or bronchial lavage previously
- Systemic steroid treatment

Severity assessment

The severity of the infection may be assessed using the Systemic Inflammatory Response Syndrome (SIRS) criteria. SIRS present if 2 or more of the following are met:

Temperature > 38.3^{0}C or < 36.0^{0}C	Heart rate > 90 beats per minute
Respiratory rate > 20 breaths per minute	White blood cell count >12 or <4 x 10^9/litre

Choosing an antibiotic

Please consult your local antibiotics guidelines for the preferred choice of agents. Here is an example protocol from University Hospital Southampton, for you to look at, but it is not intended to replace your local guidelines.

Follow up

The clinical diagnosis and continuing need for antibiotics should be reviewed regularly and the decision clearly documented.

Consider escalation of therapy:
• There is any new emerging evidence of severe sepsis
• There is no improvement in pyrexia after at least 24 hours of antibiotics

Remember that:
• C-reactive protein (CRP) may not begin to fall until 24-48 hours of antibiotic therapy
• White blood cell count can rise when oral steroids are started

Duration guide

There is considerable variation between different sources so check your local guidelines. This is an example protocol:

Hospitalised, uncomplicated patients: 5 days (if on azithromycin 3 days)
Hospitalised, complicated patients: 5-7 days (longer courses may be required for recurrent infections)

Further reading

NICE Chronic obstructive pulmonary disease in over 16s: diagnosis and management 2010.

Community acquired pneumonia (CAP)

Case definition

Diagnosis of CAP is based upon symptoms and signs of an acute lower respiratory tract infection and can be confirmed radiologically. It presents as new or worsening shadowing on the chest X-ray or CT of a patient with clinical features which usually include cough, chest pain, fever (> 38.0°C) and difficulty breathing (although these clinical features may be absent such as in older patients).

Exclusions: septic shock, immunocompromised, hospital acquired pneumonia, bronchiectasis, pneumonia expected to be a terminal event.

Typical pathogen profile

Gram positive *Streptococcus pneumoniae* (39%) *Staphylococcus aureus (1.9%)*	**Gram negative** *Haemophilus influenzae* (5.2%) *Moraxella catarrhalis* (1.9%) *Gram negative bacilli* (1.9%)
Anaerobes Consider in nursing home residents	**Atypicals** *Legionella spp.* (3.6%) *Chlamydophila pneumoniae* (13.1%) *Mycoplasma pneumoniae* (10.8%) *Chlamydophila psittaci* (2.6%) *Coxiella burnetii* (1.2%)
Viruses including influenza 13%	

Microbiology investigations

Take blood and sputum samples
Consider combined nose and throat swab for influenza and other respiratory virus detection.
Consider pneumococcal and legionella urinary antigen tests

Evidence of infection

Antibiotic treatment is guided by changes in the patient's vital signs and the presence of respiratory symptoms.

- If one respiratory complaint is present (including cough, chest pain or shortness of breath) **AND** there is at least one abnormality of the vital signs (temperature > 38.0°C, pulse > 100 beats per minute, respiratory rate > 20 breaths per minute, or pulse oximetry < 95% on room air), order X-ray and start antibiotics.
- If vital signs are normal, order X-ray and withhold antibiotics. If X-ray result is normal do not start antibiotics and monitor patient.

Risk of antibiotic resistance

Resistance to commonly used antibiotics for CAP is a major consideration when choosing empirical therapy. There are a range of risk factors:

- Recent travel to Europe or USA linked to a risk of penicillin-resistant *Pneumococcus*
- Nursing home resident
- Alcohol dependence /homelessness – risk of Gram negative enteric bacilli and *Klebsiella*
- Bronchiectasis/interstitial lung disease/enteral tube feeding - risk of *Pseudomonas*
- If recent hospital inpatient, review previous M,C&S to guide therapy

Severity assessment

There are several severity scoring systems available.

Severity criteria **C**onfusion/disorientation **U**rea > 7 mmol/litre **R**espiratory rate ≥ 30 breaths per minute **B**P systolic < 90 mmHg O_2 sats on room air < 86% Multilobar infiltrates	**High severity** ≥ 3 criteria consider referral to critical care
	Moderate severity 0-2 criteria treat on ward as moderate severity CAP

Choosing an antibiotic

Please consult your local antibiotics guidelines for the preferred choice of agents. Here is an example protocol from University Hospital Southampton for you to look at, but it is not intended to replace your local guidelines.

Follow up

There are a number of methods to assess the clinical stability of patients with pneumonia. One of these is 'Halm's stability criteria' and progress is assessed according to how many of the criteria the patient meets. These may help to inform whether a patient can be switched from intravenous to oral antibiotics, for example.

The criteria are:

1. Temperature ≤ 37.8^0C
2. Heart rate ≤ 100 beats per minute
3. Respiratory rate ≤ 24 breaths per minute
4. Systolic blood pressure ≥ 90 mmHg
5. Oxygen sats ≥ 90%
6. Normal mental status
7. Normal oral intake

Duration guide

There is considerable variation between different sources so check your local guidelines. This is an example protocol:

- Hospitalised, moderate severity: 5 days (if temperature ≤ 37.8^oC for 48 hours)

- Hospitalised, high severity: 5-7 days (stop at 5 days if temperature ≤ 37.8°C for 48 hours **AND** no more than one sign of instability (Halm's criteria 1-5) **AND** patient not immunosuppressed, not on intensive care, no chest drain required and no Legionella / Gram negative enteric bacilli /*Pseudomonas* /*S.aureus* from M,C&S results).

Further reading

NICE Pneumonia in adults: diagnosis and management 2014.

Catheter-associated urinary tract infections (CAUTI)

Case definition

UTI is a common hospital-acquired infection in the UK, with the majority associated with catheter use. The catheter provides a focus for bacterial biofilm formation. The longer the catheter is in place, the higher the risk of developing bacteriuria (bacteria in the urine). This may be asymptomatic, or lead to symptomatic UTI. Signs and symptoms such as fever, new onset confusion and suprapubic pain are common in catheterised patients without symptomatic UTI making diagnosis difficult.

However some experts have suggested that symptomatic CAUTI might be defined as;

- Culture growth of $\geq 10^3$ colony forming units (cfu)/mL of uropathogenic bacteria in the presence of symptoms or signs compatible with UTI without other identifiable source in a patient with indwelling urethral, indwelling suprapubic, or intermittent catheterisation.

- Compatible symptoms include fever, costovertebral angle tenderness, and otherwise unexplained systemic symptoms such as altered mental status, hypotension, or evidence of a systemic inflammatory response syndrome.

Exclusions: pregnancy

Risk factors

The duration of catheterisation is strongly correlated with the risk of developing an infection. Other risk factors include;

- Female gender
- Older age
- Diabetes mellitus
- Bacterial colonisation of the drainage bag
- Errors in catheter care (e.g. non-sterile technique)

Typical pathogen profile

Gram positive *Enterococcus spp.* *Staphylococcus aureus* (rare)	**Gram negative** *Escherichia coli* (most common) *Proteus spp.* *Enterobacter spp.* *Pseudomonas aeruginosa* *Klebsiella spp.*
Yeast Candida albicans	

Most CAUTIs are derived from the patient's own colonic flora.

Some of these organisms almost never cause UTI in the absence of an indwelling catheter, but the catheter offers easy access to the bladder. An example is *Candida* spp. Candiduria is a common finding in patients with indwelling bladder catheters, particularly those with diabetes or taking antimicrobials. However, most patients are asymptomatic, and progression to candidaemia is uncommon.

Microbiology investigations

- Only culture urine if patient has clinical sepsis, not because the appearance or smell of the urine suggests bacteriuria is present.
- Culture urine before starting antibiotics.
- There is no value in urine microscopy or dipstick tests.
- Samples may not accurately represent the true pathogen and often contain several bacterial species. Interpret results with caution.

Evidence of infection

- Refer to Case definition above.
- Do not treat asymptomatic bacteriuria (except for some special cases such as prior to some urological procedures).
- The absence of fever does not appear to exclude UTI and hypothermia (< 36^0C) may also indicate infection.
- Pyuria (white blood cells in the urine) or the appearance or smell of the urine, should not be used to diagnose a UTI in a patient with no other compatible signs or symptoms. Pyuria is a frequent finding in all catheterised patients with bacteruria, and absence of pyuria in symptomatic patients suggests a diagnosis other than UTI. Odorous or cloudy urine has not been demonstrated to be indicative of either bacteriuria or UTI.

Risk of antibiotic resistance

- Care home resident
- Hospitalisation for more than 7 days in the last 6 months

Severity assessment

If patient has systemic signs (e.g. fever, rigors, chills, vomiting, confusion, hypotension) consider pyelonephritis, urosepsis.

Choosing an antibiotic

Ideally base antibiotic selection on culture results. If prompt treatment is required, choice should be based upon the severity of the patient's infection, the results of any past cultures, prior use of antibiotics, local resistance, and allergy status. Empirical therapy should provide coverage against gram negative bacilli and be guided by local policy. For low risk patients in whom antibiotic resistance is unlikely, a 3rd generation cephalosporin, oral or IV fluoroquinolone or oral nitrofurantoin may be appropriate. For high risk patients, or if antibiotic resistance is suspected then a broad spectrum antibiotic may be required.

Consider changing or removing the catheter before starting antibiotics in patients with symptomatic CAUTI.

Follow up

Check response to treatment after an appropriate interval, for example 24-48 hours, depending upon clinical judgement and review urine culture results. Once antibiotic therapy has been administered the resolution of symptoms and not the absence of bacteriuria indicates that the infection has been treated.

Duration guide

Advice on the optimal duration of antibiotics is conflicting. Follow your local guidelines if you have them. In their absence, depending upon the clinical response, the pathogen and antibiotic used, the IDSA recommend 7 days in patients with prompt resolution of symptoms, or 10-14 days when there is a delayed response. A shorter regime may be appropriate for women aged ≤ 65 years without upper urinary tract symptoms after the catheter has been removed.

Lower urinary tract infections

Case definition

UTI is a common indication for empirical antimicrobial treatment in primary and secondary care but criteria for diagnosis vary widely. In primary care Public Health England recommend the following diagnostic criteria:

• Women with severe or ≥ 3 symptoms of UTI including dysuria, frequency, suprapubic tenderness, urgency, polyuria, haematuria.
• Women with mild or ≤ 2 of the above symptoms and urine dipstick indicates infection.
• Men with dysuria, frequency, urgency, nocturia, suprapubic discomfort/tenderness, haematuria or passing offensive-smelling or cloudy urine.
• Exclusions: children, pregnant women, or with indwelling catheters

Typical pathogen profile

Gram positive	**Gram negative**
Staphylococcus saprophyticus (5-10%) Less commonly: *Enterococcus spp.* *Staphylococcus aureus*	*Escherichia coli* (70-95%) *Proteus mirabilis* (more rare) Less commonly: *Proteus vulgaris* *Enterobacter spp.* *Citrobacter spp.* *Serratia marcescens* *Acinetobacter spp.* *Pseudomonas spp.* *Klebsiella spp.*
Yeast Candida albicans – may be seen in patients with an indwelling, urinary catheter or men who are immunocompromised.	

Microbiology investigations

In primary care urine M,C&S are not routinely recommended for women with suspected uncomplicated UTIs because the results are not available for immediate decision-making and, by the time they are available, most women's symptoms will be resolving. Cultures should be obtained for men with suspected UTI.

- **Do not routinely culture** women < 65 years
- **Only culture** men and women > 65 years with positive dipsticks if ≥ 2 symptoms of infection (especially dysuria, fever > 38.0^{o}C or new incontinence)
- **Culture** - women with mild or ≤ 2 symptoms of UTI but with a urine dipstick positive for leucocytes and negative for nitrites, suspected UTI in men, suspected pyelonephritis,

failed antibiotic treatment or persistent symptoms, patients with renal impairment, recurrent UTI, abnormalities of the genitourinary tract

Evidence of infection

The presence of bacteria in the urine (bacteriuria) in a patient without other signs or symptoms is rarely an indication for antibiotic treatment. The prevalence of asymptomatic bacteriuria increases with increasing age in patients > 65 years old, but treatment may cause more harm (such as side effects of the medicine) than benefit. The decision to use antibiotics is primarily based upon the patient's signs and symptoms.

Start antibiotics in;

- Women with severe or ≥ 3 symptoms of UTI and no vaginal discharge or irritation
- Women with mild or ≤ 2 symptoms of UTI and urine dipstick indicates infection
- Men with symptoms suggestive of UTI

Do not start antibiotics in;

- Women with mild or ≤ 2 symptoms of UTI and urine is not cloudy, or urine dipstick does not indicate infection
- Men and women >65 years with asymptomatic bacteriuria

Risk of antibiotic resistance

If resistance is suspected then a urine sample should be obtained and sent for culture and susceptibilities.

- Recurrent UTI (2 in 6 months, three or more in 12 months)
- Nursing home resident
- Hospitalisation for more than 7 days in the last 6 months
- Unresolving urinary symptoms
- Recent travel to a country with increased antimicrobial resistance
- Previous UTI resistance to trimethoprim, cephalosporins or quinolones
- Renal impairment

Severity assessment

Be alert for the signs and symptoms of pyelonephritis (fever, loin pain) or sepsis (nausea, vomiting, confusion, tachypnoea, tachycardia, hypotension). Consider hospital admission.

Choosing an antibiotic

Consult your local antibiotics primary care guidelines for the preferred choice of agents. Click here to read the Public Health England (PHE) antibiotic guidelines for UTI (and other conditions) in primary care.

Follow up

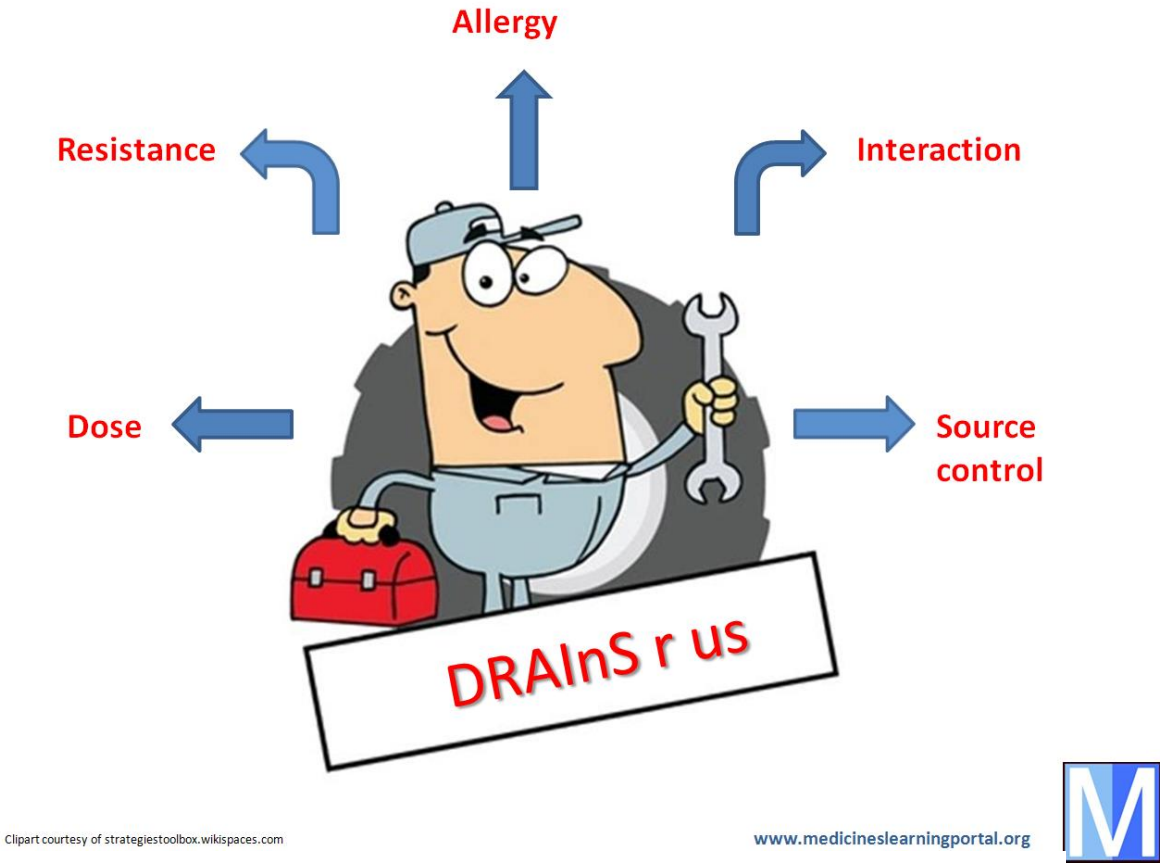
For women with uncomplicated lower UTI follow up is not routinely required. However women should be advised to seek medical attention if they develop loin pain or fever, or do not respond to first line antibiotics. For men follow up should be arranged, for example after 48 hours, depending on clinical judgement to check response to antibiotic treatment and review urine culture results.

Duration guide

- Women 3 days
- Men 7 days
- Fosfomycin – 3 gram single dose (PHE recommend a repeat [unlicensed] dose 3 days later in men)

When treatment fails

There are a number of reasons why a patient may appear not to be responding to antimicrobial treatment. The acronym **DRAInS** can help you remember some of the most common causes.



Dose – *is the dose adequate? Have any doses been missed? Is the dosing interval too long? Can the patient's plasma levels be checked to ensure the antibiotic is reaching therapeutic levels?*

Resistance – *does the antibiotic's spectrum usually cover the causative organism? Is the patient at risk of antibiotic resistance (e.g. MRSA, ESBL, E.coli, C.difficile, VRE)?*

Allergy – *could the patient's fever be due to an adverse reaction to the drug rather than the infection? Hypersensitivity is the most common cause of drug fever and usually appears within several days to weeks after an antibiotic has been started.*

Interaction – *could a drug interaction be responsible for an antibiotic not working (e.g. antacids reducing oral tetracycline bioavailability and efficacy)?*

Source control – *has any surgical intervention been adequate, such as for an infected wound? Have intravenous lines or urinary catheters been replaced or removed?*

Other considerations not covered by DRAInS include the following. We'll leave you to make up your own acronym!

Route – *is oral treatment being adequately absorbed? Is there anything to suggest the patient's gastrointestinal tract may not be functioning properly? Is the correct route being used (e.g. intravenous vancomycin is ineffective against C. difficile infection)?*

Penetration – *is the antibiotic penetrating the target site? Is the infection site poorly perfused (such as an ischaemic toe)?*

Compliance – *less of a problem in hospital but a consideration in primary care. Barriers to compliance include issues with formulation (e.g. taste of liquids, size of solid dose forms), and regimes being incompatible with a patient's daily routine (e.g. a four times daily regime in a school-age child).*

Antagonism – *is one antibiotic diminishing the effect of another (e.g. co-adminstration of a bacteriostatic agent with one that is a bactericidal such as tetracyclines and beta lactams)?*

Antibiotics: Learning exercises

Antibiotics quizzes

There is a quiz to help reinforce your learning about antibiotics here. You can look things up if you need to. Please select 'practice' as your game mode then click Start Game. There is also a 'click and drag' quiz here.

Example clinical problems: Antibiotics

To help you think about the process of clinical problem-solving, we've provided three real clinical problems for you. Click on the link to download the Word document to write in, or you might just want to look at the scenarios and discuss them with your tutor or a colleague. For each situation, please consider:

- **What background information would you need to gather if you were presented with this scenario in your practice?**
- **What sources of information would you use?**

There's no need to research a full answer unless your tutor instructs you to, but you could make notes on these scenarios and record them as a CPD exercise if you wish. Once you've had thinking time, you can see some suggestions we've made in response to each scenario here.

Additional learning

If you need a basic refresher on antimicrobial resistance, then try this e-learning programme developed by Health Education England in collaboration with Public Health England and NHS England.

Do an enquiry in a Medicines Information (MI) centre

If you have access to the MiCAL training package (subscription required) you may like to undertake question numbers 1 and 10 in its database of example MI enquiries, which involve scenarios where an antibiotic-related decision is required.

Information sources

As we have seen you could be faced with a broad range of problems about antibiotics and you may find it helpful to revisit the Information sources page in other topics such as Interactions, Drug Handling, Liver and Renal.

However the BNF, BNF for Children and SPCs are good places to start for most straightforward antibiotic questions. The BNF and BNF for Children include prophylaxis and treatment guidelines for a range of infections, dosing information and advice on therapeutic drug monitoring. SPCs may give you more detailed guidance in managing patients with special considerations such as those with renal or liver disease.

Your Trust will have local antibiotics policies. Be familiar with the basic content of these documents and know how to find them.

Subscription resources such as Martindale and the AHFS Drug Information, and Lexicomp, Micromedex or UpToDate can be very useful places to look for information on antibiotics.

You may have access to some more specialist resources such as The Sanford Guide, Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, or Kucers' The Use of Antibiotics.

NICE Evidence search may be helpful – you can filter the information to your area of interest. It covers guidance from the Royal Colleges, NICE, SIGN and the Clinical Knowledge Summaries which can be useful for infections more commonly encountered in primary care.

Don't forget to use your experts – your Trust may have a specialist anti-infectives pharmacist or you could speak to the hospital microbiology team.

Next steps in learning ...

CPPE have a range of resources to support you including CPPE Antibacterial resistance – a global threat to public health: the role of the pharmacy team. The aim of this learning programme is to update your knowledge about the issues of antimicrobial resistance and healthcare-associated infections (HCAIs) so that you can contribute to reducing their impact.

Health Education England have produced a comprehensive guide to training resources on antimicrobial resistance. It includes antimicrobial prescribing and stewardship, infection prevention and control, and treating specific infections. Many of the packages sit on the e-Learning for Healthcare platform which may be available to you through OpenAthens. Other material requires a subscription such as that produced by the Royal Pharmaceutical Society. A good starting point for pre-registration pharmacists is a 3 part series called Prudent Use of Antibiotics.