Antibiotic prescribing

Introduction

Antibiotics are commonly prescribed by junior doctors, sometimes based upon previous discussions but often when the rest of the team are unavailable, and sometimes under pressure from other members of the health-care team. Complete coverage of all issues pertinent to the prescribing of antibiotics is outside the scope of this article. The intention is to focus on clinical areas of key importance in terms of frequency of occurrence in the work of a junior doctor.

Cellulitis

Clinical features

Cellulitis is an acute spreading infection of the epidermis and dermis, characterized by erythema and oedema of the skin. The area is painful with poorly defined margins. There is usually a history of skin trauma, be that a surgical wound, ulcer, abrasion or cut which allows entry of pathogens.

Cellulitis is a serious disease because of the risk of subsequent bacteraemia, which occurs in 30% of cases. The differential diagnosis includes deep vein thrombosis and the very rare but serious necrotizing fasciitis.

The most common pathogens are bacteria found on the skin, e.g. beta-haemolytic streptococci or staphylococci. Anaerobic infection may also occur, particularly in diabetics or with peripheral vascular disease.

Antibiotics of choice would be those which cover both *Streptococcus pyogenes* and *Staphylococcus aureus* since these may be clinically indistinguishable. In a non-penicillin-allergic patient the drug of choice is flucloxacillin.

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Treatment

Penicillins

Mode of action: Penicillins are bactericidal, inhibiting cell wall synthesis by preventing cross linking of peptidoglycans.

Dose: If no systemic symptoms are present, treatment may be given orally at doses up to 1 g four times a day at least 30 minutes before food to reduce inactivation by gastric acid. More severe infections should be treated with intravenous flucloxacillin, again at 1 g four times a day. The duration of intravenous therapy may vary depending on the severity of the cellulitis, although it is usually needed for at least the first 72 hours. The total duration of therapy (intravenous plus oral) is 7–14 days. Criteria for switching to oral therapy are that the swelling, pain and erythema have reduced and that the inflammatory markers are decreasing. If the patient's condition deteriorates, review the appropriateness of the antibiotics with a microbiology colleague.

Clindamycin

For patients with non-life-threatening penicillin allergy, e.g. rash, clindamycin can be given.

Mode of action: Clindamycin works by binding to the bacterial ribosome and inhibiting protein synthesis. It is predominantly bacteriostatic.

Dose and monitoring: Clindamycin can be given orally at a dose of 300–600 mg four times a day. It is very well absorbed (approximately 90%), but it is commonly associated with colitis and therefore it is not used as a first-line treatment. Should diarrhoea occur with clindamycin it should be stopped promptly.

Vancomycin

If there is a life-threatening penicillin allergy present (anaphylaxis, urticarial rash) all beta-lactam antibiotics must be avoided, and vancomycin would be the intravenous therapy of choice. Vancomycin is also the agent of choice in patients with meticillin-resistant *Staph. aureus* (MRSA) cellulitis.

Mode of action: Vancomycin is a glycopeptide antibiotic which inhibits bacterial cell wall synthesis by preventing peptidoglycan synthesis by steric hindrance. It is principally bacteriostatic.

Dose and monitoring: Vancomycin is only effective intravenously and is renally excreted. Blood levels must be monitored to maintain therapeutic concentrations, avoid toxic concentrations and reduce length of stay in hospital. A usual starting dose for an adult is 1 g twice daily, but elderly patients will need less because they have reduced renal function. A suggested starting dose in this case would be 1g once daily.

Vancomycin takes between 24 and 48 hours to reach steady state (a half life of 6–13 hours is reported) and in patients with normal renal function a trough level (lowest level vancomycin should drop to) should be taken immediately before the third or fifth dose. The trough level should be between 5 and 15 mg/litre. Peak levels are not generally required since a trough level in the required range followed by a 1 g dose will not lead to toxic peaks. It is not necessary to wait for the results of the level before giving the next dose unless renal function is abnormal or previous levels have been high. If renal function is fluctuating levels may need to be checked daily and a dose given when the level falls to the required trough.

In cases where anaerobic infection may also occur (associated ulceration, peripheral vascular disease or diabetes) intravenous therapy of a cephalosporin plus metronidazole would be recommended, followed by oral therapy of co-amoxiclav 625 mg three times daily.

Clostridium difficile-associated diarrhoea

Clinical features

Clostridium difficile-associated diarrhoea is not a new problem in UK hospitals but with its increasing frequency and mortality there is intense debate over how best to treat it. Prevention as always is better than cure, and risk factors include the following:

- Age > 70 years
- Recent hospital admission (within the previous month)
- Recent (within the previous 6 weeks) antibacterials for any infection

- Co-prescription of proton pump inhibitors with broad spectrum antibiotics
- Recent chemotherapy.

Considerations for prevention therefore include reducing use of cephalosporin, erythromycin and quinolone antibiotics where possible (quinolones are now known to be a major risk factor for *C. difficile*-associated diarrhoea), and following hospital guidelines for antibiotic use, as well as reviewing the need for proton pump inhibitors especially if broad spectrum antibacterials are also prescribed.

Treatment

Metronidazole and vancomycin

Metronidazole is thought to prevent bacterial replication by interfering with DNA synthesis. It is almost completely absorbed following oral dosing. Metronidazole at a dose of 400 mg three times a day for 14 days should be used as first-line treatment for *C. difficile*-associated diarrhoea where there is no concurrent systemic inflammatory response. At the same time any provocative antibacterials should be discontinued. Metronidazole is of similar efficacy to oral vancomycin, and it is less expensive. About 20% of patients will get an 'antabuse' reaction if they drink alcohol within 24 hours of taking metronidazole. Taste, and therefore the patient's adherence, is better if taken with food.

In severe cases, should the oral route not be available, metronidazole may be given intravenously (500 mg three times a day) with or without oral vancomycin.

Oral vancomycin may be used in patients who have a systemic inflammatory response with no other explanation and who have failed to respond to metronidazole after 48–72 hours of treatment. The recommended dose is 125 mg four times daily. Expert advice should be sought in these cases since this may indicate infection with a more virulent strain of *C. difficile*. Note that intravenous vancomycin is not effective for *C. difficile*-associated diarrhoea.

Urinary tract infection

Clinical features

Urinary tract infections are one of the most commonly occurring bacterial infections in medicine, with 20% of women experiencing a urinary tract infection at some point in their lives. The frequency in men is lower until the age of about 50 years when the incidence rates are similar.

Common causes of urinary tract infection are usually bowel flora, most commonly *Escherichia coli*, but also Klebsiella, Proteus, Pseudomonas and Enterococcus.

Uncomplicated urinary tract infections

Lower urinary tract infections (cystitis) generally lack systemic symptoms, and are most common in women. *E. coli* is the most common cause and antibiotics chosen are targeted at this pathogen.

Short courses of antibiotics are appropriate in this case, and a 3-day course of nitrofurantoin 50 mg four times a day, or trimethoprim 200 mg twice daily is sufficient. Nitrofurantoin is readily absorbed and eliminated and antibacterial concentrations are not reached in the blood and tissue. It must be excreted into the urine to achieve antibacterial concentrations and is ineffective in patients with renal impairment. Trimethoprim, on the other hand, is almost completely absorbed and widely distributed. A quinolone (noting the risk of *C. difficile*-associated diarrhoea) may be appropriate if resistance patterns demand but should not be used generally for empirical treatment of urinary tract infection.

Complicated urinary tract infections

Patients presenting with pyelonephritis (upper urinary tract infection) warrant more aggressive treatment, since upper urinary tract infections may be accompanied by bacteraemia and are therefore potentially life threatening. A suitable choice for oral therapy would be co-amoxiclav, or ciprofloxacin if penicillin allergy is present. Treatment should continue for 14 days with co-amoxiclav, although 7 days treatment is sufficient with ciprofloxacin. If the patient is systemically unwell (tachypnoea, tachycardia, hypotension), intravenous therapy is warranted. A suitable regimen would be co-amoxiclav 1.2 g three times daily with or without gentamicin at a single dose of 5 mg/kg. Intravenous antibiotics can usually be changed to oral within 48 hours.

In males, urine infections are usually considered to be complicated as they generally occur in the presence of structural or functional abnormalities. Urine culture should be obtained if possible. Antibiotics of choice are quinolones or co-amoxiclav. Treatment should continue for 14 days with co-amoxiclav, although 7 days' treatment is sufficient with ciprofloxacin.

Pneumonia

Clinical features

Pneumonia occurs where acute respiratory infection is associated with shadowing on chest X-ray. Pneumonia can be divided into two groups according to the location where the infection was contracted: community-acquired pneumonia and hospital-acquired pneumonia. Note that pneumonias developing within the first 48 hours of hospital admission are also mostly community acquired.

Hospital-acquired pneumonia is associated with severity of illness, longer duration of hospital stay, and prior antibiotic therapy. Bacterial pneumonia is most commonly caused by *Streptococcus pneumonia* and *Mycoplasma pneumoniae*, although for hospital-acquired pneumonia enteric organisms may also be involved, e.g. Klebsiella or *E. coli*, or the non-enteric bacillus Pseudomonas.

Empirical therapy should be aimed at the most common pathogens, and the severity of the infection, for which there are scoring criteria available, e.g. CURB-65 (*Figure 1*). In all cases, antibiotics which reach high concentrations in the respiratory secretions are required, and the severity of the illness will dictate the route of administration.

Community-acquired pneumonia

For mild cases of community-acquired pneumonia oral amoxicillin at a dose of 500 mg three times a day for a 7-day course will be sufficient, and for moderate infection amoxicillin 500 mg–1 g three times daily with erythromycin 500 mg four time daily or clarithromycin 500 mg twice daily may be added. For severe community-acquired pneumonia intravenous antibiotics are required, and the choice will be guided by local policy. A suitable combination would be co-amoxiclav 1.2 g three times daily plus a macrolide, or a cephalosporin (cefuroxime, ceftriaxone or cefotaxime) plus a macrolide in the event of penicillin allergy.

Figure 1. CURB-65 scoring system for pneumonia. From British Thoracic Society Standards of Care Committee (2001).

CURB-65 is a system for scoring the severity of community-acquired pneumonia, adopted by the British Thoracic Society. There is some evidence that this score is also valid for other systemic infections.

C = confusion (new onset)

U = uraemia (urea >7 mmol/litre)

R = respiratory rate (≥30 breaths per minute)

B = blood pressure (systolic <90 mmHg or diastolic ≤60 mmHg)

65 = age ≥65 years

Score one point for the presence of each factor. The mortality for each score is as follows:

0	0.7%
1	3.2%
2	13.0%
3	17.0%
4	41.5%
5	57.0%

For treatment purposes 0–1 = mild, 2 = moderate, ≥3 = severe

Hospital-acquired pneumonia

Severe hospital-acquired pneumonia should be treated similarly, but third-line antibiotics may be required in the event of failure to respond to this regimen, previous exposure to cephalosporins in the last month, or with documented infection with Pseudomonas. Any uncertainty over treatment should be discussed with the microbiology department.

A switch from intravenous medication to oral therapy should be made as soon as clinically appropriate. If intravenous cephalosporins have been used, a broad spectrum follow-on therapy should be used, for example co-amoxiclav 625 mg three times daily. Oral cephalosporins are not recommended as follow-on therapy. Most patients can be treated with a total of 7 days therapy, or 10 days in patients with severe infection. **BJHM**

Conflict of interest: Dr Shakur is a council member for the Royal Society of Medicine's Research and Pharmaceutical section.

British Thoracic Society Standards of Care Committee (2001) BTS Guidelines for the Management of Community Acquired Pneumonia in Adults. *Thorax* **56** Suppl 4: IV1–64

KEY POINTS

- Always record time and date of sampling on laboratory request forms for drug levels. Sample in the morning if possible to enable results to be back the same day.
- Do not use intravenous vancomycin to treat *Clostridium difficile*-associated diarrhoea.
- Do not wait for vancomycin levels to come back before administering the next dose unless you are concerned about fluctuating or poor renal function.
- Familiarize yourself with your hospital's antibiotic policy. This will be in place to reduce the incidence of resistance and hospital-acquired infection and will take local resistance patterns into account.
- Monitor the duration of antibiotic course. In simple infections (e.g. acute cystitis) specify the full course on the prescription chart so the course is not unnecessarily prolonged.
- Review intravenous antibiotics regularly to avoid the risk associated with intravenous cannulae.