Fiji Antibiotic Guidelines

4th edition

Ministry of Health and Medical Services, Government of Fiji
November 2019

Foreword

Antibiotic Guidelines are an essential strategy in antimicrobial stewardship; the aim of antimicrobial stewardship is to improve patient outcomes and reduce adverse consequences associated with antimicrobial use, including antimicrobial resistance, toxicity and unnecessary costs.

Fiji has prioritised antimicrobial resistance (AMR) and in 2015 the Cabinet has endorsed the National AMR Action plan together with the formation of a multisectoral National AMR Committee.

The plan includes five key strategies to combat, or minimize the impact of, AMR:

- Improve awareness understanding of AMR through effective communication, education and training.
- Strengthen nationally coordinated surveillance systems.
- Reduce the incidence of antimicrobial resistance events through improved infection prevention and control, sanitation and hygiene, and wellness measures.
- Optimise the use of antimicrobial medicines in human and animal health.
- Establish and ensure governance, sustainable investment and actions to combat AMR.

The *Fiji Antibiotic Guidelines*, 4th edition 2019 have been extensively revised and expanded from the previous edition to include many more topics and information to guide prescribers in the use of antibiotics. Their development has included the input from a multi-disciplinary and multi-specialty team of over 40 individuals.

These guidelines are equally applicable in the private and public health sectors, in hospitals, health centres and GP clinics and all visiting medical teams. They are intended to support clinicians to make wise decisions about when to prescribe antibiotics, which antibiotics to prescribe at what dose and duration according to the best available international evidence relevant to the Fiji setting.

Apolosi Vosanibola
Acting chair, Fiji National Medicines and Therapeutics Committee

Introduction

Antimicrobial Resistance (AMR) is now a widely recognised public health concern 'compromising our ability to treat infectious diseases, as well as undermining many other advances in health and medicine[1].' Optimising the use of antimicrobials is a key priority of the global strategy to combat antimicrobial resistance.[2] Ensuring appropriate prescribing to ensure the best patient outcomes remains the sole purpose of this guideline.

The previous editions only had Essential Medicines List (EML) antimicrobials in the guideline - and the EML allows for the vast majority of this guideline's advice. However, this 4th edition aims to serve prescribers both in the public and private sectors. Local experts involved in the revision of the guideline have come from both private and and public sectors. For each indication the choice of antimicrobials are wider and allow the prescriber more options. The choices have undergone robust discussions and scrutiny to provide the best suitable option for better patient outcome.

The content has gone through multiple review by both local and international experts. Great effort has been dedicated to ensure that the recommendations align with the latest evidence which is applicable to Fiji's setting. This edition aims to ensure that the latest guideline is in keeping with other current existing guidelines.

The guideline classifies antimicrobials as either unrestricted, restricted or highly restricted where restricted or highly restricted antimicrobials are generally meant for use in a hospital setting. Further details on the classification can be found on page 12 of the guideline as well as the anti-infective section of the EML.

The synthesis of this guideline has made for a considered document that is intended for every prescriber in Fiji, be they urban or rural, public or private, from a solo medical officer in a remote setting to a specialist in a tertiary care facility.

Dr Ravi Naidu
Chair, Fiji Antibiotic Guidelines review committee

[1] https://www.who.int/antimicrobial-resistance/global-action-plan/en/
[2] http://apps.who.int/medicinedocs/documents/s23413en/s23413en.pdf

Acknowledgements

This fourth edition of the *Fiji Antibiotic Guidelines* is the culmination of the hard work of many individuals from the Ministry of Health and Medical Services (MHMS), the Fiji private health sector and Fiji National University (FNU).

The previous edition has been extensively revised, updated and expanded and much of the content is based on the Australian *Therapeutic Guidelines: Antibiotic, version 16*, 2019. We gratefully acknowledge Therapeutic Guidelines Limited (TGL) for their permission to use and adapt TGL content for use in Fiji.

Thank you also to the World Health Organization (WHO) for financial assistance in the review of these guidelines.

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Medicines recommended in these guidelines which are not currently included in the *Fiji Essential Medicines List* (EML) are denoted by [Non-EML.]

The medicines included on the Fiji EML may change during the lifetime of these guidelines, refer to the most up to date Fiji EML for more information.

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1. Principles of antimicrobial use

This topic outlines the principles of appropriate antimicrobial use. These principles are summarised in the antimicrobial creed MIND ME (Box 1.1). Appropriate antimicrobial therapy improves patient outcomes, reduces inappropriate and unnecessary antimicrobial use, and reduces adverse consequences, such as antimicrobial resistance and toxicity.

Most viral and bacterial infections are self-limiting—the immune system successfully eliminates many infections. Therefore, antimicrobial therapy is often not required.

The antimicrobial creed (Box 1.1)

M	microbiology guides therapy wherever possible
I	indications should be evidence-based
N	narrowest spectrum therapy required
D	dosage individualised to the patient and appropriate to the site and type of infection
M	minimise duration of therapy
E	ensure oral therapy is used where clinically appropriate

Appropriate antimicrobial prescribing

When prescribing antimicrobials, clearly document all antimicrobial therapy in the patient's medical records and/or medication chart. Documentation should include the indication and the intended duration of therapy before further review or cessation. Provide information about the indication and the intended plan for antimicrobial therapy, and the potential adverse effects, to the patient or the patient's carer.

Antimicrobial use may be prophylactic, empirical or directed against a known organism. In addition to the antimicrobial creed (above), the principles listed below should be closely adhered to.

Prophylactic therapy

Prophylactic use of antimicrobials aims to prevent infection when there is a significant clinical risk of infection developing.

- Restrict prophylactic antimicrobial therapy to indications for which there is evidence of efficacy or when the consequences of infection would be associated with significant morbidity or mortality.
- Base antimicrobial choice on the likely pathogen(s). Dosage should be consistent with guideline recommendations.
- For most surgical prophylaxis indications, use a single perioperative dose sufficient to achieve adequate intraoperative tissue concentration at the time that contamination is most likely. A further dose is only required in specific circumstances. For more information, see chapter 3: prevention of infection: surgical prophylaxis.

Empirical therapy

Empirical use of antimicrobials treats an established infection when the causative organism has not been identified. It is guided by the clinical presentation. Empirical use is warranted in the following circumstances: when treatment must be started before the culture susceptibility results are available; when the clinical situation is not serious enough to warrant taking cultures; or if a sample for cultures cannot be obtained.

- Restrict empirical antimicrobial use to situations where there is a clear indication for therapy and where there is likely to be a clear clinical benefit. Avoid empirical use in minor or self-limiting illness because such use is a significant driver of antimicrobial resistance.
- Before starting therapy, when indicated, obtain specimens to assist diagnosis and the targeting of antimicrobial therapy. Appropriate investigations may include blood cultures (at least two sets of blood samples from septic patients) and cultures from other appropriate sites. Depending on the presentation, other investigations that may assist clinical management include Gram stains, antigen detection tests and/or nucleic acid amplification tests.
- Base antimicrobial choice on the clinical presentation and the expected antimicrobial susceptibility of the most likely and/or important pathogen(s). The narrowest spectrum antimicrobial should be used to treat the likely pathogen(s).

- Use an antimicrobial dosage regimen consistent with guidelines, to ensure efficacy and minimise the risk of resistance and dose-related toxicity.
- Review empirical therapy at 48 to 72 hours.
  - If the diagnosis excludes infection, stop therapy.
  - If no causative organism has been identified, re-evaluate the clinical and microbiological justification for therapy. If ongoing therapy is indicated, consider de-escalation (eg change parenteral therapy to oral therapy, or change a broad-spectrum to a narrower-spectrum antimicrobial), for a defined duration.
  - If a causative organism has been identified, follow the principles of directed therapy.
- Obtain up to date information on local antimicrobial resistance patterns from pathology service providers and modify clinical guidelines as necessary.

Directed therapy

Directed use of antimicrobials

1. treats an established infection where the pathogen has been identified. Critically evaluate the results of cultures and other clinical parameters to distinguish infection from colonisation, or contamination, which does not require antimicrobial treatment. If necessary, obtain advice from an infectious diseases physician or a clinical microbiologist.
2. takes into account antimicrobial susceptibility, direct therapy in accordance with clinical guidelines, using the most effective, least toxic and narrowest spectrum drug available. Preliminary microbiology results may allow targeting of antimicrobial therapy before the definitive results are available; ongoing therapy should be modified once the pathogen and its susceptibilities are known.

- Use a single drug, unless it has been proven that combination therapy is required for efficacy (eg in polymicrobial infection), for synergy (eg in enterococcal endocarditis), or to minimise the development of resistance (eg in tuberculosis or HIV infection).
- Optimise antimicrobial dosage. Ideally, monitor the blood concentration of drugs with a narrow therapeutic index, such as aminoglycosides,

glycopeptides and azole antifungals (currently not available in Fiji).

- Use oral therapy when clinically appropriate.
- Keep the duration of therapy as short as possible. Do not exceed 7 days of therapy without a clear indication (eg endocarditis) or when recommended in these guidelines.

Route of administration

Select the most appropriate route of antimicrobial administration for the clinical presentation. For the majority of presentations, oral antimicrobial therapy is appropriate. Oral therapy avoids the need for a vascular access device and is usually associated with less serious adverse effects than parenteral therapy. It also has the advantage of lower drug and administration costs.

The antimicrobials listed in Box 1.2 can usually be given orally rather than IV, provided they are appropriate for the specific indication and safe oral administration is possible. If the oral route is unsuitable, the enteral route (eg nasogastric [NG]) may be used.

Parenteral (usually IV) administration is required in certain circumstances:

- oral administration is not tolerated or is not possible (eg a patient with difficulty swallowing)
- gastrointestinal absorption is likely to be significantly reduced (eg vomiting, gastrointestinal pathology), or reduced absorption accentuates already poor bioavailability
- an oral antimicrobial with a suitable spectrum of activity is not available
- higher doses than can be easily administered orally are required to achieve an effective concentration at the site of infection (eg endocarditis, meningitis, septic arthritis, osteomyelitis)
- urgent treatment is required for severe and rapidly progressing infection.

Reassess the need for ongoing parenteral therapy daily, and switch to oral therapy once the patient is clinically stable and tolerating oral intake.

Due to the risk of promoting resistance, the use of topical therapy should be restricted to the few recommended indications (eg bacterial conjunctivitis). Generally, antimicrobials used topically should not be from classes of drugs used for systemic therapy.

The following antimicrobials have good oral bioavailability. They can often be given orally rather than intravenously, provided the drug is appropriate for the indication, has adequate tissue penetration for the infection being treated, and the patient can tolerate oral administration.

Examples of antimicrobials for which oral therapy is as effective as parenteral therapy (Box 1.2)

- azithromycin [NB1]
- chloramphenicol
- clindamycin
- ciprofloxacin
- fluconazole
- metronidazole
- trimethoprim+sulfamethoxazole

NB1: Despite lower bioavailability, oral azithromycin is extensively distributed and achieves high intracellular concentrations.

Optimising antimicrobial dosage regimen

The selection of a dosing regimen for antimicrobial therapy should take into account patient factors as well as the pharmacodynamic properties of the drug.

In the following groups of patients with altered pharmacokinetics, dosing may be difficult and expert advice may be required:

- critically ill patients requiring intensive care support (see antibiotic dosing in patients with severe sepsis or septic shock, page 90)
- patients with severe burns
- patients with fluid sequestration into a third space (eg severe pancreatitis, bleeding, ascites)

- pregnant women
- obese patients.

Where available, monitoring of antimicrobial blood concentrations is used to improve efficacy and minimise dose-related toxicity of drugs with a narrow therapeutic index, such as aminoglycosides (eg gentamicin – see appendix 1) and glycopeptides (eg vancomycin – see appendix 2).

Duration of antimicrobial therapy

The duration of therapy for some indications is often not clearly defined from published studies. Prolonged duration of antimicrobial therapy is associated with an increased risk of adverse reactions, as well as an increase in cost. Therefore, the shortest possible duration of therapy should be used and, for the majority of infections, this should not exceed 7 days. There are certain indications, however, that require a longer duration (eg endocarditis, osteomyelitis). For these indications, treatment duration must be individualised. Recommended durations are given throughout these guidelines.

Adverse effects of antimicrobials

Overview

All antimicrobials can cause adverse effects in patients, so the possibility of harm must always be considered when prescribing an antimicrobial. Usually the adverse effects are minor and/or self-limiting; however, some can be more significant. Adverse effects of antimicrobials can be classified as direct or indirect (see Table 1.1).

Classification of the adverse effects of antimicrobials (Table 1.1)

Direct adverse effects	Indirect adverse effects
• hypersensitivity • toxicity (including in pregnancy and breastfeeding) • drug interactions	• effects on commensal flora *Clostridioides (Clostridium) difficile* infection candidiasis (eg oropharyngeal, vulvovaginal) increased risk of colonisation and/or infection with drug-resistant pathogens • effects on environmental flora risk of transmission of *C. difficile* or drug-resistant pathogens to the environment and other people

Direct adverse effects

Always check with the patient if they have a history of hypersensitivity or other adverse reaction before prescribing an antimicrobial.

Hypersensitivity reactions

It is common for a patient to report being "allergic" to an antimicrobial- usually penicillin - and this can present a dilemma. If penicillin is administered to a truly allergic patient, fatal anaphylaxis can occur. However, a history of antibiotic "allergy" often dates back to a suspected reaction during infancy or childhood and has vague features atypical of an IgE-mediated reaction, or is otherwise vague or unknown in nature, or is more consistent with a non-allergic adverse effect (eg vomiting). Further, where true hypersensitivity reactions exist, they are most commonly delayed-type (non-immediate) reactions, which do not necessarily preclude the use of the antimicrobial in the future.

Careful evaluation for antimicrobial hypersensitivity is important to ensure that patients with serious infections are not unnecessarily denied the most effective treatment, and to avoid the alternative use of broad-spectrum antibiotics, which are associated with increased antimicrobial resistance, colonisation with resistant bacterial strains and increased costs.

Types of hypersensitivity reactions

Immediate hypersensitivity reactions

Immediate IgE-mediated (allergic) hypersensitivity is characterised by a reaction ranging in severity from mild urticaria or immediate rash to more severe reactions including extensive urticaria, angioedema, bronchospasm or anaphylaxis (with objectively demonstrated hypotension, hypoxia or elevated mast-cell tryptase concentration) within 1 to 2 hours of exposure to a drug. Anaphylaxis is more likely with parenteral rather than oral administration.

> A clear history of an IgE-mediated reaction means the drug should not be administered again without appropriate precautions (eg desensitisation).

Immediate or acute reactions that do not involve an IgE-mediated mechanism can also occur; for example, vancomycin infusion-related reactions such as 'red man' syndrome. These are usually caused by direct mast-cell degranulation and may be ameliorated by prophylactic antihistamines and slowing the infusion rate.

Delayed hypersensitivity reactions

These are usually the result of T-cell mediated mechanisms and produce a range of syndromes commonly characterised by maculopapular rash. These reactions typically occur after more than one dose of a drug, with an onset days after starting treatment. However, they can occur more rapidly on rechallenge (within 6 hours).

Delayed-type reactions are more common than immediate reactions and may be caused by the infection or its treatment. Such reactions may not be reproducible upon a supervised challenge when the patient is well.

Nonsevere delayed hypersensitivity

These are characterised by macular, papular or morbilliform rash, occurring usually several days after starting treatment.

Delayed rash due to penicillins, especially amoxy/ampicillin, is not strongly predictive of a future reaction, and many patients tolerate the drug if it

is administered at a later time. Repeat exposure to beta-lactams is not necessarily contraindicated.

Severe delayed hypersensitivity

These severe reactions include:

- serum sickness—characterised by vasculitic rash, arthralgia/arthritis, influenza-like symptoms and sometimes fever and proteinuria.
- drug rash with eosinophilia and systemic symptoms (DRESS)—characterised by peripheral blood eosinophilia, desquamative dermatitis and liver dysfunction.
- Stevens-Johnson syndrome / toxic epidermal necrolysis (SJS/TEN)—a very rare, acute and potentially fatal skin reaction characterised by sheet-like skin and mucosal loss.
- acute interstitial nephritis (AIN) – a T-cell mediated hypersensitivity reaction most commonly associated with penicillins; causes kidney dysfunction and can include eosinophilia, fever and exanthematous rash.

> Severe delayed hypersensitivity reactions (including DRESS and SJS/TEN) are contraindications to further drug exposure (including desensitisation) because this can be fatal.

Patients with a known severe hypersensitivity should be strongly advised to wear an alert bracelet or necklace.

The clinical history is the single most important component in the diagnosis of antimicrobial hypersensitivity. If hypersensitivity is reported, obtain specific details about the nature of the reaction (particularly whether features of IgE-mediated immediate hypersensitivity were present), the timing of the reaction relative to drug exposure, and the outcome. Isolated minor intolerances (eg gastrointestinal disturbance) are common with antimicrobials and do not indicate hypersensitivity.

> Clinical history is the single most important component in the diagnosis of antimicrobial hypersensitivity.

Careful evaluation is important to ensure that patients with serious infections are not unnecessarily denied the most effective treatment.

Accurate, detailed documentation of antimicrobial hypersensitivity in the patient records is essential.

Sensitivity testing and desensitisation for patients with a history of immune-mediated hypersensitivity are offered in specialist centres internationally but are not currently available in Fiji.

Cross-reactivity between beta-lactams

Patients hypersensitive to penicillins are more likely to be hypersensitive to other structurally related drugs. The prevalence of cross-reactivity is not known precisely. A recent review found that only 1-2% of patients with a confirmed penicillin allergy also had a cephalosporin allergy. Cross-reactivity between penicillins and carbapenems is approximately 1%.

Historically, immune-mediated hypersensitivity was thought to be due solely to the beta-lactam ring structure common to all beta-lactam antibiotics (penicillins, cephalosporins, carbapenems and monobactams). However, recent evidence suggests that most reactions occur in response to antigenic molecules in the R1 side-chains that distinguish individual penicillins and cephalosporins from each other. Drugs with the same or similar R1 side-chains are more likely to cross-react.

The management of a patient who reports hypersensitivity to penicillins depends on many factors. As this history may alter the risk–benefit balance, a key consideration should be whether the antibiotic therapy is necessary in the first place. In patients with a history of an IgE-mediated (allergic) immediate reaction to penicillins, or severe delayed hypersensitivity (eg DRESS or SJS/TEN), avoid penicillins, cephalosporins and carbapenems; administer a non-beta-lactam antibiotic. In critical situations where an appropriate alternative is not available, seek expert advice. In patients with a history of a nonsevere delayed-type hypersensitivity reaction to penicillins (**not** DRESS or SJS/TEN), an alternative non-penicillin beta-lactam (eg a cephalosporin), or a non-beta-lactam antibiotic may be administered. If a penicillin is definitely preferred, seek expert advice.

Other direct adverse effects

Particular care should be taken in elderly patients, who often have altered pharmacokinetic or toxicodynamic profiles, making them more likely to suffer

an adverse drug reaction. In patients with kidney or liver impairment, dose and/or dose interval adjustment may be required to prevent concentration-related adverse effects (toxicity) (see appendix 6 for antimicrobial dosing in renal impairment). Consideration of pregnancy and breastfeeding may also influence appropriate antimicrobial choice (see appendix 4 for antimicrobial safety in pregnancy and breastfeeding).

Some antimicrobials can interact with other drugs, which may affect the choice or dosage regimen of the antimicrobial. The potential for interactions should always be considered; consult an appropriate resource on drug interactions if starting or stopping antimicrobials in patients taking other drugs. Contact the drug information service in divisional hospitals, or use a reliable reference. One reliable, free online resource is the Drugs.com interactions checker <www.drugs.com/drug_interactions.html>.

Indirect adverse effects

Indirect adverse effects of antimicrobials include effects on both commensal and environmental flora and are associated with higher mortality than direct adverse effects. *Clostridioides (Clostridium) difficile* is a common cause of antibiotic-associated diarrhoea. *Candida* species are normal flora in the gastrointestinal and genitourinary tract, but antibiotic therapy disrupts the normal flora, and infection caused by *Candida* species can develop. Further, antimicrobial use is associated with an increased risk of colonisation and/or infection with a drug-resistant pathogen.

Antimicrobial resistance

Unlike other drugs, the use of antimicrobials in one patient can influence their future effectiveness in other patients. The development and spread of resistance to antimicrobials is a major problem in hospitals and the community. Although the mechanisms are complex, resistance is usually due to selective pressure exerted by the widespread presence of antimicrobial drugs in the environment, together with the facilitated transfer of organisms (or their genetic material) within the environment, in both healthcare and community settings.

Antimicrobial resistance is increasing globally, including Fiji, but it may be minimised and even reversed within a specific population with the judicious use of antimicrobials, guided by the MINDME antimicrobial creed (Box 1.1)

and antimicrobial stewardship. As a limited number of new antimicrobials are becoming available, these prescribing principles must be adhered to in order to preserve their effectiveness for the future.

Antimicrobial stewardship

Antimicrobial stewardship is a multifaceted approach to improving antimicrobial use and requires multidisciplinary cooperation, including pharmacy, microbiology, nursing, medical and infection prevention and control. One important aspect of antimicrobial stewardship is the availability of and compliance with current and evidence-based guidelines.

The five essential strategies for effective antimicrobial stewardship include:

- implementing clinical guidelines that incorporate local microbiology and antimicrobial susceptibility patterns
- establishing formulary restriction and approval systems that include restriction of broad-spectrum and later generation antimicrobials to patients in whom their use is clinically justified
- ensuring laboratories use selective reporting of susceptibility results consistent with hospital antimicrobial treatment guidelines
- reviewing antimicrobial prescribing, with intervention and direct feedback to the prescriber
- usage data, auditing antimicrobial use and using indicators for the quality use of medicines.

AWARE antibiotic classification tool (Box 1.3) [NB1][NB2]

To assist in the development of tools for antibiotic stewardship at local, national and global levels and to reduce antimicrobial resistance, the Access, Watch, Reserve (AWaRe) classification of antibiotics was developed by the World Health Organization (WHO) – where antibiotics are classified into different groups to emphasise the importance of their appropriate use.

The aim is to reduce the proportion of global consumption of antibiotics most at risk of resistance. For 'access' antibiotics there is a lower risk of resistance because they are 'narrow-spectrum' antibiotics (that target a specific microorganism rather than several). They are also less costly because they are available in generic formulations.

In Fiji, the terms **unrestricted**, **restricted** and **highly restricted** are used for the different groups and prescribers must follow the relevant process when prescribing restricted or highly restricted antibiotics in line with relevant MHMS policies and the Fiji National Antimicrobial Resistance Action Plan.

Generally, restricted and highly restricted antibiotics should only be used in a hospital setting, although some may be appropriate for use in outpatients for specific indications.

Unrestricted antibiotics (equivalent to ACCESS group antibiotics)

This group includes antibiotics that have activity against a wide range of commonly encountered susceptible pathogens while also showing lower resistance potential than antibiotics in the other groups. Selected unrestricted antibiotics are recommended as essential first or second choice empiric treatment options for infectious syndromes as recommended by the Fiji Antibiotic Guidelines working group and approved by the Fiji National Medicines and Therapeutics Committee. They are essential antibiotics that should be widely available, affordable and quality assured.

These antibiotics include: amoxicillin, ampicillin, benzathine penicillin, cefalexin, cefalotin, cefazolin, chloramphenicol, cloxacillin, doxycycline, erythromycin, flucloxacillin, dapsone, gentamicin, metronidazole, nitrofurantoin, phenoxymethylpenicillin, procaine penicillin, trimethoprim, trimethoprim+sulfamethoxazole.

Restricted antibiotics (equivalent to WATCH group antibiotics)

This group includes antibiotic classes that have higher resistance potential and includes most of the highest priority agents among the 'Critically Important Antimicrobials for Human Medicine' and/or antibiotics

that are at relatively high risk of selection of bacterial resistance. These medicines should be prioritised as key targets of stewardship programs and monitoring. Selected restricted antibiotics are recommended as essential first or second choice empiric treatment options for a limited number of specific infectious syndromes as recommended by the Fiji Antibiotic Guidelines working group.

These antibiotics include: amikacin, amoxicillin+clavulanate, azithromycin, cefotaxime, ceftriaxone, ciprofloxacin, clarithromycin, clindamycin, fusidic acid, piperacillin+tazobactam, rifampicin, vancomycin

Highly restricted antibiotics (equivalent to RESERVE group antibiotics)

This group includes antibiotics and antibiotic classes that should be reserved for treatment of infections caused by multi-drug-resistant organisms in critically ill patients. Highly restricted antibiotics should be treated as "last resort" options, when all alternatives have failed or are not suitable. These medicines are protected and prioritised as key targets of stewardship programs in Fiji, and their use must involve monitoring and utilisation reporting, to preserve their effectiveness.

These antibiotics include: ceftazidime, colistimethate sodium (colistin) and meropenem.

NB1: Restricted and highly restricted antibiotics may require approval before than can be prescribed or are limited for use in specific indications.

NB2: This is not an exhaustive list of all antibiotics available in Fiji. The category of particular antibiotics may change with local policy and parenteral formulations of some antibiotics may be more restricted than oral formulations.

2. Getting to know your antimicrobials

Antibacterial drugs

Aminoglycosides

This group of antibiotics includes amikacin, gentamicin and streptomycin. Aminoglycosides are rapidly bactericidal and are predominantly used for the treatment of infections caused by aerobic Gram negative organisms. Gentamicin is active against a broad range of Gram negative bacteria, including *Pseudomonas aeruginosa*, and is the least expensive aminoglycoside. It is therefore the aminoglycoside of choice for empirical treatment of serious Gram negative infections including nosocomial infections. Gentamicin is not clinically active against Gram positive organisms but can be used in synergy with other antibiotics for the treatment of streptococcal and enterococcal endocarditis.

Aminoglycosides are not absorbed when given orally and should be administered parenterally for systemic effects.

Aminoglycosides have significant toxicity profiles, particularly when used for prolonged treatment courses. Nephrotoxicity is common but is usually reversible and is associated with longer treatment courses; a single dose is generally safe. Nephrotoxicity typically presents as a non-oliguric (or even polyuric) kidney failure. Aminoglycosides can uncommonly produce idiosyncratic ototoxicity, either vestibular (balance impairment) or cochlear (hearing loss); they should be used with caution in patients with pre-existing vestibular conditions (eg dizziness or balance problems) or hearing impairment. The therapeutic index is narrow and, where available, blood levels should be monitored for use beyond 48 hours.

The primary indication for aminoglycosides is as short-term empirical therapy pending the outcome of investigations. When used empirically, no further doses should be given beyond 48 hours (ie a maximum of 3 doses), and if continuing empirical IV therapy is required (ie an organism is not grown to enable directed therapy) therapy should be changed to an alternative less toxic drug eg ceftriaxone.

Aminoglycosides are indicated for **directed therapy (ie against a known organism) in only a few circumstances**. These include, but are not restricted to:

- infections when resistance to other safer antimicrobials has been shown
- combination therapy for serious *Pseudomonas aeruginosa* infections and brucellosis
- low doses as synergistic treatment for streptococcal and enterococcal endocarditis.

For prolonged courses (longer than 48 hours), renal function should be closely monitored for deterioration, and the patient should be questioned daily for evidence of auditory or vestibular toxicity.

> For further information about dosing, monitoring and adverse effects of gentamicin, see appendix 1.

Beta-lactams

The beta-lactam antibiotics are the penicillins, cephalosporins, carbapenems and monobactams; these antibiotics contain a beta-lactam ring in their structure.

Beta-lactams have a wide therapeutic index. In the majority of patients, beta-lactams do not cause significant adverse effects; however, some patients are hypersensitive to one or more beta-lactams (see antimicrobial hypersensitivity, page 7).

Penicillins

Narrow-spectrum penicillins

Narrow-spectrum penicillins are mainly active against Gram positive organisms, including streptococci and some anaerobes (including Clostridia), and a few other organisms including Neisseriae and Spirochaetes. However, the prevalence of penicillinase-producing *Neisseria gonorrhoea* is increasing and there are reports of decreased susceptibility of pneumococci and other streptococci to penicillin. Narrow-spectrum penicillins are inactivated by beta-lactamase enzymes; in Fiji, about 80 - 90% of *Staphylococcus aureus* are beta-lactamase producers and hence are resistant to benzylpenicillin (and the aminopenicillins).

Benzylpenicillin (penicillin G) is an intravenous preparation.

Procaine penicillin (procaine benzylpenicillin) is an intramuscular preparation that is often used as an alternative to benzylpenicillin when intravenous therapy cannot be administered (eg in rural and remote areas). An effective blood concentration is maintained for up to 24 hours after a dose.

Benzathine penicillin is given intramuscularly and results in low concentrations of benzylpenicillin for up to 4 weeks.

Phenoxymethylpenicillin (penicillin V) is acid-stable and is given orally; food impairs absorption so it should be taken on an empty stomach. It is intrinsically less active than benzylpenicillin.

Moderate spectrum penicillins (aminopenicillins)

Ampicillin and amoxicillin have a slightly broader spectrum than the narrow-spectrum penicillins because of their activity against some Gram negative bacilli including *Escherichia coli*, *Haemophilus influenzae*, *Salmonella* and *Shigella* species. They are the drugs of choice for enterococcal infections.

They are inactivated by beta-lactamase enzymes; resistance among *E.coli* and *H.influenzae* is now widespread.

These drugs are used in empirical treatment of intra-abdominal infections and in the treatment of susceptible urinary tract infections. They may also be used for typhoid fever.

Amoxicillin+clavulanate is a preparation containing amoxicillin and clavulanic acid. Clavulanic acid (clavulanate) has minimal antibacterial activity but inhibits beta-lactamase effectively. This combination is useful in the treatment of beta-lactamase–producing bacteria. It is classified as a broad-spectrum penicillin. Commonly available brands in Fiji include Augmentin® and Curam® , however there are also many others.

Anti-staphylococcal penicillins

Cloxacillin, flucloxacillin and dicloxacillin are narrow-spectrum penicillins, which are stable to staphylococcal beta-lactamases. They are used for the treatment of proven or suspected staphylococcal infections eg skin and soft tissue infections.

These drugs may cause interstitial nephritis and flucloxacillin can rarely cause cholestatic jaundice, particularly in older patients on prolonged therapy.

Some staphylococci have developed resistance to this group, by mechanisms other than beta-lactamase production. These methicillin-resistant *Staphylococcus aureus* (MRSA) will be resistant to all other beta-lactams (ie all penicillins, cephalosporins, monobactams and carbapenems).

Food impairs the absorption of flucloxacillin. It should be dosed on an empty stomach, ideally, at 6-hourly intervals. However, for practical purposes (eg in children) four-times-daily dosing, evenly spaced during waking hours, is often used.

Anti-pseudomonal penicillins

Piperacillin+tazobactam is the only anti-pseudomonal penicillin available in Fiji. It has broad-spectrum Gram positive, Gram negative and anaerobic activity.

The beta-lactamase enzyme inhibitor, tazobactam, has little inherent antibacterial activity; it inhibits the beta-lactamase enzymes produced by *Staphylococcus aureus*, *Bacteroides fragilis*, *Haemophilus influenzae*, and some of the beta-lactamase enzymes produced by *Escherichia coli* and *Klebsiella* species.

Beta-lactamase inhibitor combinations should be reserved for infections caused by bacteria that produce beta-lactamase enzymes. Additional treatment for anaerobic bacteria (eg metronidazole) is usually not required with beta-lactamase inhibitor combinations.

When used to treat *Pseudomonas aeruginosa*, piperacillin+tazobactam must be dosed 6-hourly.

Cephalosporins

The cephalosporins are traditionally divided into “generations” based on their spectrum of activity; there are currently five generations of cephalosporins; agents from the first three are available in Fiji:

1st generation cephalosporins	2nd generation cephalosporins	3rd generation cephalosporins
cefalexin	cefaclor	ceftriaxone
cefalotin (cephalothin)	cefuroxime	cefotaxime
cefazolin		ceftazidime

First generation cephalosporins include among others, cefalexin (oral), cefalotin and cefazolin. The spectrum of activity is similar, being active against many Gram positive cocci including streptococci and staphylococci (not MRSA) and a few Gram negative enteric bacilli (including *E. coli* and some *Klebsiella* species). They are not active against enterococci, *Listeria monocytogenes* or any Gram negative anaerobic organisms. They may be used in some patients with penicillin hypersensitivity (excluding immediate (IgE-mediated) hypersensitivity and severe delayed hypersensitivity). Cefazolin has replaced cefalotin in these guidelines because cefazolin is as effective as cefalotin, and the short half-life of cefalotin makes it inadequate for the treatment of Gram negative infections and for surgical prophylaxis.

Second generation cephalosporins, including cefaclor and cefuroxime (oral) are more stable to some Gram negative beta-lactamase enzymes than first generation agents, and are therefore more active against *Haemophilus influenzae*. Their activity against Gram positive organisms is similar to, or less than, that of the first generation cephalosporins and they have varying degrees of activity against anaerobes. These drugs have a limited role in therapy and are more expensive.

The third generation cephalosporins, including ceftriaxone, cefotaxime and ceftazidime, have a broad-spectrum of activity that includes the majority of community-acquired enteric Gram negative rods. They are less active against staphylococci than earlier generation cephalosporins but maintain excellent streptococcal activity. They are inactive against MRSA, enterococci and listeria; activity against anaerobes varies. A major advantage of these agents is their ability to reach the central nervous system. Ceftriaxone and cefotaxime are useful in serious Gram negative infections, including hospital-acquired infections, and in the treatment of meningitis. However, they are not effective against *Pseudomonas*. Ceftazidime has specific antipseudomonal activity.

Some organisms (the ESCAPPM group, including *Enterobacter*, *Serratia* and *Citrobacter*) have chromosomal resistance in the form of cephalosporinase enzymes; while they may test sensitive initially, resistance can develop during treatment.

Ceftriaxone should be used with caution in neonates as it is associated with an increased risk of bilirubin encephalopathy; cefotaxime is preferred.

Cephalosporins have been shown to select MRSA, vancomycin-resistant enterococci and multi-resistant Gram negative bacilli. Therefore, indications for their use should be limited where narrower-spectrum drugs are appropriate.

Carbapenems

The only carbapenem available in Fiji is meropenem. Carbapenems are very broad-spectrum drugs with activity against enteric Gram negative rods (including isolates producing extended-spectrum beta-lactamase enzymes [ESBLs], and *Pseudomonas aeruginosa*) comparable to that of aminoglycosides, and excellent activity against anaerobic organisms (including *Bacteroides fragilis*) and many Gram positive organisms (including streptococci, methicillin sensitive staphylococci and *Nocardia* species).

Carbapenems are inactive against MRSA, VRE, *Enterococcus faecium, Mycoplasma, Chlamydia (and Chlamydophila)*, and *Stenotrophomonas maltophilia*.

Widespread use of carbapenems has been linked with increasing prevalence of infections caused by multi-resistant organisms, therefore their use should be reserved. Carbapenem resistance is emerging worldwide, often due to the production of various carbapenemase enzymes, which also confer resistance to other antibiotics.

Chloramphenicol

Chloramphenicol is a broad-spectrum antibiotic active against many Gram positive and Gram negative bacteria, including anaerobes, and *Rickettsia* and *Chlamydia/Chlamydophila*. However, it is ineffective against *Pseudomonas aeruginosa*.

Chloramphenicol can be used topically, orally or parentally. **Bioavailability**

after oral administration is as good as parenteral use and the oral preparation can be used to initiate treatment in emergencies if the injection is not available.

Chloramphenicol is generally well tolerated, however its use has been restricted in many countries due to a potential for severe haematological toxicity. It can produce a predictable, dose-dependent, reversible anaemia, but also rarely an idiosyncratic, irreversible aplastic anaemia (incidence 1 in 24,000-40,000 courses). It is not safe in pregnancy and in neonates as it may cause Grey baby syndrome. Its use as far as possible should be limited to specific indications like meningitis, brain abscess and occasionally anaerobic infections.

Folic acid antagonists (trimethoprim and sulfamethoxazole)

Trimethoprim+sulfamethoxazole (co-trimoxazole, TMP-SMX) is a combination of two antimicrobials which act synergistically to inhibit bacterial DNA synthesis. It is active against a wide variety of aerobic Gram positive and Gram negative organisms, including most non-multidrug-resistant MRSA *Burkholderia cepacia*, *Stenotrophomonas maltophilia* and *Nocardia* species, and against *Pneumocystis jiroveci* and some protozoa. It is not active against most anaerobes.

Sulfamethoxazole may cause GIT upset and hypersensitivity reactions, most commonly skin rash but on occasion severe dermatologic reaction (eg Stevens-Johnson syndrome) or anaphylaxis. Adverse reactions are more common in HIV-infected patients and the elderly. Prolonged use, particularly in high doses, can be associated with bone marrow toxicity, most commonly leucopoenia. It can cause, or exacerbate pre-existing, renal impairment and should be used with caution in patients with advanced renal insufficiency.

Trimethoprim inhibits tubular secretion of creatinine, which can elevate serum creatinine without any true decrease in glomerular filtration rate. Trimethoprim also inhibits tubular excretion of potassium and can cause hyperkalaemia. Monitor serum potassium after 3 days of treatment with trimethoprim in patients at increased risk of hyperkalaemia (eg patients with renal impairment, patients who are taking a high dose of trimethoprim or other drugs that can cause hyperkalaemia). For the treatment of

some infections, particularly uncomplicated urinary tract infections, and acute otitis media in children, trimethoprim alone is as effective as the combination drug and is preferred.

Trimethoprim and trimethoprim+sulfamethoxazole should generally be avoided in the first trimester of pregnancy due to a risk of congenital malformations. Trimethoprim+sulfamethoxazole should be avoided in the last month of pregnancy, and in infants younger than 1 month, due to the risk of kernicterus. Oral bioavailability is good.

Fusidic acid

Fusidic acid (fusidate sodium) has a narrow spectrum of activity. It is active against *Staphylococcus aureus* including methicillin-resistant *Staphylococcus aureus* (MRSA). Resistance develops readily, so it should always be used concomitantly with other antibiotics. It should not be used topically.

Glycopeptides

Vancomycin (and teicoplanin) are active against a wide range of Gram positive organisms. However, the drug is principally reserved for treating Gram positive infections resistant to beta- lactams, particularly methicillin-resistant *Staphylococcus aureus* (MRSA) and ampicillin- resistant enterococci, and for patients with immediate hypersensitivity to beta-lactams. Gram negative organisms are not susceptible. Vancomycin is not absorbed orally; it is used orally only to treat *Clostridioides (Clostridium) difficile* diarrhoea unresponsive to metronidazole.

Vancomycin must be given as a slow IV infusion to prevent “red man” syndrome (flushing, pruritus, hypotension). See appendix 6 for safe administration. Renal toxicity can occur, especially if given with aminoglycosides. Attention should be paid to dosing schedules (see appendix 2) and renal function, and serum levels where available should be monitored.

Lincosamides

Clindamycin (and lincomycin) are active against most Gram positive aerobic bacteria including streptococci and staphylococci (but not *Enterococcus* species) and most anaerobic bacteria. They are not active against Gram

negative organisms. They are commonly used, particularly in skin and soft tissue infections, as second-line therapy for patients who do not tolerate conventional therapy eg with beta-lactams, or for infections resistant to other antibiotics (eg non-multi-resistant methicillin-resistant *Staphylococcus aureus*). They are used in combination with penicillin therapy for necrotising skin and soft tissue infections (eg necrotising fasciitis or myositis) and other invasive group A streptococcal infections associated with toxic shock syndrome.

Although clindamycin is inherently more active than lincomycin for most indications the same dosage is appropriate. Clindamycin and lincomycin have common adverse effects, in particular antibiotic-associated diarrhoea.

Macrolides

Azithromycin, clarithromycin, erythromycin and roxithromycin have a broad-spectrum of activity, including Gram positive cocci, *Legionella*, *Corynebacterium*, Gram negative cocci, *Mycoplasma*, *Chlamydia* and Gram positive and Gram negative anaerobic bacteria. Erythromycin, azithromycin and clarithromycin are also active against *Bordetella*.

Clarithromycin is active against nontuberculous mycobacteria, including *Mycobacterium avium* complex (MAC), and is used in combination with other drugs for this indication. It is also used in combination with other drugs in the eradication of *Helicobacter pylori* infection.

Azithromycin is less active than erythromycin against Gram positive bacteria but is active against some Gram negative bacteria (eg *Salmonella* species and the causative organisms of atypical pneumonia), some anaerobic organisms, nontuberculous mycobacteria including MAC, and some parasites (eg *Toxoplasma gondii*).

Macrolides attain high intracellular concentrations that are theoretically beneficial for the treatment of infections caused by intracellular pathogens.

Erythromycin and clarithromycin are potent inhibitors of the cytochrome P450 (CYP3A4) enzyme system, so they have significant drug interactions. Consult an appropriate drug interactions resource when starting macrolides in patients taking other drugs or contact a divisional hospital drug information service. A free online interactions checker is available at <www.drugs.com/drug_interactions.html>.

Azithromycin, erythromycin and clarithromycin prolong the QT interval.

Oral formulations of erythromycin have variable absorption and are poorly tolerated due to gastrointestinal adverse effects. Furthermore, poor adherence is likely due to the four-times-daily dosing schedule. These factors limit the use of erythromycin in practice. Erythromycin is not recommended for neonates (up to 28 days old); infantile hypertrophic pyloric stenosis has been associated with the use of erythromycin and azithromycin, particularly during the first 2 weeks of life, but the risk is greater with erythromycin.

Mupirocin

Only available as a topical preparation, mupirocin has a limited role in therapy. Prolonged or widespread use causes high-level resistance to mupirocin in methicillin-resistant *Staphylococcus aureus* (MRSA).

Nitrofurantoin

Nitrofurantoin is active against organisms that commonly cause urinary tract infection, many Gram negative bacilli (eg *Escherichia coli*) and Gram positive cocci (eg *Enterococcus faecalis*).

Nitrofurantoin is excreted by the kidneys. Effective treatment of urinary tract infection depends on an adequate concentration in the urine, so even in mild renal impairment, treatment is considerably less effective. Use should be avoided if the eGFR is below 60mL/min/1.73m2.

Nitroimidazoles

Metronidazole and tinidazole are active against almost all Gram negative anaerobic bacteria (eg *Bacteroides fragilis*), and most Gram positive anaerobic bacteria (eg *Clostridioides (Clostridium)* species). They are also active against protozoa including *Trichomonas vaginalis*, *Giardia lamblia* and *Entamoeba histolytica*. Metronidazole is well-absorbed and can be administered IV, orally or rectally. The rectal preparation produces high levels and can be used to treat serious infections. Metronidazole crosses the blood–brain barrier.

Metronidazole is usually well tolerated. Common minor side effects include nausea, vomiting and a metallic taste in the mouth. The nitroimidazoles may

cause a disulfiram like reaction with alcohol, characterised most commonly by flushing, tachycardia, palpitations and nausea and vomiting. Patients should be advised to avoid alcohol during treatment and for 48 hours after finishing the course. Prolonged courses of >2 weeks may be associated with peripheral neuropathy; caution should be used.

Tinidazole has a longer half-life than metronidazole allowing less frequent dosing.

Polymixins

Colistimethate sodium (also called colistin methanesulfonate and often referred to as colistin) is a polymyxin antibiotic with bactericidal activity against many Gram negative bacteria (including strains of *Pseudomonas aeruginosa* and *Acinetobacter baumannii*) that are resistant to other drug classes. Dosing of colistimethate sodium is complex (dosing recommended in the product information is not appropriate) and use of this drug is associated with severe adverse effects including renal and neurotoxicity. Colistimethate sodium should only be used with **specialist supervision**.

Fluoroquinolones (quinolones)

Fluoroquinolones (including ciprofloxacin, moxifloxacin, levofloxacin and norfloxacin) should generally be reserved for treatment of infections where there are no other therapeutic options eg for organisms resistant to other drugs, or as oral therapy when alternative antibiotics are not available eg *Pseudomonas aeruginosa* infections. Ciprofloxacin is also used for the treatment of enteric fever (typhoid). Ofloxacin is used topically to treat eye infections.

Resistance to fluoroquinolones is now widespread, particularly in enteric Gram negative rods, *Pseudomonas aeruginosa*, *Campylobacter* species and *Neisseria gonorrhoeae* and local susceptibility information is important.

The fluoroquinolones have potent activity against aerobic Gram negative bacteria, including *Haemophilus influenzae*, the Enterobacteriaceae (enteric Gram negative rods), *P. aeruginosa* (particularly ciprofloxacin) and Gram negative cocci including *Neisseria* species and *Moraxella catarrhalis*. Ciprofloxacin and norfloxacin have poor activity against streptococci, but the newer drugs (levofloxacin and moxifloxacin) have improved coverage against

Gram positive cocci, including streptococci. Ciprofloxacin, levofloxacin and moxifloxacin are active against the organisms causing atypical pneumonia (*Legionella pneumophilia*, *Mycoplasma pneumoniae* and C*hlamydia (Chlamydophila) pneumoniae)* and various species of mycobacteria; moxifloxacin may be used in the treatment of TB. Ciprofloxacin and norfloxacin have no clinical activity against anaerobic bacteria.

Moxifloxacin, an extended-spectrum fluoroquinolone, has increased activity against Gram positive bacteria (including staphylococci and streptococci) and is active against many Gram negative aerobic bacteria, but has no clinical activity against *P. aeruginosa*. Moxifloxacin has good activity against anaerobic bacteria and most atypical pathogens that cause pneumonia. It is also used for the management of some mycobacterial infections.

Fluoroquinolones should be used with caution in children younger than 14 years and in pregnant or breastfeeding women, due to concerns from animal studies re: potential joint damage. Fluoroquinolones may cause tendinitis, commonly involving the Achilles tendon, though other tendons can be affected. Risk factors for developing tendinitis are concomitant corticosteroid use, advanced age, renal impairment and prolonged therapy. Fluoroquinolones have many clinically significant drug interactions and can prolong the QT interval.

Rifamycins

Rifampicin is used in the treatment of tuberculosis, and for infections with *Staphylococcus aureus* (including MRSA). It is also used as prophylaxis in contacts of patients with *Haemophilus influenzae* type B and meningococcal disease. Since resistance emerges rapidly, **it should always be used in combination** with other antibiotics (except where used as prophylaxis).

Rifamycins colour urine, tears and other body fluids orange-red; patients should be warned prior to commencing therapy. Rifampicin may also cause hepatitis; liver function tests should be monitored regularly. Rifamycins can accelerate the metabolism and reduce the effectiveness of other drugs including oral contraceptives, warfarin and phenytoin.

Tetracyclines

Tetracyclines (including tetracycline, doxycycline and minocycline) have a

broad spectrum of activity that includes many Gram positive and Gram negative bacteria, *Chlamydia (Chlamydophila) species*, *Rickettsia* species, *Mycoplasma* species, spirochaetes (including Leptospira and Treponema species), some nontuberculous mycobacteria and some protozoa (eg *Entamoeba histolytica*, and *Plasmodium* species causing malaria). **Doxycycline** is the preferred tetracycline in most situations. For chlamydial and rickettsial infections this is the drug of first choice.

The spectrum of activity of different tetracyclines is very similar, but they are different in their pharmacokinetics. Tetracycline is excreted predominantly through the kidneys; doxycycline, which is excreted via the GIT, is safer in patients with renal impairment, but caution is required in patients with advanced hepatic disease. Doxycycline has a longer half-life than tetracycline.

Minocycline is active against some bacteria that are resistant to other tetracyclines, including strains of staphylococci. However, benign intracranial hypertension, vestibular adverse effects and, rarely, skin pigmentation limit the use of minocycline.

Oesophagitis can occur with doxycycline and, less commonly, minocycline. Tetracyclines should be taken with food and a full glass of water, and the patient should be instructed to remain upright for at least an hour after administration. Photosensitivity reactions can occur with tetracyclines.

Because of their effect on growing bones and teeth (discolouration and enamel dysplasia), these drugs are generally contraindicated in pregnancy, lactating mothers and in children younger than 8 years. However, these concerns may be outweighed by the superior effectiveness of doxycycline for some infections (eg Q fever, rickettsial infections). Additionally, the risk of these adverse effects is thought to be minimal if single short courses are used.

Antimycobacterial drugs

Dapsone

Dapsone is used for the treatment of leprosy and toxoplasmosis, for the prevention of malaria, and for treatment and prevention of *Pneumocystis jiroveci* infection. Exclude glucose-6-phosphate dehydrogenase deficiency

before starting treatment, because patients who are deficient are at risk of developing severe haemolytic anaemia. Peripheral neuropathy can occur, particularly with daily doses exceeding 200 mg.

Dapsone is structurally similar to sulphonamides; the cross-reactivity rate between dapsone and sulfamethoxazole is 9-12%. Do not use dapsone in patients with immediate hypersensitivity or another severe reaction (eg drug rash with eosinophilia and systemic symptoms [DRESS] or Stevens-Johnson syndrome / toxic epidermal necrolysis [SJS/TEN]) to sulfonamides.

Ethambutol

Ethambutol is used for the treatment of tuberculosis and nontuberculous mycobacterial infections, including *Mycobacterium avium* complex (MAC). Ethambutol can cause optic neuritis; check visual acuity and colour vision before starting treatment and instruct patients to report any changes in vision. Stop treatment with ethambutol immediately if visual symptoms occur.

Ethambutol has not been routinely used in children younger than 6 years due to the difficulty in assessing visual acuity in this age group. However, ethambutol is now considered safe in children of all ages.

Isoniazid

Isoniazid is used as part of combination treatment for *Mycobacterium tuberculosis* and other mycobacterial infections. Although peripheral neuropathy can occur, the risk is minimised by concomitant treatment with pyridoxine. Severe hepatitis has been reported with isoniazid; the risk increases with age, hazardous alcohol consumption and pre-existing liver disease.

Pyrazinamide

Pyrazinamide is used exclusively as part of combination treatment of *Mycobacterium tuberculosis*. It is not effective for the treatment of other types of mycobacterial infection.

Rifamycins

See rifamycins above.

Antifungal drugs

Azoles

There are two main groups; those for systemic use and those for topical use.

Azoles for systemic use

Includes the triazoles (fluconazole, itraconazole and voriconazole) and the imidazole ketoconazole. These drugs vary significantly with regards to spectrum of activity, pharmacokinetics and toxicities.

Fluconazole and ketoconazole are active against most yeasts, including *Candida* species (but not *Candida kruseii*), and *Cryptococcus* species and have some activity against *Histoplasma*. These agents are useful in the treatment of systemic infections due to these organisms. They have no activity against moulds (including Aspergillus species). Fluconazole is well-absorbed following oral administration and has good CNS penetration.

Voriconazole is active against yeasts (*Candida* species including *C.kruseii* and *Cryptococcus* species), and some moulds including *Aspergillus* and *Scedosporium* species. Where available, it is the first line agent for the treatment of invasive aspergillosis.

Systemic azole antifungals interact with many other drugs (including commonly prescribed drugs such as amiodarone, clopidogrel, phenytoin and warfarin). They are generally well tolerated but can cause GIT upset and hepatic dysfunction. QT interval prolongation has been reported with voriconazole; other azoles may also prolong the QT interval under certain conditions (eg when administered with other drugs that prolong the QT interval). For more information on drugs that prolong the QT interval, see the CredibleMeds website <https://crediblemeds.org/>.

Azoles for topical use

Miconazole, clotrimazole and econazole. These are used in the treatment of superficial candidiasis and dermatophytosis.

It is important to be aware that miconazole oral gel, when used to treat oral thrush, is systemically absorbed and may cause clinically significant drug interactions.

Amphotericin B

Amphotericin is useful against most invasive fungal infections. Specifically, it is active against a wide range of yeasts, including *Candida* and *Cryptococcus* species, most Aspergillus species (but not *A.terreus* or *A.nidulans*), and other fungi, including some *Fusarium* species, zygomycetes and phaeohyphomycetes and *Leishmania* species.

Amphotericin is associated with significant toxicity, including infusion-related "flu-like" reactions, nephrotoxicity, electrolyte abnormalities and anaemia. Adverse reactions are particularly common with amphotericin B desoxycholate (the 'conventional' form of amphotericin); the lipid complex or liposomal formulations are generally better tolerated and can replace conventional amphotericin if severe infusion reactions or nephrotoxicity occur. To minimise toxicity, patients should be pre-hydrated with sodium chloride 0.9% (0.5 to 1 L IV) before amphotericin infusion. Pre-treatment with hydrocortisone, antihistamines, antiemetics, opioids or an antipyretic may also be used to provide symptomatic relief.

The dosage and infusion rates for each amphotericin formulation (conventional, lipid complex or liposomal) are significantly different—exercise caution when prescribing and administering, because errors have caused fatalities.

Griseofulvin

When given orally, it concentrates in keratinised tissues and prevents further invasion by dermatophytes.

Terbinafine

Effective against dermatophytes when used orally or topically.

Nystatin

Nystatin is mainly active against *Candida* species. It is poorly absorbed orally and is not absorbed through skin or mucous membranes when applied topically. Nystatin suspension is used to treat oral thrush.

Antiviral drugs

Guanine analogues

Aciclovir, famciclovir and valaciclovir are active against herpesvirus infections, particularly herpes simplex virus (HSV) (types I and II) and varicella-zoster virus. Aciclovir is poorly and erratically absorbed orally. Valaciclovir, a prodrug of aciclovir, and famciclovir, are well-absorbed after oral administration, so are dosed less frequently than aciclovir. Only aciclovir is currently available on the EML. Topical application or oral therapy is used for skin, mucous membrane and eye infections. Intravenous aciclovir is used for the treatment of HSV encephalitis; renal function should be closely monitored.

Neuraminidase inhibitors

Oseltamivir (oral), zanamivir (inhaled or intravenous) and peramivir (intravenous) inhibit influenza virus A and B neuraminidase (an enzyme required for viral replication) and are used for the treatment and prevention of influenza in selected patient groups.

Neuropsychiatric adverse effects have been reported rarely in children and adolescents taking neuraminidase inhibitors.

Tenofovir

Tenofovir is a nucleotide reverse transcriptase inhibitor which is used for the treatment of chronic hepatitis B virus (HBV) infection (and HIV-1, in combination with other agents). It is generally well tolerated but can cause nephrotoxicity and should be used with caution in patients with pre-existing renal insufficiency. Tenofovir may cause decreased bone mineral density and increased fracture risk. Resistance in HBV is rare; however, cessation of therapy has been associated with severe acute exacerbations of hepatitis.

Antiparasitic drugs

Antiprotozoal drugs

Artemisinin derivatives

Artemisinin (qinghaosu) derivatives (artesunate and artemether) have potent activity against all human malaria parasites. Artesunate is used to treat severe malaria.

Artemether+lumefantrine is used to treat acute uncomplicated malaria. It should be taken with fatty food or full-fat milk to ensure adequate absorption of lumefantrine.

Atovaquone+proguanil (Malarone®)

Atovaquone+proguanil is used for prophylaxis and treatment of malaria. It should be taken with fatty food or full-fat milk to ensure adequate absorption of atovaquone. Consider alternative therapy for patients with severe chronic diarrhoea because absorption can be significantly reduced.

Atovaquone, as a single drug, is used for the prevention and treatment of *Pneumocystis jiroveci* infection in patients who do not tolerate other therapies.

Chloroquine

Chloroquine is no longer recommended for the treatment or prophylaxis of malaria. Chloroquine-resistant *Plasmodium falciparum* has spread to most malaria-endemic areas of the world, and high-grade chloroquine-resistant *Plasmodium vivax* now occurs in several areas of the Asia–Pacific region.

Mefloquine

Mefloquine is used for the prophylaxis of malaria. Neuropsychiatric disturbances (eg headache, nightmares, depression, psychosis) occur infrequently, usually within the first 4 weeks of treatment, and can continue for many months after stopping therapy. Mefloquine can prolong the QT interval, so it should not be used with other drugs that prolong the QT interval or in patients with a cardiac conduction abnormality.

Nitazoxanide

Nitazoxanide is an oral antiprotozoal drug with activity against *Cryptosporidium parvum* and *Giardia intestinalis*. Adverse effects are usually mild and can include nausea, abdominal pain, diarrhoea and headache.

Paromomycin

Paromomycin is an aminoglycoside that is not systemically absorbed. It is active against protozoa, including *Entamoeba histolytica* and *Giardia*. It is used to eradicate cysts after the initial treatment of amoebic colitis (dysentery) or liver abscess, and for giardiasis. Adverse effects are limited to gastrointestinal intolerance, particularly diarrhoea.

Primaquine

Primaquine is essential for the treatment of malaria caused by *Plasmodium vivax* and *Plasmodium ovale* because it eradicates dormant parasites that would otherwise persist in the liver. Adverse effects include gastrointestinal disturbances and methaemoglobinaemia. Exclude glucose-6-phosphate dehydrogenase deficiency before starting treatment because patients who are deficient are at risk of developing haemolytic anaemia.

Pyrimethamine

Pyrimethamine is used in combination with another drug (eg sulfadiazine) for the prevention and treatment of toxoplasmosis. Concomitant administration of calcium folinate reduces the incidence of bone marrow suppression.

Quinine

Quinine is used to treat malaria. Hypersensitivity or drug accumulation may lead to cinchonism (tinnitus, impaired hearing, headache, gastrointestinal disturbances and visual disturbances). Other adverse effects include urticaria, fever, rash, dyspnoea, and, in patients with glucose-6-phosphate dehydrogenase deficiency, haemolytic anaemia.

Sulfadoxine-pyrimethamine (Fansidar®)

Fansidar® is a combination agent of two folic acid antagonists which is used for the prevention and treatment of acute uncomplicated *P. falciparum* malaria. Gastrointestinal upset and headache are common. Haematological

toxicity in the form of bone marrow suppression can occur, and haemolytic anaemia may occur in patients with G6PD-deficiency. The sulfur component may be associated with severe allergic cutaneous reactions (eg Stevens-Johnson syndrome; toxic epidermal necrolysis). Fansidar® should be used with caution in those with renal or hepatic dysfunction. Global resistance rates are high.

Anthelmintic drugs

Benzimidazoles

Albendazole and **mebendazole** are predominantly used to treat intestinal worm infections such as roundworm (*Ascaris lumbricoides*), threadworm or pinworm (*Enterobius vermicularis*), hookworm (*Ancylostoma duodenale* and *Necator americanus*), whipworm (*Trichuris trichiura*) and strongyloidiasis (*Strongyloides stercoralis*).

Albendazole is used as adjunctive therapy for hydatid disease in combination with surgery. It is used for the treatment of cutaneous larva migrans as an alternative to ivermectin.

The main adverse effects of both drugs are elevated liver transaminases, gastrointestinal symptoms and haematological abnormalities (eg leucopenia). Avoid albendazole in pregnant women and in children weighing 10 kg or less.

For treating systemic infections, albendazole and mebendazole should be taken with a fatty meal to improve absorption. In contrast, for treating intestinal worms, they should be taken on an empty stomach to limit systemic absorption.

Ivermectin

Ivermectin is used for filariasis, strongyloidiasis, scabies, head lice and cutaneous larva migrans. It is not recommended for children weighing less than 15 kg. Absorption of ivermectin is improved when taken with food.

Ivermectin can cause sensitivity reactions when used for filarial infections, due to its effect on the microfilariae. These reactions are usually transient and respond to analgesics and antihistamines.

Praziquantel

Praziquantel is used for tapeworm and fluke infections, such as cysticercosis and schistosomiasis. It is sometimes used as adjunctive therapy for hydatid disease. Adverse effects are transient and include gastrointestinal upset, headache, dizziness and drowsiness.

Pyrantel

Pyrantel is effective against roundworm (*Ascaris lumbricoides*), hookworm (*Ancylostoma duodenale* and *Necator americanus*), and threadworm or pinworm (*Enterobius vermicularis*). Adverse effects are uncommon.

Topical antiparasitic drugs

Benzyl benzoate

Benzyl benzoate is used to treat scabies. The mechanism of action is uncertain; it may work by disrupting the nervous system of the mite. When applied topically at the recommended dose, systemic toxicity is unlikely, but irritation is common.

Maldison

Maldison (malathion) is an organophosphate cholinesterase inhibitor. It is an effective insecticide used to treat infestation by lice and their eggs (nits).

Maldison is detoxified more rapidly in humans than in arthropods, so it is one of the least toxic organophosphates. When used topically at the recommended dose, systemic toxicity has not been reported.

Permethrin

Permethrin is a pyrethroid insecticide used to treat infestation by lice or scabies. Permethrin disrupts the electrochemical balance across cell membranes in insects, causing sensory hyperexcitability, incoordination and prostration. In mammals, permethrin is rapidly hydrolysed to inactive metabolites.

Pyrethrins

Pyrethrins are used to treat infestation by lice. They block nerve impulse transmission in arthropods, causing paralysis and death. Piperonyl butoxide

has little or no intrinsic insecticidal activity but is used to potentiate the action of pyrethrins.

Pyrethrins and piperonyl butoxide are poorly absorbed through intact skin, so they are unlikely to cause systemic toxicity when used topically.

3. Prevention of infection: surgical prophylaxis

General principles

Principles for appropriate prescribing of surgical antibiotic prophylaxis (Box 3.1)

The following principles guide antibiotic prophylaxis to prevent postoperative infection:

- Do not use antibiotic prophylaxis unless there is a clear indication for its use ie when there is a significant risk of infection or if postoperative infection would have serious consequences.
- Antibiotic selection may need to be modified according to patient risk factors such as pre-existing infection, recent antimicrobial use, known colonisation with multidrug-resistant organisms, prolonged hospitalisation or the presence of prostheses.
- Antibiotic pharmacokinetics are altered in obese patients, so dosage adjustment may be necessary. Obesity is an independent risk factor for postoperative infection.
- The optimal timing for preoperative IV antibiotic administration is within the 60 minutes before surgical incision. Due to its long infusion time, vancomycin should ideally be started 15 to 120 minutes before surgical incision.
- A single dose of antibiotic(s) is sufficient for the significant majority of procedures. A repeat intraoperative dose is required if the procedure is prolonged and the drug has a short half-life. The interval between the pre- and intraoperative doses should be equal to approximately two half-lives of the drug (eg cefazolin should be administered every 4 hours). A repeat intraoperative dose may also be required if there is excessive blood loss during the procedure.
- Postoperative doses of IV antibiotics (up to 24 hours) are only required in defined circumstances (eg some cardiac and vascular surgeries, lower limb amputation).

- Prophylaxis should not extend beyond 24 hours, regardless of the surgical procedure; neither IV nor oral antibiotic prophylaxis offers a benefit beyond this period. Extended prophylaxis is associated with an increased risk of adverse effects, including subsequent infection with resistant pathogens or *Clostridioides (Clostridium) difficile*.
- Urinary or intravascular catheters or indwelling surgical drains that remain *in situ* are not a justification to extend the duration of antibiotic prophylaxis. Antibiotic prophylaxis at the time of urinary catheter insertion or removal is not recommended, other than in some high-risk patients after urological procedures.

Introduction

Appropriate surgical antibiotic prophylaxis reduces the rate of superficial and deep surgical site infections, as well as postoperative pneumonia and urinary tract infection. Appropriately timed prophylaxis is crucial; short courses (either a single dose or, in specific circumstances, up to 24 hours) are as effective as longer courses. If the risk of postoperative infection is low, surgical antibiotic prophylaxis is not usually indicated because the risks associated with antibiotic exposure outweigh the benefits of prophylaxis.

A first generation cephalosporin (cefazolin / cefalotin (cephalothin)) remains the preferred drug for the majority of procedures that require prophylaxis.

Adherence to the following principles maximises the potential benefit of surgical antibiotic prophylaxis while minimising adverse effects, including the development of drug-resistant pathogens.

Indications

Consider prophylaxis if there is a significant risk of postoperative infection (eg colonic resection), or if postoperative infection would have serious consequences (eg infection associated with a prosthetic heart valve), even when such infection is uncommon.

Antibiotics for infective endocarditis prophylaxis may be needed for patients with specific cardiac conditions who are undergoing a surgical procedure; see chapter 4: prevention of infection: endocarditis. In these patients, endocarditis prophylaxis may be required even if surgical antibiotic prophylaxis is not indicated.

Non-antibiotic measures

Surgical antibiotic prophylaxis should not be the only strategy used to reduce the risk of postoperative infection. Minimising the risk requires a comprehensive approach to patient management, including optimal perioperative medical management (eg perioperative glycaemic control in patients with diabetes), adequate debridement and good surgical technique.

Antibiotic selection

General principles

The prophylactic antibiotic regimen should be directed against the organism(s) most likely to cause postoperative infection. It need not necessarily include antibiotics that are active against every potential pathogen. Cefazolin is the preferred drug for the majority of procedures that require prophylaxis.

Most postoperative infections are caused by organisms that already colonise the patient; this may include multidrug-resistant organisms when there has been prolonged hospitalisation or repeated antibiotic use.

The choice of antibiotic(s) should take into account patient factors (such as pre-existing infection, the potential for colonisation with multidrug-resistant organisms) and environmental factors (such as the organisms causing infection within the institution). Avoid using broad-spectrum antibiotics, including broad-spectrum cephalosporins (eg cefotaxime, ceftriaxone), for surgical antibiotic prophylaxis.

Additional antibiotic prophylaxis is not required if the patient is being treated with antibiotic therapy for established infection, provided the regimen has an appropriate spectrum of activity for prophylaxis. Timing of the antibiotic dose should be adjusted so that adequate plasma and tissue concentrations are achieved at the time of surgical incision and for the duration of the procedure.

Surgical antibiotic prophylaxis for patients with a penicillin or cephalosporin allergy

Cefazolin is the mainstay of surgical antibiotic prophylaxis. It is a beta-lactam antibiotic that shares no common side-chains with other beta-

lactams (see page 10), and is often tolerated in patients with a penicillin or cephalosporin allergy.

For patients with **delayed nonsevere** hypersensitivity to penicillins, cefazolin can be used. Other cephalosporins may also be appropriate—seek expert advice.

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, a non–beta-lactam antibiotic must be used instead of cefazolin—for alternatives, see the relevant procedure in Table 3.1.

Principles of gentamicin prophylaxis

The Gram negative spectrum of cefazolin is considered adequate for most surgical procedures where there is a risk of contamination with Gram negative bacteria. However, gentamicin continues to be recommended for a limited number of indications where a broader spectrum of Gram negative activity is required, or as an alternative when cefazolin is contraindicated.

The risk of gentamicin toxicity is low when it is given as a single dose for prophylaxis.

There is divergent practice in gentamicin dosing for surgical prophylaxis; doses from 1.5 to 5 mg/kg are used. The doses recommended in this guideline are based on extensive clinical experience and the pharmacokinetic/pharmacodynamic properties of gentamicin.

The appropriate dose depends on the duration of prophylaxis required.

- A 2 mg/kg dose is recommended when a short duration (up to 6 hours) of prophylaxis is required because it provides an adequate concentration for the duration of the procedure.
- If there is a moderate likelihood that a procedure will continue for longer than 6 hours, consider using a 5 mg/kg dose.

Principles of vancomycin prophylaxis

Avoid the routine use of vancomycin prophylaxis to reduce selection of vancomycin-resistant organisms. Vancomycin is not as effective as cefazolin for preventing postoperative skin and soft tissue infections caused by methicillin-susceptible *S. aureus* (MSSA).

Vancomycin is not as effective as cefazolin for preventing postoperative infections caused by MSSA.

Vancomycin should not be used for surgical prophylaxis, except for patients who have:

- Immediate or delayed severe hypersensitivity to penicillins
- An increased risk of postoperative infection caused by methicillin-resistant *S. aureus* (MRSA).

Vancomycin is used as a **replacement** for the cephalosporin component of a regimen in patients who are hypersensitive to penicillins. If there is a significant risk of contamination of the surgical site with Gram negative organisms, give vancomycin in **combination** with gentamicin.

Consider **adding** vancomycin to the cephalosporin-containing regimen if there is an increased risk of postoperative infection with MRSA. This includes the following circumstances:

- patients known or suspected to be infected or colonised preoperatively with MRSA (healthcare- or community-associated)
- patients with a history of infection or colonisation with MRSA

A postoperative vancomycin dose is only required in some cardiac and vascular surgeries, and lower limb amputation.

Multidrug-resistant Gram negative organisms

Prophylaxis for patients colonised with multidrug-resistant Gram negative organisms should be guided by the results of susceptibility testing—seek expert advice.

Preoperative decolonisation to reduce or eliminate faecal carriage of multidrug-resistant Gram negative organisms is not currently feasible.

Antibiotic administration

Route

The route of administration is usually parenteral (either IV or IM) but in some circumstances rectal or oral administration is appropriate. Applying antimicrobials (eg ointments, solutions, powders) to the surgical incision

to prevent surgical site infection is not recommended, because there is potential for harm (eg hypersensitivity reactions, bacterial resistance) and inadequate evidence to support a benefit.

Timing

A key consideration in surgical antibiotic prophylaxis is the achievement of effective plasma and tissue concentrations at the time of incision and for the duration of the surgical procedure, when the risk of bacterial contamination is maximal.

For short-acting antibiotics, such as cefazolin, the dose should be administered no more than 60 minutes before surgical incision. For antibiotics that are not short acting, the dose should be administered no more than 120 minutes before surgical incision.

> Surgical antibiotic prophylaxis must be administered before surgical incision.

Vancomycin requires a slow infusion, at a rate not exceeding **10 mg/min**. Start the vancomycin infusion within 15 to 120 minutes before surgical incision to ensure adequate blood and tissue concentrations at the time of incision and allow potential infusion-related toxicity to be recognised before induction. The infusion can be completed after surgical incision.

> Vancomycin requires a slow infusion but surgical incision can occur before the infusion is completed.

Administer IM antibiotics at the time of premedication for surgery.

Duration

> Continuing prophylactic antibiotics until residual surgical drains or intravascular or urinary catheters are removed is not supported by current evidence and increases the risk of adverse outcomes.

Successful prophylaxis requires effective antibiotic concentrations in blood and tissue at the time of incision and for the duration of the procedure. A

single preoperative dose of a parenteral drug is sufficient to achieve this for the majority of procedures. A second intraoperative dose may be necessary under the following circumstances:

- a significant delay in starting the operation
- a short-acting antibiotic is used (eg cefalotin, cefazolin, flucloxacillin) and the operation is prolonged beyond 3 to 4 hours (ie more than two half-lives of the drug)
- excessive blood loss during the procedure.

When measuring the time to a second intraoperative or postoperative dose, measure the interval from the time of the first preoperative dose rather than the beginning of the operation.

Postoperative doses are only required for specific indications (eg some cardiac and vascular surgeries, lower limb amputation) for which a benefit for up to 24 hours of prophylaxis has been demonstrated in clinical trials.

Complete prophylaxis within 24 hours of incision in **all** circumstances; continuing prophylactic antibiotics until residual surgical drains or intravascular or urinary catheters are removed is not supported by current evidence. Postoperative (IV or oral) antibiotics beyond 24 hours do not provide benefit and increase the risk of subsequent infections with resistant pathogens and *Clostridioides (Clostridium) difficile*.

Surgical antibiotic prophylaxis for specific procedures

Surgical antibiotic prophylaxis for specific procedures (Table 3.1)

Procedure	Antibiotic	Antibiotic if major beta-lactam allergy (immediate or delayed severe hypersensitivity)	Postoperative doses required
ABDOMINAL SURGERY			
Biliary surgery (including laparoscopic surgery)	cefazolin	clindamycin plus gentamicin	No
Colorectal surgery	cefazolin plus metronidazole	clindamycin plus gentamicin OR gentamicin plus metronidazole	No
Gastroduodenal or oesophageal procedure which enters GIT lumen	cefazolin	clindamycin plus gentamicin	No
Hernia repair with mesh[M]	cefazolin	vancomycin	No
Small intestinal surgery (non-endoscopic procedures only)	cefazolin (if obstruction is present, add metronidazole)	clindamycin plus gentamicin OR gentamicin plus metronidazole	No

BREAST SURGERY			
Breast cancer surgery, reduction mammoplasty, insertion of prosthetic material or reoperation of previous breast surgery[M]	cefazolin	vancomycin	No
BURNS SURGERY			
Burns or extensive skin loss undergoing surgical debridement	cefazolin in the first 48 hrs post burn. After 48 hrs add gentamicin	vancomycin in the first 48 hours post burn. After 48 hrs add gentamicin	No
GASTROINTESTINAL ENDOSCOPIC PROCEDURES			
ERCP	gentamicin	gentamicin	No
Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA)	cefazolin plus metronidazole	gentamicin plus metronidazole	No
Gastrostomy or jejunostomy tube insertion[M]	cefazolin: add metronidazole if there is an obstruction	vancomycin: add metronidazole if there is an obstruction	No
EAR, NOSE & THROAT / HEAD & NECK SURGERY			
Procedure involving incision through mucosal surfaces	cefazolin plus metronidazole	clindamycin	No

Clean procedure with insertion of prosthetic material	cefazolin	clindamycin	No
NEUROSURGERY			
Craniotomy (if prolonged procedure, re-exploration, microsurgery or prosthetic material inserted)	cefazolin	vancomycin	No
Insertion of shunts, ventricular drains or pressure monitors	cefazolin	vancomycin	No
IMPLANTABLE CARDIAC DEVICE INSERTION			
Permanent pacemaker	cefazolin	vancomycin plus gentamicin	No
OBSTETRIC & GYNAECOLOGICAL SURGERY			
Caesarean section	cefazolin	clindamycin	No
Surgical termination of pregnancy	doxycycline	N/A	No
Vaginal hysterectomy	cefazolin plus metronidazole	clindamycin	No
Abdominal hysterectomy	cefazolin	clindamycin	No

OPHTHALMIC SURGERY			
Cataract surgery	cefuroxime 1 mg intracamerally at the end of surgery Non-EML	consider vancomycin intracamerally at the end of surgery	chloramphenicol drops for up to 4 weeks post-surgery
ORTHOPAEDIC SURGERY			
Arthroscopic procedure	cefazolin	vancomycin	No
Prosthetic joint replacement, insertion of prosthetic/ transplant material or internal fixation of fracture[M]	cefazolin	vancomycin	No
PLASTIC SURGERY			
Clean-contaminated procedure[M]	cefazolin	vancomycin	No
UROLOGICAL SURGERY • If there is clinical evidence of a UTI or confirmed bacteriuria and the patient has not been treated preoperatively, give gentamicin 3 mg/kg IV, as a single preoperative dose. • If there is risk of entry into the bowel (eg ileal conduit or rectocele repair), add metronidazole to antibiotic regimen.			
Diagnostic cystoscopy	none	none	none

Endoscopic intrarenal or ureteric stone procedure or other endoscopic procedure in high-risk patient[M]	gentamicin (if gentamicin is contraindicated, use cefazolin)	N/A	No
TURP[M]	gentamicin (if gentamicin is contraindicated, use cefazolin)	N/A	No
Transrectal prostate biopsy	ciprofloxacin	N/A	No
Open or laparoscopic procedures – urinary tract NOT entered			
Procedure with insertion of prosthetic material[M]	cefazolin plus gentamicin (if gentamicin is contraindicated, seek expert advice)	vancomycin plus gentamicin	No
Open or laparoscopic procedures – urinary tract entered[M]			
General procedure	cefazolin plus gentamicin (if gentamicin is contraindicated, seek expert advice)	vancomycin plus gentamicin	No
Procedure with insertion of prosthetic material	cefazolin plus gentamicin (if gentamicin is contraindicated, seek expert advice)	vancomycin plus gentamicin	No

Radical prostatectomy	cefazolin plus gentamicin (if gentamicin is contraindicated, seek expert advice)	vancomycin plus gentamicin	No
VASCULAR SURGERY			
Brachial or carotid surgery with insertion of prosthetic material or vascular reconstruction surgery[M]	cefazolin	vancomycin (if at risk of Gram negative infection, add gentamicin)	24 hours (incl. perioperative dose)
Arteriovenous fistula formation[M]	cefazolin	vancomycin (if at risk of Gram negative infection, add gentamicin)	No
Lower limb amputation[M]	cefazolin (if limb is ischaemic, add metronidazole)	vancomycin plus gentamicin (if limb is ischaemic, add metronidazole)	24 hours (incl. perioperative dose)
[M] If the patient is known to be, or at high risk of MRSA colonisation or infection, ADD vancomycin to cefazolin.			
Where cefazolin is not available, use cefalotin (cephalothin). Where IV clindamycin is not available, in patients with a major beta-lactam allergy vancomycin may be used as an alternative; metronidazole should be added to vancomycin (but NOT clindamycin) where anaerobic cover is required.			

Surgical antibiotic prophylaxis for patients receiving antibiotics (Table 3.2)

<table>
<tr><th colspan="5">If the patient requires surgical antibiotic prophylaxis and is already on IV antibiotic(s) for treatment of infection prior to procedure:</th></tr>
<tr><td rowspan="2">Does the antibiotic have adequate spectrum of cover for pathogens likely to cause postoperative infection (staphylococcal and streptococcal cover in most cases)?</td><td rowspan="2">YES</td><td rowspan="2">Was the last dose of antibiotic administered within 60 minutes before incision?</td><td>YES</td><td>No additional surgical antibiotic prophylaxis required.</td></tr>
<tr><td>NO</td><td>Give perioperative dose of antibiotic(s) as above.</td></tr>
<tr><td>NO</td><td colspan="3">Give perioperative dose of antibiotic(s) as above.</td></tr>
</table>

Administration and timing of antibiotics for surgical prophylaxis (Table 3.3)

Antibiotic	Adult dose	Paediatric dose	Administration	Timing	Dose adjustment for weight	Redosing interval [NB1][NB2]
cefalotin (cephalothin)	2 g	50 mg/kg up to 2 g	IV bolus over 3-5 minutes	Within 60 minutes before incision	≥ 120 kg (actual body weight): 3 g IV	2 hours
cefazolin	2g	30mg/kg up to 2 g		Within 60 minutes before incision	≥ 120 kg (actual body weight): 3 g IV	4 hours
ciprofloxacin[RA]	500 mg	N/A	oral	Within 120 minutes before procedure	N/A	N/A
clindamycin	600mg	15mg/kg up to 600mg		Within 120 minutes before incision		6 hours
doxycycline	400 mg	N/A	oral	Take 60 minutes before procedure	N/A	N/A

gentamicin	2 mg/kg (5 mg/kg for vascular surgery)	2 mg/kg (5 mg/kg for vascular surgery)	IV bolus over 3-5 minutes	Within 120 minutes before incision	use ideal body weight	redosing not required [NB3]
metronidazole[RA]	500 mg	12.5 mg/kg up to 500 mg	IV infusion over 20 minutes	Start infusion within 120 minutes before incision	N/A	12 hours
vancomycin[RA]	15 mg/kg	15 mg/kg	IV infusion at 10 mg/minute	Start infusion within 120 minutes before incision	use actual body weight	12 hours

NB1: The redosing interval is the time at which a repeat intraoperative dose is required. The interval is measured from the initial preoperative dose, rather than the beginning of the operation. For a specific drug, the redosing interval is approximately equivalent to two half-lives.

NB2: The redosing intervals in this table only apply to patients with normal kidney function. For patients with impaired kidney function, seek expert advice.

NB3: Despite gentamicin's short half-life, redosing is not required because of its 'post-antibiotic effect', whereby bacterial killing continues for many hours after plasma concentration is undetectable.

4. Prevention of infection: endocarditis

General considerations

Infective endocarditis is a relatively uncommon illness with high morbidity and mortality. For many years, antibiotic prophylaxis was routinely administered before dental and other procedures to patients with cardiac conditions that carry a high lifetime risk of infective endocarditis. However, endocarditis after dental or other procedures is infrequent, so prophylaxis prevents very few cases. Infective endocarditis is more likely to result from bacteraemia associated with daily activities than from specific dental procedures, so the maintenance of good oral health and hygiene is more important than periprocedural antibiotics. No randomised controlled trial has been performed to determine the role of antibiotic prophylaxis, and there are no human studies showing that it can prevent endocarditis. Consequently, guidelines rely on expert consensus. Since 2002, many international guidelines have significantly reduced the number of indications for antibiotic prophylaxis for endocarditis.

In Fiji, antibiotic prophylaxis remains recommended for patients with a cardiac condition associated with the highest risk of adverse outcomes from endocarditis (see Box 4.1) who are undergoing certain dental procedures (see Table 4.1) or other procedures (see Table 4.2 and Table 4.3). **This includes patients with documented rheumatic heart disease.** All patients with cardiac abnormalities should be reminded to practise good oral hygiene and have regular dental check-ups, with preventive dental and periodontal treatment to ensure optimal oral health.

If, after careful evaluation of both the cardiac condition (see Box 4.1) and the procedure (see Tables 4.1, 4.2 and 4.3), antibiotic prophylaxis is considered necessary, give a single dose of antibiotic before the procedure. There is no proven value to giving a dose after the procedure.

Cardiac conditions associated with the highest risk of adverse outcomes from endocarditis (Box 4.1)

Antibiotic prophylaxis is recommended in patients with the following cardiac conditions who are undergoing certain dental procedures (see Table 4.1) or other procedures (see Table 4.2 and Table 4.3):

- rheumatic heart disease
- prosthetic cardiac valve or prosthetic material used for cardiac valve repair
- previous infective endocarditis
- congenital heart disease *but* only if it involves:
  - unrepaired cyanotic defects, including palliative shunts and conduits
  - completely repaired defects with prosthetic material or devices, whether placed by surgery or catheter intervention, during the first 6 months after the procedure (after which the prosthetic material is likely to have been endothelialised)
  - repaired defects with residual defects at or adjacent to the site of a prosthetic patch or device (which inhibit endothelialisation)

Procedures and antibiotic recommendations

Dental procedures

Bacteraemia associated with dental procedures usually involves viridans group streptococci, which are known to cause infective endocarditis. The key factors of a bacteraemia of oral origin are the incidence, magnitude and duration of viridans streptococcal bacteraemia. Whether a procedure necessitates prophylaxis depends on these factors.

Prophylaxis is not recommended for procedures with a low incidence of bacteraemia.

If a patient is having more than one procedure requiring antibiotic prophylaxis, dentists should plan treatment so that all of the procedures can be completed in a single or at most two sittings, if possible, thus avoiding the need for multiple antibiotic doses.

In patients taking long-term IM benzathine penicillin therapy for prevention of recurrent rheumatic fever, theoretical concerns exist that antibiotic resistance may develop in oral flora, rendering traditional beta-lactam based infective endocarditis prophylaxis ineffective. Accordingly, the 2018 *Fiji Guidelines for Acute Rheumatic Fever and Rheumatic Heart Disease Diagnosis, Management and Prevention* recommend that people who receive regular benzathine penicillin or oral penicillin for secondary ARF prophylaxis should be given a different antibiotic (azithromycin or, where indicated, vancomycin) for peri-procedural infective endocarditis prophylaxis. However, currently available evidence suggests that the amoxicillin susceptibility of viridans streptococci in the oral flora is not significantly affected by the benzathine penicillin prophylaxis. It is therefore the consensus expert opinion of the authors of these guidelines that amoxicillin remains an appropriate choice for endocarditis prophylaxis in this setting.

In contrast, in patients currently taking or who have recently taken a treatment course of beta-lactam therapy, evidence suggests that the amoxicillin susceptibility of viridans streptococci may be affected. Therefore, a non–beta-lactam antibiotic, such as clindamycin or azithromycin, may be considered for prophylaxis in this setting.

For standard prophylaxis, use:

amoxicillin 2 g (child: 50 mg/kg up to 2 g) orally, 1 hour before the procedure

OR

ampicillin 2 g (child: 50 mg/kg up to 2 g) IV, within the 60 minutes before the procedure

OR

ampicillin 2 g (child: 50 mg/kg up to 2 g) IM, 30 minutes before the procedure

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefalexin 2 g (child: 50 mg/kg up to 2 g) orally, 1 hour before the procedure [Non-EML]

OR

cefazolin [Non-EML]/ cefalotin 2 g (child: 30 mg/kg up to 2 g) IV, within the

60 minutes before the procedure

OR

cefazolin [Non-EML]/ cefalotin 2 g (child: 30 mg/kg up to 2 g) IM, 30 minutes before the procedure

For patients with **immediate or delayed severe** hypersensitivity to penicillins (and consider in patients who have recently taken a treatment course of beta-lactam therapy), use:

clindamycin 600 mg (child: 20 mg/kg up to 600 mg) orally, 60 to 120 minutes before the procedure [Non-EML]

OR

clindamycin 600 mg (child: 20 mg/kg up to 600 mg) IV over at least 20 minutes, within the 120 minutes before the procedure [Non-EML]

OR

azithromycin 500 mg (child: 15 mg/kg up to 500 mg), orally 30 to 60 minutes before the procedure

OR

vancomycin (adult and child) 15 mg/kg (up to 2 g in adults and 1 g in children) IV infusion (at a maximum rate of 10 mg/minute), started within 15 to 120 minutes before the procedure (infusion can continue during procedure)[1]

Dental procedures and their requirement for endocarditis prophylaxis in patients with a cardiac condition listed in Box 4.1 (Table 4.1)

[1] Note: This is different to the recommendation in the Fiji Guidelines for Acute Rheumatic Fever and Rheumatic Heart Disease Diagnosis, Management and Prevention 2018 which recommends vancomycin 20 mg/kg up to 500 mg

Prophylaxis always required	Prophylaxis required in some circumstances	Prophylaxis not required
• dental extractions • periodontal procedures including surgery, subgingival scaling and root planing • dental implant placement • gingival surgery • initial placement of orthodontic appliances • placement of orthodontic bands • replanting avulsed teeth • other surgical procedures (eg apicoectomy, biopsies, soft tissue surgeries) • surgical drainage of dental abscess (if not already on treatment antibiotics) • maxillary or mandibular osteotomies • surgical repair fractured jaw (mandible and maxilla) • Endodontic surgery and instrumentation	*Consider prophylaxis for the following procedures if multiple procedures are being conducted, the procedure is prolonged or periodontal disease is present:* • full periodontal probing for patients with periodontitis • supragingival calculus removal/ cleaning • rubber dam placement with clamps (where there is a risk of damaging gingiva) • restorative matrix band/ strip placement • endodontics beyond the apical foramen • placement of interdental wedges	• oral examination • infiltration and block local anaesthetic injection • restorative dentistry • supragingival rubber dam clamping and placement of rubber dam • intracanal endodontic procedures • removal of sutures • impressions and construction of dentures • orthodontic bracket placement and adjustment of fixed appliances • application of gels • intraoral radiographs • supragingival plaque removal • conservative treatment of fractured jaws (mandible and maxilla)

Upper and lower respiratory tract procedures

Bacteraemia associated with respiratory procedures predominantly involves viridans group streptococci, which are known to cause infective endocarditis. Prophylaxis is only recommended for procedures that have a high risk of bacteraemia (see Table 4.2) in patients with a specific cardiac condition (see Box 4.1).

For standard prophylaxis, antibiotic choice is the same as for dental procedures (see page 54).

In patients who undergo an invasive respiratory tract procedure to treat an established infection, such as drainage of an abscess, the antibiotic regimen administered should include a drug active against viridans group streptococci. If the infection is known or suspected to be caused by *Staphylococcus aureus*, the regimen should include a drug active against *S. aureus*.

Respiratory tract procedures and their requirement for endocarditis prophylaxis in patients with a cardiac condition listed in Box 4.1 (Table 4.2)

Procedure	Recommendation
invasive ear/nose/throat or respiratory tract procedure to treat an established infection (eg drainage of abscess)	Empirical antibiotic therapy should include a drug active against viridans group streptococci and, in some circumstances, *Staphylococcus aureus* (see relevant respiratory tract infection for appropriate regimen). Adjust timing of therapy so that an oral dose is administered 60 minutes before the procedure, an IM dose 30 minutes before the procedure, or an IV dose within the 60 minutes before the procedure.
tonsillectomy and/or adenoidectomy	Endocarditis prophylaxis recommended – use regimens given for regimens.

respiratory tract procedure where surgical antibiotic prophylaxis **is** routinely recommended (clean-contaminated surgery) (eg laryngectomy, pharyngectomy, complex septorhinoplasty)	Routine surgical antibiotic prophylaxis is sufficient (see Table 3.1 for regimen). Specific endocarditis prophylaxis is not required.
respiratory tract procedure where surgical antibiotic prophylaxis **is not** routinely recommended (eg tracheostomy, endotracheal intubation, bronchoscopy *with or without* incision or biopsy, tympanoplasty)	Neither surgical nor endocarditis antibiotic prophylaxis is required.

Genitourinary and gastrointestinal tract procedures

Bacteraemia associated with genitourinary and gastrointestinal tract procedures predominantly involves enterococci, which are known to cause infective endocarditis. However, antibiotic prophylaxis solely to prevent endocarditis is not routinely recommended for patients undergoing genitourinary or gastrointestinal tract procedures (see Table 4.3).

In patients with a cardiac condition listed in Box 4.1 **and** who:

- have an established genitourinary or intra-abdominal infection (see relevant infection for routine empirical regimen), or
- require surgical antibiotic prophylaxis for a genitourinary (see Table 3.1, page 47) or gastrointestinal tract procedure (see Table 3.1, page 45)

the regimen selected should include an antibiotic active against enterococci (eg amoxicillin, amoxicillin+clavulanate, piperacillin+tazobactam or vancomycin, depending on the clinical indication). If the regimen does not include an antibiotic active against enterococci, **add**:

ampicillin 2 g (child: 50 mg/kg up to 2 g) IV, within the 60 minutes before the procedure

OR

ampicillin 2 g (child: 50 mg/kg up to 2 g) IM, 30 minutes before the procedure.

For patients with hypersensitivity to penicillins use:

vancomycin (adult and child) 15 mg/kg up to 2 g in adults and 1 g in children, IV infusion (at a maximum rate of 10 mg/minute), started within 15 to 120 minutes before the procedure (infusion can continue during procedure)[2]

For patients colonised or infected with vancomycin-resistant enterococci, seek expert advice about an appropriate antibiotic regimen.

Genitourinary and gastrointestinal tract procedures and their requirement for endocarditis prophylaxis in patients with a cardiac condition listed in Box 4.1 (Table 4.3)

Condition or procedure	Recommendation
suspected or confirmed genitourinary tract or intra-abdominal infection (regardless of whether a procedure is involved)	Therapy should include an antibiotic active against enterococci (see relevant infection for routine empirical regimen). If the routine empirical regimen does not include an antibiotic active against enterococci, see text for recommendations. If undergoing a genitourinary or gastrointestinal tract procedure, adjust timing of the antienterococcal antibiotic so that an oral dose is administered 60 minutes before the procedure, an IM dose 30 minutes before the procedure, or an IV dose within the 60 minutes before the procedure.
genitourinary or gastrointestinal tract procedure where surgical antibiotic prophylaxis **is** routinely indicated	Surgical prophylaxis should include an antibiotic active against enterococci (see Table 3.1 for routine regimen). If routine surgical prophylaxis does not include an antibiotic active against enterococci, see text above for recommendations. Bacteriuria should be treated before all elective urological procedures.

[2] Note: This is different to the recommendation in the Fiji Guidelines for Acute Rheumatic Fever and Rheumatic Heart Disease Diagnosis, Management and Prevention 2018 which recommends vancomycin 20 mg/kg up to 500 mg

genitourinary or gastrointestinal tract procedure where surgical antibiotic prophylaxis **is not** routinely indicated (eg insertion or removal of intrauterine contraceptive device, transoesophageal echocardiography, routine endoscopy +/– biopsy, including colonoscopy)	Neither surgical nor endocarditis antibiotic prophylaxis is required. Bacteriuria should be treated before all elective urological procedures.
obstetric indications	Endocarditis antibiotic prophylaxis is not required. However, routine antibiotic prophylaxis is required for the following obstetric indications: surgical prophylaxis for caesarean section, prevention of group B streptococcal disease, prophylaxis in the setting of preterm prelabour rupture of membranes, and prophylaxis for third- or fourth-degree perineal tear. See relevant chapters for details.

Other procedures

Antibiotic prophylaxis solely to prevent endocarditis is not required for procedures other than those covered in this topic. However, for patients with a cardiac condition associated with a high risk of adverse outcomes from infective endocarditis (see Box 4.1) and who are undergoing incision and drainage of a local abscess or a surgical procedure through infected skin, skin structure or musculoskeletal tissue, it is particularly important that the therapeutic antibiotic regimen selected is active against the suspected or confirmed pathogens.

5. Prevention of infection: medical

Prevention of recurrent rheumatic fever

For more detailed information on the diagnosis and management of acute rheumatic fever (ARF) and rheumatic heart disease (RHD), see *Fiji Guidelines for Acute Rheumatic Fever and Rheumatic Heart Disease 2018*.

Patients with a history of ARF, or with RHD confirmed on echocardiogram, should receive antibiotic prophylaxis against *Streptococcus pyogenes* infection. Use:

benzathine penicillin IM every 4 weeks
adult and child 20 kg or more: 1.2 million units
child less than 20 kg: 600 000 units

OR (for patients refusing or unable to have IM benzathine penicillin)

phenoxymethylpenicillin (all ages) 250 mg orally, 12-hourly

Intramuscular benzathine penicillin is preferred, especially in remote areas, because it is more effective and patient adherence is more likely.

Administration of benzathine penicillin every 4 weeks is the standard prophylaxis recommended for most patients. Administration every 3 weeks is recommended for patients who have had a confirmed breakthrough of ARF despite adherence to benzathine penicillin given every 4 weeks, and for selected patients with moderate or severe carditis or a history of cardiac valve surgery (provided adherence to the more frequent injections is likely).

Assess patients reporting hypersensitivity to penicillins. For patients with true hypersensitivity to penicillins, use:

erythromycin 250 mg (child 1 month or older: 10 mg/kg up to 250 mg) orally, 12-hourly

The minimum recommended duration of antibiotic prophylaxis is:

- 10 years after the most recent episode of ARF, or until 21 years of age (whichever is longer)
- until 35 years of age in patients with moderate rheumatic heart disease

- until 40 years of age or lifelong in patients with severe rheumatic heart disease and in those who are having or have had cardiac valve surgery for rheumatic heart disease.

The decision to stop antibiotic prophylaxis should be based on clinical and echocardiographic assessment. Lifelong prophylaxis is preferable for patients who have had cardiac valve surgery.

Meningitis chemoprophylaxis

Neisseria meningitidis (meningococcus)

For more detailed information, see *Meningococcal Disease Public Health Management Guideline, March 2018*.

After an episode of *Neisseria meningitidis* (meningococcal) meningitis or other invasive disease (eg sepsis), clearance antibiotics are recommended for close contacts of the index case. The time period of interest is from 7 days prior to the onset of symptoms in the case to the time the case has completed 24 hours of appropriate antibiotic therapy. The highest risk is to contacts living within the same household as the case, which includes a household-like living arrangement like dormitories. Other "higher risk" contacts requiring chemoprophylaxis are included in the box below:

Meningococcal disease high-risk contacts (Box 5.1)

Household contacts	Including recent visitors who have stayed overnight in the 7 days before onset of the case's illness (or contacts in a household where the case has spent the night during that time). Includes roommates in dormitory style room
Travel contacts	Passengers seated in the seat immediately adjacent to the case on any journey more than 8 hours duration in the 7 days before onset of illness
Sexual contacts	All sexual contacts, including intimate kissing partners

Childcare / day-care contacts	Only children and staff at the childcare/day-care facility that were with the case in the same room group for 4 hours or longer in the 7 days before onset of illness
School or university	Only school or university contacts who can also be defined as household contacts eg boarding schools, or university dormitories/halls-of-residence, or school friends who have stayed the night
Healthcare worker contacts	Only medical personnel directly exposed to the case's nasopharyngeal secretions eg the person who intubated the case

Lower risk contact groups should be given information only. The Divisional Outbreak Response Team is in general responsible for contract tracing.

Disease can occur despite prophylaxis. It is essential to provide education about frequent, careful observation and the need for medical attention at the first signs of an unexplained illness. The risk is highest in the first 7 days following the onset of symptoms in the case, then falls rapidly but remains elevated for 30 days if chemoprophylaxis is not given.

Prophylaxis should ideally be given within 24 hours of identification of the index case; where unavoidable delays occur it may be given up to 30 days after the last exposure. Suitable regimens for *Neisseria meningitidis* (meningococcus) chemoprophylaxis are:

rifampicin 600 mg (neonate: 5 mg/kg; child: 10 mg/kg up to 600 mg) orally, 12-hourly for 2 days.

OR

ceftriaxone 250 mg (child 1 month to < 15 years: 125 mg) IM, as a single dose (preferred option for pregnant women)[3]

OR, as a less preferred option

ciprofloxacin 500 mg (child: 20mg/kg up to 500mg) orally, as a single dose

[3] IM injection of ceftriaxone is painful; reconstitute with lignocaine 1%.

Rifampicin interacts significantly with many drugs (eg with the oral contraceptive pill) and is contraindicated in pregnancy and severe liver disease.

Ciprofloxacin is no longer the first line preferred antibiotic for chemoprophylaxis due to the recent increase in resistant isolates within Fiji.

Vaccination may be considered by public health authorities in outbreak situations.

Haemophilus influenzae type b

Chemoprophylaxis of meningitis, or other infections caused by H*aemophilus influenzae type b (Hib)*, may be offered to close contacts of the index case. The presence or absence of young children within the household (and the vaccination status of those children) should be considered; seek expert advice.

A suitable regimen for *H. influenzae* type b (Hib) chemoprophylaxis is:

> rifampicin 600 mg (neonate: 10 mg/kg; child: 20 mg/kg up to 600 mg) orally, daily for 4 days

Rifampicin interacts significantly with many drugs (eg with the oral contraceptive pill) and is contraindicated in pregnancy and severe liver disease.

Although data are limited, ceftriaxone can be used if rifampicin is not suitable:

> ceftriaxone 1 g (child 1 month or older: 50 mg/kg up to 1 g) IM or IV, daily for 2 days[4]

Invasive group A streptococcal infection

For a **single probable or confirmed case of invasive group A streptococcal (iGAS) infection**, antibiotic prophylaxis for close contacts may be indicated; seek expert advice.

Consider giving antibiotic prophylaxis to all household contacts, but particularly the following (who are at higher risk of infection):

[4] IM injection of ceftriaxone is painful; reconstitute with lignocaine 1%.

- mother–neonate contacts, if either the mother or a neonate develops invasive group A streptococcal infection during the first 28 days after birth
- household contacts older than 75 years.

Antibiotic prophylaxis may be considered for other close contacts in some circumstances.

If antibiotic prophylaxis is given to close contacts, offer prophylaxis to all household members to prevent re-colonisation.

An **outbreak of invasive group A streptococcal infection** may be suspected if two or more epidemiologically linked cases (eg inpatient facility, childcare centre, community cluster) are confirmed. The appropriate local public health authority should be notified. The outbreak management plan should include consideration of a screening and antibiotic prophylaxis strategy.

Prophylaxis regimens for iGAS infection

If antibiotic prophylaxis is indicated for close contacts of patients with probable or confirmed invasive group A streptococcal infection, start prophylaxis as soon as possible; secondary cases usually occur shortly after the index case infection. The optimal antibiotic prophylaxis regimen for invasive group A streptococcal (iGAS) infection has not been determined—suitable regimens include:

benzathine penicillin intramuscularly, as a single dose,
adult or child 20 kg or more: 1.2 million units
neonate and child 6 kg or less: 300 000 units
child 6 kg to less than 12 kg: 450 000 units
child 12 kg to less than 16 kg: 600 000 units
child 16 kg to less than 20 kg: 900 000 units

OR

cefalexin 1 g (neonate and child: 25 mg/kg up to 1 g) orally, 12-hourly for 10 days Non-EML

For close contacts with **delayed nonsevere** hypersensitivity to penicillins, cefalexin can be used.

For close contacts with **immediate** or **delayed severe** hypersensitivity to

penicillins, antibiotic choice depends on the susceptibility of the isolate from the index case (as rates of resistance to non–beta-lactam antibiotics are higher). If susceptibility results are not available, a reasonable regimen is:

azithromycin 500 mg (child: 12 mg/kg up to 500 mg) orally, daily for 5 days

Prevention of infection in asplenic and hyposplenic patients

Fulminant sepsis can occur in patients who have had a splenectomy or who are hyposplenic. The risk of overwhelming infection is highest in children and immunocompromised patients, and the risk remains lifelong. The most common pathogens are encapsulated bacteria, especially *S. pneumoniae, N. meningitidis* and *H. influenzae* type b (Hib). Measures to prevent infection in asplenic and hyposplenic patients are education (including advice about the risk of overwhelming infection, and the provision of a fever action plan), immunisation and antibiotic prophylaxis.

Pneumococcal, meningococcal, Hib and influenza vaccination (where available) are recommended for asplenic and hyposplenic patients. For elective splenectomy, vaccination should be completed, if possible, at least 2 weeks before surgery.

The aim of antibiotic prophylaxis is to reduce the risk of *S. pneumoniae* infection. The optimal duration of prophylaxis remains controversial, but should be based on patient factors, including the risk of invasive pneumococcal disease, and drug tolerability and the likelihood of adherence. Factors associated with a high risk of invasive pneumococcal disease in asplenic and hyposplenic patients include:

- age younger than 16 years or older than 50 years
- previous invasive pneumococcal disease
- splenectomy for haematological malignancy, particularly if there is ongoing immunosuppression.

For prophylaxis, use:

amoxicillin 250 mg (child: 20 mg/kg up to 250 mg) orally, daily

OR

phenoxymethylpenicillin 250 mg (child younger than 1 year: 62.5 mg; 1 to 5 years: 125 mg) orally, 12-hourly

Due to the increasing prevalence of macrolide resistance in *S. pneumoniae*, penicillins are preferred for prophylaxis; if the patient reports hypersensitivity to penicillins, confirm the presence of hypersensitivity before using a macrolide. If required, use:

erythromycin 250 mg (child 1 month or older: 10 mg/kg up to 250 mg) orally, daily

OR

roxithromycin 150 mg (child: 4 mg/kg up to 150 mg) orally, daily Non-EML

The minimum recommended duration of antibiotic prophylaxis is:

- up to the age of 5 years in asplenic children
- up to the age of 5 years in children who are hyposplenic due to sickle cell anaemia or another congenital haemoglobinopathy
- at least 3 years after splenectomy
- at least 6 months after an episode of severe sepsis.

Consider lifelong prophylaxis for:

- asplenic patients who are severely immunosuppressed
- patients who have had a splenectomy for haematological malignancy, particularly those with ongoing immunosuppression
- patients who have had an episode of severe sepsis, particularly after a second episode.

Adherence to prophylactic therapy is often a problem. **Give patients clear instructions to seek prompt medical attention if a fever develops.** Give an "open card" for paediatric patients. All patients should also have an emergency supply of antibiotics to take before medical review in the event of a sudden onset of unexplained fever, particularly if medical review is not readily available.

For **adults**, suggested regimens include:

amoxicillin 2 g orally for the first dose, then 1 g 8-hourly until medical review

OR, for **delayed nonsevere** penicillin hypersensitivity, where available:

cefuroxime 500 mg orally 12-hourly until medical review Non-EML

OR, for **immediate** or **delayed severe** penicillin hypersensitivity, or where cefuroxime is not available, use:

erythromycin 1 g orally, 6-hourly until medical review

OR

roxithromycin 300 mg orally, daily until medical review Non-EML

For **children**, suggested regimens include:

amoxicillin+clavulanate 15 mg/kg amoxicillin component up to 500+125 mg orally, 8-hourly until medical review

For children hypersensitive to penicillins, seek expert advice.

Prevention of infection in patients with cirrhosis

Patients with upper gastrointestinal bleeding

Antibiotic prophylaxis is recommended for all inpatients who have cirrhosis with upper gastrointestinal bleeding.

Use:

ceftriaxone 1 g (child 1 month or older: 50 mg/kg up to 1 g) IV, daily[5]

OR

ciprofloxacin 400 mg (child: 10 mg/kg up to 400 mg) IV, 12-hourly

OR

ciprofloxacin 500 mg (child: 12.5 mg/kg up to 500 mg) oral, 12-hourly

OR

norfloxacin 400 mg (child: 10 mg/kg up to 400 mg) orally, 12-hourly Non-EML

Once the patient is haemodynamically stable and able to tolerate oral medication switch to oral prophylaxis. To reduce the emergence of antibiotic resistance, use the shortest possible duration of prophylaxis (IV + oral)—3 days is recommended as a minimum standard. The maximum duration is 7

[5] If ceftriaxone is unavailable, use cefotaxime 1 g (child: 25 mg/kg up to 1 g) IV, 8-hourly

days. Consider stopping antibiotic prophylaxis once bleeding has resolved. At this stage, switching to oral prophylaxis is not required if prophylaxis has already been given for the minimum duration (ie 3 days).

Prevention of spontaneous bacterial peritonitis

After a first episode of spontaneous bacterial peritonitis (SBP), the use of **secondary antibiotic prophylaxis** to prevent subsequent episodes of SBP in patients with ascites due to cirrhosis has been well established.

For secondary prophylaxis, use:

trimethoprim+sulfamethoxazole 160+800 mg (child 1 month or older: 4+20 mg/kg up to 160+800 mg) orally, daily

If trimethoprim+sulfamethoxazole is contraindicated or has previously failed, seek expert advice.

Pneumocystis jiroveci pneumonia

Pneumocystis jiroveci pneumonia (PJP) prophylaxis is recommended for some patients with marked immunosuppression (eg advanced HIV/AIDS, early renal transplantation), or receiving long-term high dose steroids (≥20mg prednisolone daily for 1 month or longer) in combination with a second immunosuppressive drug or additional cause of significant immunocompromise; seek expert advice.

Where indicated, the preferred regimen for prophylaxis is:

trimethoprim+sulfamethoxazole 80+400 or 160+800 mg orally, daily

OR

trimethoprim+sulfamethoxazole 160+800 mg orally, 3 times weekly

If trimethoprim+sulfamethoxazole is contraindicated use dapsone 100 mg daily, except in patients with **severe** hypersensitivity to trimethoprim+sulfamethoxazole (eg anaphylaxis, DRESS, SJS/TEN). Do **not** give dapsone because there is a possibility of cross-reactivity between dapsone and sulfamethoxazole. Seek specialist advice.

In HIV exposed/positive infants and children <5 years old: Start trimethoprim+sulfamethoxazole at 4-6 weeks of age or at first encounter

with healthcare system and continued until HIV is excluded. Use:

> trimethoprim+sulfamethoxazole 5+25 mg/kg up to 160+800 mg orally, daily

Refer to *Fiji HIV Care and Antiretroviral Therapy Guidelines, 3rd Edition 2019* for more information.

Postexposure prophylaxis against bloodborne viruses

Introduction

Bloodborne viruses include hepatitis B virus (HBV), hepatitis C virus (HCV), and HIV. Transmission of a bloodborne virus can occur after:

- percutaneous injury (eg needlestick injury, injury with a sharp object)
- contact of mucous membranes or nonintact skin (eg exposed skin that is chapped or abraded) with blood, tissue, or other potentially infectious body fluids (eg after sexual exposure).

This topic covers the general principles of postexposure prophylaxis (PEP) in adults; detailed local or regional protocols for occupational and non-occupational exposures should be available from individual health services. For PEP in children, seek expert advice.

Perform the following after all exposures to bloodborne viruses:

- Immediately treat the exposure site (eg wash thoroughly with soap and water).
- Obtain details of the exposure, including the time and nature of the exposure, and details of the exposed person and the source.
- Perform a risk assessment of the exposure, taking into account the type of exposure, the type and amount of fluid involved, the infectious status of the source (if known), and the susceptibility of the exposed person.
- Test the source (if known) for HBV surface antigen (HBsAg), HCV antibody and HIV antibody/antigen. Follow standard consent procedures.
- Test the exposed person for baseline HBV surface antibody, and retain the blood sample in case further testing (eg HBsAg, HCV antibody,

HIV antibody/antigen or baseline alanine aminotransferase [ALT]) is required.

- Provide counselling and follow-up for all exposed people. This should include information about the need for any special precautions to prevent secondary infection at work, in the household and in the community during the follow-up period.

Hepatitis B

The general principles of PEP against hepatitis B are summarised in Table 5.1 below.

Postexposure management of people exposed to hepatitis B virus (Table 5.1)

	Exposed person is immune [NB1]	**Exposed person is not immune [NB1]**
Source is HBsAg negative and unlikely to be in window period	No further follow-up testing required. No preventive measures required.	No further follow-up testing required. Start a course of hepatitis B vaccination as soon as possible, preferably within 24 hours of exposure.
Source is HBsAg positive or status unknown	No further follow-up testing required. No preventive measures required.	Test the exposed person for HBsAg at baseline, 3 months and 6 months after the exposure. Start a course of hepatitis B vaccination as soon as possible, preferably within 24 hours of exposure. Administer HBIG within 72 hours of exposure.

HBIG = hepatitis B immunoglobulin; HBsAg = hepatitis B virus surface antigen NB1: A person is immune if they have evidence of seroconversion to hepatitis B vaccination or natural immunity from past infection.		

Post-exposure prophylaxis is also required for neonates of mothers who are HBsAg positive. All such neonates should receive immunoglobulin ideally within 48 hours of birth in addition to vaccination.

Where immunoglobulin is required, use:

> HBV immunoglobulin 400 international units (child: see manufacturer's information) IM, as a single dose

A full course of hepatitis B vaccine should be given, starting at the same time as the immunoglobulin.

Pre-exposure

Hepatitis B vaccination is routinely given to:

- All newborns
- Those at increased risk of contracting infection eg health care workers (including clinical staff and workers who may be exposed to bodily fluids in a health care setting).

It is also recommended for:

- Sexual partners of HBsAg positive individuals
- HIV patients & their partners

In these cases, a full course of hepatitis B vaccine should be administered. The vaccine is given at 0, 1 and 6 months (except for infants – refer to immunisation schedule). For dosage, refer to manufacturer's instructions.

Hepatitis C

General principles:

- If the source is HCV antibody negative and unlikely to be in the window period, no further follow-up testing of the source or exposed person is required.
- If the source is HCV antibody positive, perform follow-up testing of the exposed person, including HCV antibodies at baseline and 4 months after exposure.
- Effective passive or active immunoprophylaxis is not currently available.

HIV

It is essential to seek expert advice from a physician experienced in the management of HIV or to consult local guidelines before initiating PEP against HIV infection.

General principles:

- If the source is HIV antibody/antigen negative and unlikely to be in the window period, no further follow-up testing of the source or exposed person is required.
- In all other circumstances, the exposed person should have HIV antibody testing at baseline, 6 weeks, 3 months and 6 months after exposure.
- The risk of HIV transmission from a single exposure is determined by the nature of the exposure, the likelihood that the source is HIV-positive (if their status is unknown), and other factors associated with the source and the exposed person.
- If PEP against HIV is indicated (source known to be HIV-positive, or at high risk of HIV infection if status unknown), it should be started as soon as possible after exposure and within 72 hours. If it has been longer than 72 hours since the exposure, PEP should only be offered in exceptional circumstances with expert advice.
- Inform people receiving PEP of the potential adverse effects of treatment and the possibility of drug interactions.

PEP for non-occupational exposures eligibility criteria:

- Less than 72 hours has elapsed since exposure; AND
- The exposed individual is not known to be HIV-positive; AND

- The person who is the source of the exposure is HIV-positive or has an unknown HIV status: AND
- A defined risk of exposure, such as:
  - Receptive vaginal or anal intercourse without a condom or with a condom that broke or slipped; OR
  - Receptive oral sex with ejaculation; OR
  - Sexual assault (including: contact between the perpetrator's blood or ejaculate and mucous membrane or non-intact skin during the assault; the person who was sexually assaulted was drugged or otherwise unconscious at the time of the alleged assault and is uncertain about the nature of the potential exposure; the person was gang-raped).

HIV PEP regimen for adults / adolescents above 10 years

tenofovir disoproxil fumarate (TDF) 300 mg orally, daily for 28 days

PLUS

lamivudine (3TC) 150 mg orally, 12-hourly OR 300 mg orally, daily for 28 days

PLUS

lopinavir+ritonavir (LPV/r) 400+100 mg (2x 200+50 mg tablets) orally, 12-hourly for 28 days

PLUS

atazanavir+ritonavir (ATV/r) 300+100 mg orally, daily for 28 days

Where available dolutegravir (DTG), raltegravir (RAL), darunavir+ritonavir (DRV/r) or efavirenz (EFV) may be considered as alternative options. **Seek expert advice.**

Enhanced adherence counselling is suggested.

HIV PEP regimen for children ≤10 years:

zidovudine (AZT) 180-240 mg/m^2 up to 300 mg orally, 12-hourly for 28 days

PLUS

lamivudine (3TC) 4 mg/kg up to 150 mg orally, 12-hourly for 28 days

PLUS

lopinavir+ritonavir (LPV/r) 320-350 mg/m^2 up to 400+100 mg orally, 12-hourly for 28 days

Where an age-appropriate alternative is available, atazanavir+ritonavir A(TV/r), dolutegravir (DTG), raltegravir (RAL), darunavir (DRV), efavirenz (EFV) and nevirapine (NVP) may be considered as alternative options. **Seek expert advice.**

Enhanced adherence counselling is suggested.

If there is exposure to drug-resistant HIV or adverse effects of the above regimens limit their use, seek expert advice.

For further information about assessing the risk of HIV transmission and regimens for PEP against HIV, see the *Fiji HIV Care and Antiretroviral Therapy Guidelines 3rd Edition 2019*.

Prophylaxis in obstetric patients

Prevention of neonatal *Streptococcus agalactiae* (group B streptococcus) disease

Streptococcus agalactiae (group B streptococcus [GBS]) is a commensal organism of the gastrointestinal and genital tracts in up to 30% of healthy women of childbearing age. Other than in pregnancy, it is generally an incidental finding and should be ignored unless there are symptoms of vaginitis or evidence of a urinary tract infection.

The use of intrapartum benzylpenicillin or ampicillin for pregnant women who are colonised with GBS reduces vertical transmission, with a reduction in the incidence of early onset neonatal GBS infections. Guidelines for the prevention of early onset GBS disease describe risk-based and screening approaches to identifying pregnant women who need intrapartum prophylaxis. If screening is undertaken, GBS carriage is best predicted by antenatal screening at 35 to 37 weeks' gestation (using both low vaginal and anorectal swabs, placed into a selective enrichment broth medium).

Intrapartum antibiotic prophylaxis is indicated in the following situations:

- GBS identified by the results of screening cultures from either vaginal or rectal swabs in late gestation during the current pregnancy
- invasive GBS disease in a neonate from a previous pregnancy
- GBS bacteriuria detected during any trimester of the current pregnancy
- unknown antepartum GBS status (cultures not performed, results incomplete or not available) **and** any of the following:
  - intrapartum fever (38ºC or more)
  - preterm onset of labour (before 37 weeks' gestation)
  - prolonged rupture of membranes (18 hours or longer)

In these situations, antibiotic therapy should be started on admission to hospital for labour or rupture of membranes, ideally at least 4 hours before delivery, and continued until the neonate is delivered.

For intrapartum antibiotic therapy, use:

benzylpenicillin 5 million units (3 g) IV, for the first dose, then 3 million units (1.8 g) IV, 4-hourly until delivery

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefazolin 2 g IV, 8-hourly until delivery[6] Non-EML

For patients with **immediate or delayed severe** hypersensitivity to penicillins if the GBS isolate is known to be susceptible to clindamycin, use:

clindamycin 600 mg IV, 8-hourly until delivery Non-EML

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins if the GBS isolate is resistant to clindamycin or the results of susceptibility testing are not available, use:

vancomycin 15 to 20 mg/kg actual body weight up to 2 g IV infusion; see appendix for dosing intervals and administration

If intra-amniotic infection (chorioamnionitis) is suspected clinically (ie maternal fever with other clinical manifestations such as uterine tenderness and purulent amniotic fluid), the antibiotic regimen should be broadened from prophylaxis to treatment, and must include a drug active against GBS (eg gentamicin plus ampicillin) – seek expert advice.

[6] If cefazolin is unavailable, use cefalotin 2 g IV, 6-hourly

Premature rupture of membranes

Preterm prelabour rupture of membranes (PPROM) (ie membrane rupture before 37 weeks' gestation and before the onset of uterine contractions) is the commonest cause of preterm birth. The use of antibiotic prophylaxis in preterm labour in the absence of membrane rupture is not supported by evidence. For PPROM with suspected or confirmed intra-amniotic infection (chorioamnionitis) (ie fever 38°C or more) with other clinical manifestations such as uterine tenderness and purulent amniotic fluid), treat as for intra-amniotic infection (chorioamnionitis) – seek expert advice.

Pre-term:

Use:

ampicillin 2 g IV, 6-hourly for 48 hours

Followed by:

amoxicillin 250 mg orally, 8-hourly

PLUS

erythromycin 250 mg orally, 6-hourly

Total duration of therapy (IV + oral) is usually 7 days or until delivery (whichever is sooner).

For patients hypersensitive to penicillins, give erythromycin as a single drug for 10 days.

At term:

Start antibiotic therapy and induce labour. Use:

ampicillin 2 g IV, 6-hourly

Continue antibiotic coverage for pre-labour, during labour and post-labour for a total of 72 hours.

Prophylaxis for caesarean section

See caesarean section in Table 3.1, page 46.

Prophylaxis for third- or fourth-degree perineal tear

Give a single preprocedural dose of antibiotic(s) before the repair of an obstetric anal sphincter injury (OASIS) (including third- or fourth-degree perineal tears). Use (including for patients with **delayed nonsevere** hypersensitivity to penicillins):

cefazolin 2 g IV, as early as possible[7] Non-EML

PLUS

metronidazole 500 mg IV, as early as possible

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, as a single agent, use:

clindamycin 600 mg IV, as early as possible

See Table 3.3 for redosing intervals but do not give additional intravenous doses once the procedure is completed.

The role of postoperative antibiotic therapy is unclear, but therapy is recommended following anal sphincter repair because infection in this setting carries a high risk of anal incontinence and fistula formation. Use:

amoxicillin+clavulanate 500+125 mg orally, 8-hourly for 5 days

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefalexin 500 mg orally, 6-hourly for 5 days Non-EML

PLUS

metronidazole 400 mg orally, 12-hourly for 5 days

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

trimethoprim+sulfamethoxazole 160+800 mg orally, 12-hourly for 5 days

PLUS

[7] If cefazolin is unavailable, use cefalotin 2 g IV

metronidazole 400 mg orally, 12-hourly for 5 days

There is no evidence to recommend antibiotic prophylaxis for other indications following vaginal delivery.

6. Severe sepsis and septic shock

Sepsis definitions

Sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection. Important clinical features include an acutely altered mental status, tachypnoea, tachycardia and hypotension, often associated with a fever and elevated white cell count (WCC). Lactate is also frequently elevated. In septic shock, the sepsis is associated with persistent hypotension despite adequate fluid resuscitation, requiring vasopressor support; the associated circulatory and metabolic/cellular dysfunction is profound enough to cause substantially increased mortality.

Initial management of severe sepsis and septic shock in adults

Early recognition of severe sepsis and septic shock is vital, because rapid initiation of antibiotic therapy and control of the source, together with appropriate resuscitation and organ support, saves lives.

For patients with severe sepsis or septic shock, collect two sets of blood samples (ie four bottles, ideally from two different sites) for cultures, and administer appropriate broad-spectrum antibiotics, **within one hour** of Emergency Department presentation or, for ward-based patients, recognition.

> Collect two sets of blood samples for cultures, and administer appropriate broad-spectrum antibiotics, within one hour.

Begin initial resuscitation of a patient with severe sepsis or septic shock with rapid assessment and appropriate support of airway, breathing and circulation—the 'ABC' approach. This may include administration of high-flow oxygen. Consider intubation and mechanical ventilation if gas exchange is inadequate.

Hypotension or organ hypoperfusion should be managed initially with IV fluid boluses. If hypotension is not responsive to fluid resuscitation, give vasopressor support to maintain the mean arterial pressure (MAP) and

transfer to a divisional hospital.

Empirical therapy in adults – no obvious source of infection

Staphylococcus aureus is the most common cause of septicaemia in Fiji, but Gram negative organisms are also frequently implicated. For empirical therapy use:

cloxacillin 2 g IV, 4-hourly

PLUS

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients

For patients with **delayed nonsevere** hypersensitivity to penicillins, **replace** cloxacillin with:

cefazolin 2 g IV, 6-hourly [8] Non-EML

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, **replace** cloxacillin with:

vancomycin IV infusion: 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals

If typhoid fever, leptospirosis or meningococcal disease are suspected, **add** to the above regimen (except in **immediate** or **delayed severe** hypersensitivity to penicillins):

ceftriaxone 2 g IV, daily[9]

Seek expert advice for patients with **immediate** or **delayed severe** penicillin hypersensitivity.

If infection with methicillin-resistant *Staphylococcus aureus* (MRSA) is suspected (see Box 6.1), **add**:

[8] If ceftriaxone is unavailable, for suspected leptospirosis or meningococcal disease benzylpenicillin 2 million units IV, 6-hourly may be used as a less preferred alternative
[9] If cefazolin is unavailable, use cefalotin 2 g (child: 50 mg/kg up to 2 g) IV 4-hourly

vancomycin IV infusion: 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals

Risk factors for infection with MRSA (Box 6.1)

- Previous colonisation or infection with MRSA, particularly if recent or associated with the current episode of care
- Frequent stays, or a prolonged current stay, in a hospital with a high prevalence of MRSA, particularly if associated with antibiotic exposure or recent surgery

Empirical therapy may need to be modified if a patient has risk factors for infection with a multidrug-resistant Gram negative organism (for risk factors, see Box 6.2). For empirical therapy, seek expert advice.

Risk factors for infection with a multidrug-resistant Gram negative organism (such as ESBL-producing organisms) (Box 6.2)

- recent (within 6 months) international travel to areas with a high prevalence of multidrug-resistant Gram negative organisms (eg Asia, including India)
- prolonged hospitalisation
- previous colonisation or infection with a resistant Gram negative organism

Empirical therapy in children – no obvious source of infection

Neonatal sepsis

Any neonate (up to 1 months of age) who is unwell must be considered at risk of sepsis. Symptoms and signs of neonatal sepsis may be non-specific including, poor tolerance to handling, hypoglycaemia. The consequences of untreated sepsis are devastating. Commence antibiotic treatment as soon as possible after taking cultures.

Babies with confirmed sepsis should generally be managed in the Special Care Nursery (SCN) where they can be observed closely. However, in some cases where antibiotics are commenced while sepsis is being ruled out it may be appropriate for the baby to be managed in the post-natal ward to keep mother and baby together.

> All babies with suspected sepsis should be under the care of a paediatric consultant.

Early onset sepsis – within the first 72 hours of life

Risk factors

Maternal risks and signs

- Maternal GBS colonisation
- Premature, preterm or prolonged rupture of membranes (>18 hours)
- Maternal urinary tract infections
- Maternal fever
- Mother on antibiotics
- Poor prenatal care
- Chorioamnionitis (maternal uterine tenderness, fever)
- Multiple obstetric procedures, including cervical sutures
- History of GBS infection in previous infant

Neonatal risks and signs

- Prematurity
- Low birth weight
- Difficult delivery
- Birth asphyxia
- Meconium staining
- Congenital abnormalities
- Foetal distress

Investigations include full blood count, glucose, CRP where available, blood cultures (at least 1 mL). Consider doing lumbar puncture (LP).

Start empirical antibiotics, use:

gentamicin 5 mg/kg IV – see appendix for dosing frequency

PLUS

ampicillin 50 mg/kg IV

First week of life: 12-hourly

Week 2-4 of life: 8-hourly

OR, if ampicillin is not available

benzylpenicillin 100 000 units/kg (60 mg/kg) IV

First week of life: 12-hourly

Week 2-4 of life: 6-hourly

Change antibiotics according to sensitivity results. Follow up blood cultures after 48 to 72 hours. If cultures are negative and sepsis is unlikely **stop** antibiotics. If there is a strong suspicion of sepsis despite negative cultures complete 7 days of treatment.

For empirical therapy for term neonates with early onset sepsis or septic shock who are **severely unwell** and may have **meningitis** (not ruled out by lumbar puncture), use:

cefotaxime 50 mg/kg IV

First week of life: 8-hourly

Week 2-4 of life: 6-hourly

PLUS

benzylpenicillin 100 000 units/kg (60 mg/kg) IV

First week of life: 12-hourly

Week 2-4 of life: 6-hourly

Late onset sepsis - from 72 hours of life

Do full blood count, blood cultures (at least 1 mL), glucose, urea & electrolytes, chest X-ray, suprapubic urine aspirate (SPA), and **lumbar puncture unless contraindicated** - discuss with consultant.

Suspect meningitis if baby has convulsions, opisthotonus, unconsciousness, lethargy or bulging anterior fontanelle.

For community-acquired late onset neonatal sepsis, use:

gentamicin 5 mg/kg IV – see appendix for dosing frequency

PLUS

ampicillin 50 mg/kg

First week of life: 12-hourly

Week 2-4 of life: 6-hourly

If suspicion of *Staphylococcal* infection, **add**

cloxacillin 50 mg/kg

First week of life: 12-hourly

Week 2-4 of life: 8-hourly

For suspected or confirmed meningitis, or if not responding to initial therapy, use:

ampicillin ***100 mg/kg***

First week of life 12-hourly

Week 2-4 of life: 8-hourly

PLUS

cefotaxime 50 mg/kg

First week of life: 8-hourly

Week 2-4 of life: 6-hourly

Duration of antibiotics

- 7 to 10 days for pneumonia and proven neonatal sepsis
- 7 days for strong suspicion of sepsis (culture-negative)
- 14 days for Group B streptococcal meningitis
- At least 21 days for Gram negative meningitis
- For neonates at increased risk of **MRSA** infection (eg exposed to a care-giver colonised with MRSA) add vancomycin to the above regimens.

For nosocomial infections choice of antibiotics depend on the prevalent organisms in NICU and their sensitivities. Outbreaks will dictate temporary changes in above empiric regimens.

Infants and children

Empirical therapy in infants (> 1 month) and children – no obvious source of infection

ampicillin 50 mg/kg up to 2 g IV, 6-hourly

PLUS

gentamicin IV: see appendix for dose and dosing intervals

If a skin or bone source is suspected, **replace** gentamicin with:

cloxacillin 50 mg/kg up to 2 g IV, 4-hourly

For patients with **delayed nonsevere** hypersensitivity to penicillins, **replace** ampicillin or cloxacillin with:

cefazolin 50 mg/kg up to 2 g IV, 8-hourly[10] Non-EML

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, **replace ampicillin** with:

chloramphenicol 25 mg/kg up to 1 g IV 6-hourly

OR

erythromycin 25 mg/kg up to 1 g IV 6-hourly

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins where a skin or bone source is suspected, **replace cloxacillin** with:

vancomycin IV infusion: 15 mg/kg actual body weight up to 750 mg 6-hourly; see appendix for additional dosing information

If typhoid fever, leptospirosis or meningococcal disease are suspected, **add** to any of the above regimens:

ceftriaxone 50 mg/kg up to 2 g IV, 12-hourly

Seek expert advice for patients with **immediate** or **delayed severe** penicillin hypersensitivity.

[10] If cefazolin is unavailable, use cefalotin 50 mg/kg up to 2 g IV, 6-hourly

If infection with methicillin-resistant *Staphylococcus aureus* (MRSA) is suspected in children with sepsis or septic shock, **add** vancomycin to any of the above regimens:

vancomycin IV infusion: 15 mg/kg actual body weight up to 750 mg 6-hourly; see appendix for additional dosing information

Empirical therapy may need to be modified if a patient has risk factors for infection with a multidrug-resistant Gram negative organism (for risk factors, see Box 6.2). For empirical therapy, seek expert advice.

Septic shock in infants (> 1 month) and children

See the *PICU Clinical Practice Guidelines 2019* for further information on the management of shock in children. For empirical treatment where there is no obvious source of infection, use:

ceftriaxone 50 mg/kg up to 1 g IV, 12-hourly

PLUS

cloxacillin 50 mg/kg up to 2 g IV, 6-hourly

If infection with methicillin-resistant *Staphylococcus aureus* (MRSA) is suspected in children with sepsis or septic shock, **add** vancomycin:

vancomycin IV infusion: 15 mg/kg actual body weight up to 750 mg 6-hourly; see appendix for additional dosing information

Empirical therapy may need to be modified if a patient has risk factors for infection with a multidrug-resistant Gram negative organism (for risk factors, see Box 6.2). For empirical therapy, seek expert advice.

Sepsis in neutropaenic patients (neutrophils less than 0.5 x 10^9/L)

For sepsis in neutropaenic children, also refer to the paediatric protocol: I*nfection in the Immunocompromised Patient*.

All neutropenic patients with suspected or proven septicaemia should be referred to a divisional hospital for ongoing specialist care.

Antibiotic therapy is aimed primarily at *Enterobacteriaceae and Pseudomonas*

aeruginosa, but Gram positive organisms including *Staphylococcus aureus* must also be covered. Use:

piperacillin+tazobactam 4+0.5 g (child: 100+12.5 mg/kg up to 4+0.5 g) IV, 6-hourly

PLUS

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

Alternatively, use:

ceftazidime 2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly Non-EML

PLUS

cloxacillin 2 g (child: 50 mg/kg up to 2 g) IV, 4-hourly

PLUS, if clinically indicated for anaerobic cover

metronidazole 500 mg (child: 12.5 mg/kg up to 500 mg) IV, 8-hourly OR metronidazole 400 mg (child: 10 mg/kg up to 400 mg) orally, 12-hourly

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

ceftazidime 2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly Non-EML

PLUS

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

PLUS, if clinically indicated for anaerobic cover

metronidazole 500 mg (child: 12.5 mg/kg up to 500 mg) IV, 8-hourly OR metronidazole 400 mg (child 10 mg/kg up to 400 mg) orally, 12-hourly

If ceftazidime is not available, **replace** in either of the above regimens with:

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

PLUS

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

PLUS, if clinically indicated for anaerobic cover

metronidazole 500 mg (child: 12.5 mg/kg up to 500 mg) IV, 8-hourly OR metronidazole 400 mg (child 10 mg/kg up to 400 mg) orally, 12-hourly

Empirical therapy may need to be modified if a patient has risk factors for infection with a multidrug-resistant Gram negative organism (for risk factors, see Box 6.2), seek expert advice.

Empirical therapy - source of infection clinically apparent

When the source of sepsis or septic shock is apparent (eg sepsis or septic shock that develops in a patient with pneumonia), antibiotic choice is guided by the usual susceptibility of common pathogens associated with the source.

However, in critically ill patients with severe sepsis or septic shock (usually those requiring intensive care support), dose modification is frequently necessary to achieve adequate drug exposure. For example:

- **cefotaxime** - use an increased dose, ie cefotaxime 2 g (child: 50 mg/kg up to 2 g) IV, 6- or 8-hourly depending on the likely source of infection.
- **ceftriaxone** - use a 12-hourly dosing regimen, ie ceftriaxone 1 g (child: 25 mg/kg up to 1 g) IV, 12-hourly.
- **cefazolin** Non-EML - use a 6-hourly dosing regimen for adults, ie cefazolin 2 g IV, 6-hourly; use an 8-hourly dosing regimen for children, ie 50 mg/kg up to 2 g IV 8-hourly.
- **cefalotin** - use a 4-hourly dosing regimen for adults, ie cefalotin 2 g IV, 4-hourly; use a 6-hourly dosing regimen for children, ie 50 mg/kg up to 2 g IV 6-hourly.

- **cloxacillin** - use a 4-hourly dosing regimen, ie cloxacillin 2 g (child: 50 mg/kg up to 2 g) IV, 4-hourly.
- **gentamicin –** use an increased dose, ie for adults (CrCl > 60 mgL/minute) 7 mg/kg, see appendix 1 for further information on calculating doses and dosing intervals including in critically ill patients with CrCl 60 mL/min or less or unknown renal function.
- **piperacillin+tazobactam** - consider giving the 6-hourly dose of piperacillin+tazobactam as an extended infusion over 3 to 4 hours (this increases the percentage time above minimum inhibitory concentration [MIC] and may achieve better outcomes).
- **vancomycin** - consider a 25 to 30 mg/kg vancomycin loading dose for adults in ICU setting, see appendix 2.

Treatment recommendations for common sources of sepsis:

- Source of infection: **lung**
  - Treat as for severe pneumonia (see page 116).
- Source of infection: **urinary tract**
  - Treat as for severe pyelonephritis (see page 246).
- Source of infection: **biliary or gastrointestinal tract**
  - Treat as for intra-abdominal infection (see page 189).
- Source of infection: **female genital tract**
  - Treat as for severe pelvic inflammatory disease – either sexually or non-sexually acquired as appropriate (see page 262).
- Source of infection: **skin**
  - Carbuncle and cellulitis: treat as for severe cellulitis (see page 212).
  - Diabetic foot infection: treat as for severe diabetic foot infection (see page 225).

Source of infection: intravenous cannulae, including central venous catheters

Coagulase-negative staphylococci and *Staphylococcus aureus* are the most common causes of sepsis associated with intravascular devices. Many other organisms, including Gram negative rods and Candida species, also cause infection.

Remove peripheral intravascular catheters immediately if an intravascular device source of infection is suspected.

A central catheter should also usually be removed if possible, after consultation with the treating team. Send the tip, together with two sets of blood samples (ie four bottles) taken from another site, for cultures. Rarely, catheter salvage can be attempted—seek expert advice.

Initial empirical therapy targets *S. aureus* and aerobic Gram negative organisms. Use:

cloxacillin 2 g (child: 50 mg/kg up to 2 g) IV, 4-hourly

PLUS

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefazolin 2 g (child: 50mg/kg up to 2g) IV, 6-hourly[11]

PLUS

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

PLUS

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

If MRSA or coagulase-negative *Staphylococcus* is the suspected cause of sepsis, **add** vancomycin to the above regimens. Use:

[11] If cefazolin is unavailable, use cefalotin 2 g (child: 50 mg/kg up to 2 g) IV 4-hourly

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

If *Candida* species is isolated from blood cultures, seek expert advice.

The results of susceptibility testing guide ongoing therapy. If susceptibility results are not available by 72 hours and empirical IV therapy is still required, cease the gentamicin-containing regimen and seek expert advice.

Intravenous cannula-related sepsis may resolve quickly after the infected device is removed if it is caused by a relatively low virulence pathogen (eg coagulase-negative staphylococci), so continuing antimicrobial therapy may not be necessary. If infection is caused by a more virulent pathogen (eg *S. aureus* or *Candida* species), therapy must be prolonged because deep-seated infection such as endocarditis, osteomyelitis or endophthalmitis may develop.

For patients with sepsis or septic shock **requiring ICU support**, remove the line (if alternative access is available) and use meropenem and vancomycin to cover ESBL Gram negative organisms and MRSA pending culture and sensitivity results.

Directed therapy (ie organism identified)

Gram positive bacilli

Listeria monocytogenes

For severe sepsis caused by *Listeria monocytogenes*, see *Listeria* meningitis page 182 for drug choice.

Gram positive cocci

Staphylococcus aureus

Staphylococcus aureus bacteraemia is associated with significant morbidity and mortality. Take repeat blood cultures 48 to 72 hours after antibiotic therapy is started and repeat at two-day intervals until cultures are negative. Continue antibiotic therapy (in adults intravenously) for a **minimum of 14 days**. Close review is essential to detect relapse or the development of metastatic infection (eg infective endocarditis; osteomyelitis).

For methicillin-susceptible *S. aureus* (MSSA), use:

cloxacillin 2 g (child: 50 mg/kg up to 2 g) IV, 4- to 6-hourly

Use a 4-hourly cloxacillin dosing interval for critically ill patients with severe sepsis or septic shock (usually those requiring intensive care support).

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefazolin (adult) 2 g IV, 6- to 8-hourly

cefazolin (child) 50 mg/kg up to 2 g IV, 8-hourly [12] Non-EML

Use a 6-hourly cefazolin dosing interval for critically ill **adults** with severe sepsis or septic shock (usually those requiring intensive care support).

For methicillin-resistant *S. aureus* (MRSA), or for patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

For the treatment of *S. aureus* bacteraemia use IV antibiotics for the entire duration of therapy.

The **duration** of antibiotic therapy depends on whether the patient has complications of infection (eg metastatic spread, endocarditis). Patients meeting **all** of the following criteria have uncomplicated *S. aureus* bacteraemia and are treated for 14 days only:

- rapid resolution of fever
- negative blood culture results 48 to 72 hours after starting appropriate antibiotics
- normal valvular morphology and no evidence of valvular lesions, regurgitation or endocarditis on transthoracic echocardiogram (TTE) or transoesophageal echocardiogram (TOE)
- an identifiable source of infection that has been removed (eg IV catheter, drainable skin abscess)
- no evidence of a metastatic focus (eg vertebral osteomyelitis, endocarditis)

[12] If cefazolin is unavailable, use cefalotin 2 g IV 4-hourly (child: 50 mg/kg up to 2 g IV 6-hourly)

- no intravascular prosthetic material (eg pacemaker, prosthetic cardiac valve, prosthetic arteriovenous graft)
- no significant immunocompromise.

In **adults**, if all of the above criteria are not met then the patient has a complicated infection and a minimum of 4 weeks of IV therapy is required. Criteria for diagnosing complicated infection in **children** are not as well defined—seek expert advice on the duration of therapy and whether oral continuation therapy may be appropriate. Patients with complicated infections, or who are not improving as expected, should be referred to a divisional hospital for further management.

In *S. aureus* sepsis associated with an intravascular device, the device should be removed promptly where possible.

In **adults**, infective endocarditis can complicate *S. aureus* bacteraemia and must be excluded by echocardiogram.

In **children**, do not perform echocardiography unless the child has a known intracardiac or valvular abnormality, prolonged fever or persistently positive blood cultures.

Haematogenous seeding of prosthetic material (eg prosthetic joints) by *S. aureus* results in metastatic infection at the prosthetic site. See, for example, prosthetic valve endocarditis page 182.

Streptococcus pyogenes

Streptococcus pyogenes (group A streptococcus) causes a range of infections including severe, invasive disease such as necrotising fasciitis, toxic shock syndrome, pneumonia and bacteraemia. *S. pyogenes* bacteraemia usually follows infection at a primary site, most commonly the skin or soft tissues. When *S. pyogenes* bacteraemia is associated with necrotising fasciitis, urgent surgical debridement is required.

Use:

benzylpenicillin 3 million units (1.8 g) (child: 75 000 units/kg up to 3 million units) IV, 4-hourly

PLUS

clindamycin 600 mg (child: 15 mg/kg up to 600 mg) IV or oral, 8-hourly

for a minimum of 72 hours until organ function has significantly improved Non-EML

For patients with **delayed nonsevere** hypersensitivity to penicillins, **replace** benzylpenicillin in the above regimen with:

cefazolin (adult) 2 g IV, 6- to 8-hourly

cefazolin (child) 50 mg/kg up to 2 g IV, 8-hourly[13] Non-EML

Use a 6-hourly cefazolin dosing interval for critically ill **adults** with severe sepsis or septic shock (usually those requiring intensive care support).

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, **replace** benzylpenicillin in the above regimen with vancomycin. Use:

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

Once the patient has clinically improved, switch to oral therapy. Use:

amoxicillin 1 g (child: 25 mg/kg up to 1 g) orally, 8-hourly

For patients with **delayed nonsevere** hypersensitive to penicillins, therapy may be completed with oral cefalexin or for **immediate** or **delayed severe** hypersensitivity, with clindamycin.

Data to inform the duration of antibiotic therapy are limited—seek expert advice. A total treatment duration of 7 to 10 days (IV + oral) is often adequate.

Consider prophylaxis for close contacts of patients with invasive *S. pyogenes* infections, including bacteraemia (see page 66).

Gram negative enteric bacteria

For severe sepsis or septic shock caused by Gram negative enteric bacteria (eg *E. coli*, *Klebsiella* species, *Proteus* species), treat according to the results of susceptibility testing, when available. Until then, use:

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese

[13] If cefazolin is unavailable, use cefalotin 2 g IV 4-hourly (child: 50 mg/kg up to 2 g IV 6-hourly)

patients, and dosing in children

OR

ceftriaxone 2 g (child 1 month or older: 50 mg/kg up to 2 g) IV, daily

OR

cefotaxime 2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly

Use the results of susceptibility testing to guide ongoing therapy. If the results of susceptibility testing are not available by 72 hours and empirical IV therapy is still required, cease gentamicin and use ceftriaxone or cefotaxime as above.

The incidence of infections with **multidrug-resistant Gram negative organisms** is increasing. Consider local microbiological data. If an organism that produces extended-spectrum beta-lactamase (ESBL) enzymes is identified by susceptibility testing, or the patient is at high risk of infection with an ESBL-producing organism (see Box 6.1), use meropenem (1 g [child: 40 mg/kg up to 1 g] IV, 8-hourly) as a single drug initially, and seek expert advice.

Some Gram negative organisms are now extensively drug-resistant, due to the production of carbapenemase enzymes. This renders them resistant to carbapenem antibiotics (eg meropenem). While extensively drug-resistant Gram negative organisms remain rare, treatment choices for infections caused by these pathogens are extremely limited—seek expert advice.

Usually a source of infection can be identified (most commonly the biliary or urinary tract); refer to the recommendations for the primary source of infection for duration of therapy. If there is no obvious source of infection and the patient responds rapidly, 5 to 7 days of therapy is adequate.

Pseudomonas aeruginosa

For severe sepsis caused by *Pseudomonas aeruginosa*, until the results of susceptibility testing are available, use:

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

PLUS EITHER

piperacillin+tazobactam 4+0.5 g (child: 100+12.5 mg/kg up to 4+0.5 g) IV, 6-hourly

OR

ceftazidime 2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly Non-EML

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, until the results of susceptibility testing are available, use:

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

PLUS

ciprofloxacin 400 mg (child: 10 mg/kg up to 400 mg) IV, 8-hourly

Once the results of susceptibility testing are known, continue treatment as monotherapy according to the results, preferably with a non-aminoglycoside antibiotic.

Refer to the recommendations for the primary source of infection for duration of therapy. If there is no obvious source of infection, seek expert advice.

Gram negative cocci

Neisseria meningitidis (meningococcal sepsis)

Management before hospitalisation

If *Neisseria meningitidis* infection is suspected on clinical grounds, initiate management immediately; **antibiotics should be given within 30 minutes of presentation**. Antibiotics should be administered intravenously where possible; where not the intramuscular route may be used.

> All patients with suspected meningococcal sepsis must be referred to the nearest divisional hospital as soon as possible.

Before the administration of antibiotics, if possible, collect samples for blood cultures, and swabs or aspirates of punctured skin lesions. Collection of specimens should NOT delay antibiotic therapy. Send all samples with the patient to hospital.

Prior to transfer, use:

ceftriaxone 2 g (child 1 month or older: 50 mg/kg up to 2 g) IV or IM [14]

OR

cefotaxime 2 g (infant or child: 50 mg/kg up to 2 g) IV or IM

For infants less than 1 month, ADD to the above:

ampicillin 50 mg/kg IV or IM

If ceftriaxone / cefotaxime are not available, or for patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

chloramphenicol 1 g (child 1 month or older: 12.5 mg/kg up to 1 g) IV

Where the above agents are not available, a less preferred alternative (due to rising rates of resistance) is:

benzylpenicillin 4 million units (2.4 g) (child: 100 000 units/kg up to 2.4 g) IV or IM

Doses may need to be repeated if there is a delay in reaching the divisional hospital.

Subsequent (divisional hospital) management

Treat acute or chronic meningococcaemia as for meningococcal meningitis (see page 165 for treatment recommendations).

Neisseria gonorrhoeae (gonococcal sepsis)

For the treatment of gonococcal sepsis, use:

ceftriaxone 2 g (child: 50mg/kg up to 2 g) IV, daily

OR

cefotaxime 2 g (child: 50mg/kg up to 2 g) IV, 8-hourly

Where susceptibility to penicillin is proven, use:

ampicillin 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly

Continue IV therapy until the patient has been afebrile for 48 hours, then

[14] IM injection of ceftriaxone is painful; consider reconstituting with lignocaine 1%.

switch to oral regimens based on the results of cultures and susceptibility testing. Total duration of therapy (IV + oral) is 7-14 days.

For patients with **immediate severe** or **delayed severe** hypersensitivity to penicillins, seek expert advice.

Patients with gonococcal infection have frequent undiagnosed coinfection with *Chlamydia trachomatis*. Treat presumptively with:

azithromycin 1 g orally, as a single dose

Candida species

The management of sepsis caused by *Candida* species is complex - seek expert advice. Treatment choice should be based on local susceptibility data. If the infection is associated with an intravascular catheter, the catheter must be removed to prevent relapse.

Use:

fluconazole 800 mg (child: 12 mg/kg up to 800 mg) IV, for the first dose, then 400 mg (child: 6 mg/kg up to 400 mg) IV, daily.

Alternatively, amphotericin B desoxycholate or lipid formulations (currently not available in Fiji) may be used; dosing is dependent upon the formulation used and expert advice should be sought. Alternative antifungals are often preferred eg echinocandins; none are currently available in Fiji.

Following clinical improvement, for susceptible species, continue treatment with:

fluconazole 450 mg (child: 6 mg/kg up to 450 mg) orally, daily for a total treatment course (IV and oral) of at least 14 days[15]

All patients with candidaemia require an ophthalmological examination to exclude endophthalmitis, and a liver scan to exclude liver abscess. Blood cultures should be repeated at 48 to 72 hours after antibiotic therapy is started, and repeated at two-day intervals until negative; persistent candidaemia is suggestive of metastatic infection. If metastatic infection is present, prolonged treatment is required eg 4-6 weeks.

[15] Only 150 mg are capsules available in Fiji, therefore doses must be in multiples of 150 mg

7. Respiratory tract infections

Acute sore throat (acute pharyngitis and tonsillitis)

Many sore throats are viral in origin and do not require antibiotic treatment. Paracetamol or non-steroidal anti-inflammatory drugs (NSAIDs) eg ibuprofen, provide valuable symptomatic relief.

Acute bacterial tonsillitis, most commonly caused by *Streptococcus pyogenes* (Group A streptococcus, GAS), is difficult to distinguish clinically from viral aetiology, but is more likely if patients have a majority, or all, of the following features:

- Fever > 38^0 C
- Tender cervical lymphadenopathy
- Tonsillar swelling or exudates
- No cough
- A scarlet fever-type rash is highly suggestive of GAS infection

AND, absence of:

- Coryza, hoarse voice, cough

A Fiji-specific Clinical Decision Rule should be used to guide the administration of antibiotic therapy (sensitivity 85%; specificity 29%) in children ≤ 15 years:

'A patient presenting with a sore throat in the absence of a runny nose or a hoarse voice should be treated with antibiotics.'

If the patient has a runny nose or a hoarse voice, this suggests a viral infection that does **not** require antibiotic therapy.

For adults (> 15 years), if GAS is the suspected cause of sore throat antibiotics should also be given.

If bacterial (GAS) infection is suspected, use:

benzathine penicillin IM as a single dose

Age in months	Weight in kg	Dose in units	Volume in mL
0 up to 3	2.5 – 5.9	300 000	1.3
4 – 12	6 – 10	450 000	1.9
13 – 36	11 – 14	600 000	2.5
37 – 60	15 – 18	900 000	3.8
> 60	> 18	1 200 000	5.0
Benzathine penicillin 2.4 million units per vial. Mix with 8 mL of water for injection to make 10 mL			

Alternatively, as a less preferred option

phenoxymethylpenicillin 500 mg (child: 15 mg/kg up to 500 mg) orally, 12-hourly for 10 days

S. pyogenes, which is the organism of concern, remains highly susceptible to phenoxymethylpenicillin. Amoxicillin should not be used for streptococcal pharyngitis and tonsillitis. Amoxicillin exposes the patient to unnecessary broader spectrum treatment and can cause a rash if the patient has undiagnosed Epstein-Barr virus (EBV) infection.

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefalexin 1 g (child: 25 mg/kg up to 1 g) orally, 12-hourly for 10 days[Non-EML]

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

erythromycin 500 mg (child: 10 mg/kg up to 500 mg) orally, 6-hourly for 10 days

NOTE: When oral therapy is given it is important to complete the 10 day course, even once the patient has clinically improved, to produce maximal pharyngeal GAS eradication to prevent rheumatic fever, which is still a common problem in Fiji.

For further information, see *Fiji Guidelines for Sore Throat and Skin Disease 2018*.

Acute otitis externa

Inflammation of the external auditory canal, presenting with ear pain, discharge, pruritus and/or hearing loss. Where bacterial, usual organisms include *Pseudomonas aeruginosa* and *Staphylococcus aureus*; other bacteria or fungi may be involved.

Topical therapy is the mainstay of management. The external ear canal must be kept as dry as possible. Remove discharge or other debris from the ear canal by dry aural toilet, not by syringing with water. Dry aural toilet involves dry mopping the ear with rolled tissue spears (ear wick) or similar, 6-hourly until the external canal is dry. Dry aural toilet should be followed by instillation of topical steroid and antibiotic combination drops.

Use:

> chloramphenicol 5% ear drops, 5 drops instilled into the affected ear(s) twice daily for 7 days
>
> OR
>
> dexamethasone+framycetin+gramicidin (eg Sofradex®) 0.05%+0.5%+0.005% ear drops, 3 drops instilled into the affected ear(s) 3 times daily for 7 days Non-EML
>
> OR
>
> triamcinolone 0.1%, neomycin 0.25%, gramicidin 0.025%, nystatin 100 000 units/g (eg Kenacomb Otic®) ear drops, 3 drops instilled into the affected ear(s) 2 or 3 times daily for 7 days Non-EML

If possible, avoid products containing chloramphenicol or an aminoglycoside (eg gentamicin, framycetin, neomycin) in patients with a perforated tympanic membrane or if the tympanic membrane cannot be visualised, in case it is perforated.

Systemic antibiotic therapy is NOT indicated unless there is fever, spread of inflammation to the pinna, or folliculitis. In these situations, *Staphylococcus* and *Streptococcus* are the likely pathogens: use:

> flucloxacillin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly for 7 to 10 days

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefalexin 500 mg (child: 25 mg/kg up to 500 mg) orally, 6-hourly for 7 to 10 days Non-EML

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

clindamycin 450 mg (child: 10 mg/kg up to 450 mg) orally, 8-hourly for 7 to 10 days Non-EML

Rarely, acute diffuse otitis externa may be complicated by the spread of infection to adjacent cartilage and bone; necrotising (malignant) otitis externa. Suspect if apparent treatment failure (eg fever, severe persistent pain, or cranial neuropathies), particularly in patients with diabetes or the elderly. If suspected, refer urgently to specialist. Broad-spectrum antibiotic cover, including anti-Pseudomonal cover and surgical input are generally required.

Acute bacterial otitis media

This may be either viral or bacterial, most commonly *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis*. Regardless of aetiology it is usually self-limiting and often does not require antibiotic therapy. Symptomatic therapy such as pain relief should be provided for the first 2 days; for patients who will be difficult to follow up or those with high-grade fever or systemically unwell, provide antibiotic treatment at the first visit.

Acute otitis media <u>without</u> perforation

Use:

amoxicillin 1 g (child: 25 mg/kg up to 1 g) orally, 12-hourly for 7 days

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefaclor SR 375 mg orally 12-hourly for 5 days (adult)[16]

OR

[16] Cefuroxime is preferred to cefaclor, but is more expensive. Where available, use cefuroxime 500 mg (child 3 months or older: 15 mg/kg up to 500 mg) orally, 12-hourly

cefaclor 10 mg/kg up to 250 mg, orally, 8-hourly for 5 days (child) Non-EML

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

trimethoprim+sulfamethoxazole 160+800 mg (child 1 month or older: 4+20 mg/kg up to 160+800 mg) orally, 12-hourly for 7 days.

Review after 4-7 days, if ear drum is still bulging **increase** amoxicillin dose to:

amoxicillin 2 g (child: 50 mg/kg up to 2 g) orally, 12-hourly for 7 days

Patients who have an inadequate response to high dose amoxicillin therapy after a further 4 to 7 days may have infection caused by a beta-lactamase–producing strain of *H. influenzae* or *M. catarrhalis*; adding clavulanate provides increased activity against these pathogens. Use:

amoxicillin+clavulanate 1500+375 mg (child: 45 mg/kg amoxicillin component up to 1500 mg) orally, 12-hourly for 7 days[17]

Acute otitis media with perforation

Use a higher dose of amoxicillin initially:

amoxicillin 2 g (child: 50 mg/kg up to 2 g) orally, 12-hourly for 14 days

Review after 7 days, if there is still pus or perforation change to:

amoxicillin+clavulanate 1500+375 mg (child: 45 mg/kg amoxicillin component up to 1500 mg) orally, 12-hourly for 7 days[14]

PLUS

ciprofloxacin 0.3% ear drops, 5 drops instilled into the affected ear, 12-hourly until the middle ear has been free of discharge for at least 3 days[18] Non-EML

PLUS

recommend ear wicks three times a day

[17] The dose of amoxicillin+clavulanate used in the treatment of AOM is much higher than for other indications

[18] If ciprofloxacin ear drops are unavailable, use povidone-iodine 5% (e.g. Betadine®) 5 drops into the affected ear 8-hourly

For patients with hypersensitivity to penicillins, use:

trimethoprim+sulfamethoxazole 160+800 mg (child 1 month or older: 4+20 mg/kg up to 160+800 mg) orally, 12-hourly for 7 days

Review after 7 days, if there is still pus or perforation ADD ciprofloxacin ear drops and ear wicking as above.

Teach parents how to clean/dry mop ears with tissue spears and put in ear drops. If not resolved within 2 weeks, treat as for chronic suppurative otitis media.

Chronic suppurative otitis media

Chronic suppurative otitis media is an infection of the middle ear with a perforated eardrum and discharge for at least 2 weeks. Chronic suppurative otitis media can cause hearing impairment and disability. Occasionally, serious complications can occur, such as intracranial infection and acute mastoiditis.

For patients with chronic suppurative otitis media (whether or not a tympanostomy tube has been inserted), cleaning the external ear canal by dry aural toilet is important and should be performed before instilling ear drops. Dry aural toilet can be performed by a healthcare professional (using mechanical suction or, under direct visualisation, cotton wool on a probe) or the patient or their carer (by dry mopping the ear with rolled tissue spears or similar, 6-hourly until the external canal is dry).

Aminoglycoside-based ear drops have previously been used for chronic suppurative otitis media; however, due to concerns about safety, in particular the risk of auditory and vestibular toxicity, quinolone ear drops are now preferred.

To treat chronic suppurative otitis media, use topical antibiotic therapy alone:

ciprofloxacin 0.3% ear drops, 5 drops instilled into the affected ear, 12-hourly until the middle ear has been free of discharge for at least 3 days Non-EML

There is inadequate evidence to support the use of topical corticosteroids in combination with topical antibiotics for the treatment of chronic suppurative otitis media.

Persistent discharge may require prolonged courses of treatment. Refer to ENT clinic if not resolved within 3 months.

Immediately refer any patients with sudden deafness, sudden vertigo, sudden facial palsy, posterior auricular swelling and meningitis symptoms (severe headache with fever, neck stiffness) for urgent specialist review.

Acute rhinosinusitis

Characterised by the rapid onset of inflammation of the nose and paranasal sinuses, with ≥ 2 additional symptoms of:

- nasal blockage
- nasal discharge
- facial pain or pressure
- loss of sense of smell.

Usually viral; may be complicated by bacterial infection in between 0.5 to 2% of cases. Acute bacterial rhinosinusitis is usually caused by *S. pneumoniae* or *H. influenzae*, and less frequently by *M. catarrhalis*.

Antibiotic therapy is generally NOT required. Consider antibiotic therapy, as well as intranasal corticosteroids, for patients with severe rhinosinusitis symptoms (purulent nasal discharge, nasal congestion and/or facial pain or pressure) for more than 5 to 7 days plus any of the following features:

- high fever (38.4 °C or more)
- unilateral maxillary sinus tenderness
- severe headache
- worsening symptoms after initial improvement.

If antibiotics are indicated, use:

> amoxicillin 500 mg (child: 15 mg/kg up to 500 mg) orally, 8-hourly for 5 days

For patients with **delayed nonsevere** hypersensitivity to penicillins, use

cefaclor SR 375 mg orally 12-hourly for 5 days (adult)[19]

OR

cefaclor 10 mg/kg up to 250 mg, orally, 8-hourly for 5 days (child) Non-EML

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, alternatives include:

doxycycline 100 mg (children 8 years and older: 2 mg/kg up to 100 mg) orally, 12-hourly for 5 days

OR

trimethoprim+sulfamethoxazole 160+800 mg (child 1 month or older: 4+20 mg/kg up to 160+800 mg) orally, 12-hourly for 5 days

Patients who have an inadequate response to amoxicillin therapy within 48 to 72 hours may have infection caused by a beta-lactamase–producing strain of *H. influenzae* or *M. catarrhalis*; adding clavulanate provides increased activity against these pathogens. Use:

amoxicillin+clavulanate 500+125 mg (child: 15 mg/kg amoxicillin component up to 500 mg) orally, 8-hourly for 5 days

Consider referral to ENT clinic for patients who have an inadequate response to amoxicillin+clavulanate therapy within 3 days. For patients with penicillin hypersensitivity who are failing to respond to first line treatment, seek expert advice.

Acute epiglottitis

Inflammation of the epiglottis and adjacent supraglottic structures which can progress rapidly to life-threatening airway obstruction. Suspect if severe sore throat, associated with:

- stridor
- drooling
- dysphagia

[19] Cefuroxime is preferred to cefaclor, but is more expensive. Where available, use cefuroxime 500 mg (child 3 months or older: 15 mg/kg up to 500 mg) orally, 12-hourly

- respiratory distress
- anxiety
- "tripod" position

Patients with epiglottitis often have sepsis or septic shock.

> Patients with acute epiglottitis require urgent transfer to hospital for airway management and intravenous antibiotic therapy.

Commonly caused by *H influenzae (type b and other strains)* or *S. pneumoniae*, but consider other pathogens including *S. aureus* if slow to improve. For empirical therapy, use:

ceftriaxone 2 g (child 1 month or older: 50 mg/kg up to 2 g) IV, daily

OR

cefotaxime 1 g (infant or child: 25 mg/kg up to 1 g) IV, 8-hourly

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use

chloramphenicol 1 g (child: 50 mg/kg up to 1 g) IV, 6-hourly

Switch to appropriate oral therapy once the patient improves, guided by results of susceptibility testing, for a total duration of 7-10 days (IV and oral).

Where susceptibility results are not available, use:

amoxicillin+clavulanate 500+125 mg (child: 15 mg/kg amoxicillin component up to 500 mg) orally, 8-hourly

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefuroxime 500 mg (child 3 months or older: 15 mg/kg up to 500 mg) orally, 12-hourly Non-EML

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, or if cefuroxime is not available, use:

> chloramphenicol 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly

The addition of corticosteroids to reduce airway inflammation is controversial but widespread; corticosteroids should **not** be used in children. If used in **adults**, a suitable regimen is:

> dexamethasone 10mg IV as a single dose; repeat at 24 hours if required

Pertussis

Pertussis (whooping cough) is caused by *Bordetella pertussis*. It typically presents with a persistent cough (longer than 2 weeks' duration) with one or more of the following features:

- paroxysms of coughing
- inspiratory whoop
- post-tussive vomiting.

Infants younger than 6 months are at the highest risk of morbidity and mortality from pertussis, and may require hospitalisation for supportive care of complications such as apnoea, hypoxia and feeding difficulties. Clinical suspicion is important; no specific diagnostic tests are available in Fiji.

Treatment to prevent disease transmission

Although antibiotics effectively eliminate *B. pertussis*, the evidence that they alter the course of the disease (when given in the catarrhal or early paroxysmal stage) is not conclusive.

Treatment of established disease minimises transmission to susceptible contacts; however, patients are rarely infectious if the cough has been present for longer than 3 weeks. Patients should avoid contact with others, especially young children and infants, until antibiotic therapy has been taken for at least 5 days. Use:

azithromycin 500 mg (child 6 months or older: 10 mg/kg up to 500 mg) orally, for the first dose, then 250 mg (child 6 months or older: 5 mg/kg up to 250 mg) orally, daily for a further 4 days (neonate and child younger than 6 months: 10 mg/kg orally, daily for 5 days)

OR

trimethoprim+sulfamethoxazole 160+800 mg (child 1 month or older: 4+20 mg/kg up to 160+800 mg) orally, 12-hourly for 7 days

OR

clarithromycin 500 mg (child: 7.5 mg/kg up to 500 mg) orally, 12-hourly for 7 days Non-EML

OR

erythromycin 500 mg (child: 10 mg/kg up to 500 mg) orally, 6-hourly for 14 days

To prevent transmission, **household contacts** of the index case should also receive antibiotic prophylaxis using doses and durations as above.

Acute bronchitis

In an immunocompetent patient, acute bronchitis is most often viral and does *not* require antibiotic therapy. Randomised controlled trials show that antibiotic therapy provides no overall benefit to the patient and may cause harm.

If severe, particularly if sputum is voluminous and purulent and the patient is febrile, secondary bacterial infection may be present. Consider treating as for mild community-acquired pneumonia (see page 114).

Acute exacerbation of chronic obstructive pulmonary disease (COPD)

Acute exacerbations of COPD can be triggered by viral and bacterial infections or by noninfective causes.

Although bacteria are isolated from cultures in around 50% of acute exacerbations, many patients with COPD are persistently colonised with

Haemophilus influenzae, *Moraxella catarrhalis* or *Streptococcus pneumoniae*, and a positive sputum culture is not necessarily indicative of acute infection. Mild exacerbations do not require antibiotic therapy. Moderate to severe exacerbations may require hospital admission and antibiotic therapy.

If antibiotics are indicated, use:

amoxicillin 500 mg orally, 8-hourly for 5 days

OR

doxycycline 200 mg orally, for the first dose, then 100 mg orally, daily for a total of 5 days

OR

chloramphenicol 500 mg orally, 6-hourly for 5 days

Long-term antibiotic prophylaxis for patients with frequent exacerbations is in general **not** recommended.

Pneumonia

Community-acquired pneumonia in adults and children over 5 years

Community-acquired pneumonia (CAP) is pneumonia in individuals who are not hospitalised or have been hospitalised for less than 48 hours.

In adults the most common bacterial cause of CAP is *Streptococcus pneumoniae*. Other important causes are the atypical pathogens *Mycoplasma pneumoniae*, *Chlamydophila (Chlamydia) pneumoniae* and *Legionella species*. *M. pneumoniae* is particularly common in young adults. In patients who are significantly immunocompromised or have chronic suppurative lung disease (eg bronchiectasis), a broader range of pathogens may need to be considered.

Haemophilus influenzae is predominantly seen in patients with chronic obstructive pulmonary disease (COPD). Gram negative bacilli, including *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*, are uncommon but are more likely to cause severe disease. *Staphylococcus aureus* is an important consideration in patients with severe disease, particularly in Fiji.

Viruses cause a significant proportion of CAP. Consider influenza based on the season and local epidemiology, and review the need for isolation (for patients in hospital) and empirical antiviral therapy while awaiting the results of investigations (see influenza, page 145).

Clinical and microbiological assessment

Initial assessment, in addition to a thorough **history and examination**, should include:

- **chest X-ray**, which usually establishes the diagnosis.
- **oxygen saturation** (while breathing room air), arterial blood gases in severely ill patients.
- **sputum Gram stain** and **cultures** can indicate the likely pathogen, provided good quality specimens are collected before starting antibiotic therapy.
- **blood samples for cultures** should be collected in patients requiring hospital admission, ideally before starting antibiotic therapy. If a pathogen is identified, use directed therapy.

A careful assessment of all patients with CAP is required to determine the need for clinical review, inpatient management and the most appropriate empirical antibiotic therapy. The presence of 'red flags' likely indicate more severe disease and the need for hospital admission:

'Red flags' for community-acquired pneumonia in adults (Box 7.1)

The presence of any of the following features indicates patients who need close clinical review and are more likely to require inpatient management:

- respiratory rate higher than 30 breaths per minute
- systolic blood pressure lower than 90 mm Hg
- oxygen saturation lower than 92%
- acute onset confusion
- heart rate higher than 100 beats per minute
- multilobar involvement on chest X-ray.

In addition to disease severity, consider the patient's age, comorbidities, social situation, ability to tolerate and absorb oral therapy, and need for supportive oxygen therapy, when deciding whether inpatient management is necessary.

Treatment stratification

A number of scoring systems are available to stratify patients with CAP according to disease severity. Two such well validated tools are CORB and SMART-COP (see appendix page 339). These tools can be used, in addition to clinical judgement, to sort patients into groups for which appropriate empirical antibiotic treatment can be recommended, based upon disease severity.

Mild disease

Patients with mild CAP are usually managed as outpatients with oral antibiotic therapy (though a single dose of benzylpenicillin 2 million units (1.2 g) IV may be administered in addition in the Emergency Department). Clinical review within 48 hours is generally recommended.

For patients with mild CAP, use:

amoxicillin 1 g (child: 25 mg/kg up to 1 g) orally, 8-hourly for 5 to 7 days

OR

doxycycline 100 mg (child over 8 years: 2 mg/kg up to 100 mg) orally, 12-hourly for 5 to 7 days.

OR, in remote areas where supervised administration is preferred

procaine penicillin 1.5 million units (1.5 g) (child: 50,000 unit/kg up to 1.5 million units) IM daily for 5 days

If doxycycline is not appropriate (eg in pregnant women or children less than 8 years) or poorly tolerated, use:

erythromycin 500 mg (child: 10 mg/kg up to 500 mg) orally 6-hourly for 5 to 7 days

OR

clarithromycin 500 mg (child: 7.5 mg/kg up to 500 mg) orally, 12-hourly for 5 to 7 days Non-EML

If the patient is not improving after 48 hours of monotherapy, consider escalating to combination therapy with amoxicillin **plus** doxycycline (or clarithromycin or erythromycin) (doses as above), and reassess the patient's need for hospital admission. If clinical review within 48 hours is not possible, use combination therapy from the outset.

For patients hypersensitive to penicillins, use doxycycline (or erythromycin or clarithromycin) monotherapy as above.

If atypical pathogens (*Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, or *Legionella*) are suspected, doxycycline (or clarithromycin or erythromycin) monotherapy (dose as above) is preferred for initial therapy.

Moderate (non-severe) disease

Patients with moderate severity CAP require admission to hospital. Use:

> benzylpenicillin 2 million units (1.2 g) (child: 50,000 units/kg up to 2 million units) IV, 6-hourly until significant improvement,
> ***then switch to*** amoxicillin 1 g (child: 25 mg/kg up to 1 g) orally, 8-hourly for a total of 5 to 7 days (IV + oral)
>
> PLUS
>
> doxycycline 100 mg orally (child over 8 years 2 mg/kg up to 100 mg), 12-hourly for 5 to 7 days

For patients with **delayed nonsevere** hypersensitivity to penicillins or if Gram negative bacilli are identified in the sputum, use:

> ceftriaxone 2 g IV, daily until significant improvement,
> ***then switch to*** cefaclor[20] 500 mg orally, 8-hourly for a total of 5 to 7 days (IV + oral)
>
> PLUS
>
> doxycycline 100 mg orally (child over 8 years 2 mg/kg up to 100 mg), 12-hourly for 5 to 7 days

Alternatively (including for **immediate** or **delayed severe** penicillin hypersensitivity) use:

> chloramphenicol 1 g oral/IV 6-hourly until improved, ***then switch to***

[20] Cefuroxime is preferred to cefaclor, but is more expensive. Where available, use cefuroxime 500 mg orally, 12-hourly

chloramphenicol 500 mg oral 6-hourly for a total of 5 to 7 days

PLUS:

doxycycline 100 mg orally (child over 8 years: 2 mg/kg up to 100 mg), 12-hourly for 5 to 7 days

Gentamicin plus benzylpenicillin (instead of ceftriaxone) remains an effective alternative for patients with Gram negative bacilli identified in the sputum, who are not hypersensitive to penicillins.

In all of the above regimens, if doxycycline is not appropriate (eg in pregnant women or children less than 8 years) or poorly tolerated, **replace** it with:

erythromycin 500 mg (child: 10 mg/kg up to 500 mg) orally 6-hourly for 5 to 7 days

OR

clarithromycin 500 mg (child: 7.5 mg/kg up to 500 mg) orally, 12-hourly for 5 to 7 days Non-EML

Modify therapy based on the results of cultures and susceptibility testing.

Severe disease

General principles

Patients with severe CAP are more likely to require intensive respiratory or vasopressor support, usually in an intensive care unit. Empirical antibiotic therapy should treat a broad range of pathogens, including *S. pneumoniae*, *Legionella*, enteric Gram negative bacilli and *S. aureus*. Importantly, also consider whether influenza is a potential cause of disease and treat accordingly. Investigation to identify the pathogen(s) is important. Collect blood and sputum samples for cultures, ideally before starting antibiotic therapy.

Use:

ceftriaxone 2 g (child: 50 mg/kg up to 2 g) IV, daily

PLUS

cloxacillin 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly

PLUS

azithromycin 500 mg (child: 10 mg/kg up to 500 mg) IV [Non-EML] or 1 g (child: 20 mg/kg up to 1 g) orally, daily for 5 days.

OR (where azithromycin is not available)

erythromycin 1 g (child: 25 mg/kg up to 1 g) IV 6-hourly until significant improvement, then 500 mg (child: 10 mg/kg up to 500 mg) orally, 6-hourly for a total of 10-14 days (IV + oral)

Once significant improvement occurs, change to oral therapy:

amoxicillin+clavulanate 500+125mg (child: 15 mg/kg amoxicillin component up to 500 mg) orally, 8-hourly to complete 7-to 14 days (IV + oral)

Alternatively, where staphylococcal pneumonia is considered unlikely, change to oral therapy with:

amoxicillin 1 g (child: 25 mg/kg up to 1 g) orally, 8-hourly to complete 7 to 14 days (IV plus oral)

PLUS

doxycycline 100 mg (child over 8 years: 2 mg/kg up to 100 mg) orally, 12-hourly to complete 7 to 14 days (IV plus oral)

If ceftriaxone is not available, **replace** in the above intravenous regimen with benzylpenicillin 2 million units (1.2g, child: 50,000 units/kg up to 2 million units) IV 6-hourly plus gentamicin.

For patients with **delayed nonsevere** hypersensitivity to penicillins **replace** cloxacillin with vancomycin, then step down to oral cefaclor (or cefuroxime) PLUS doxycycline as for moderate CAP.

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

PLUS

ciprofloxacin 400 mg (child: 10 mg/kg up to 400 mg) IV 8-hourly

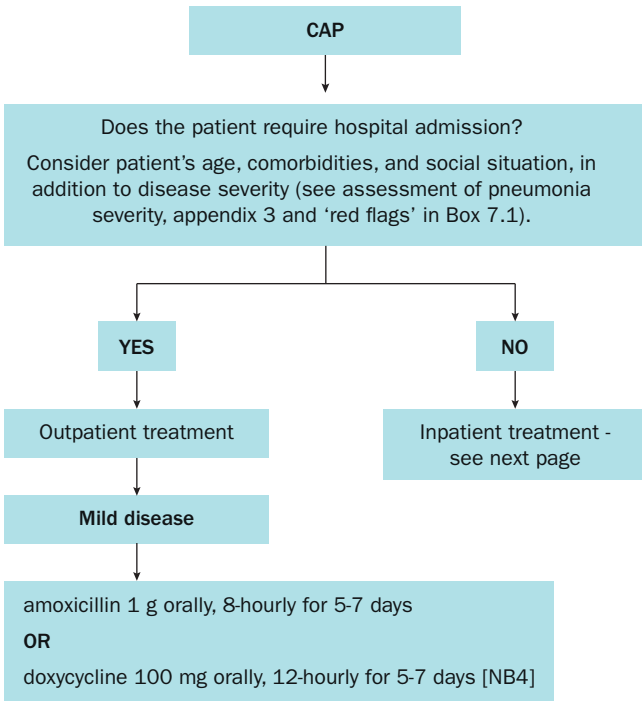
Seek expert advice for an appropriate oral step down regimen.

If Gram negative bacilli are identified by cultures of sputum or blood, or if the patient has a history of previous colonisation of sputum with *Pseudomonas aeruginosa*, add gentamicin until the pathogen is identified and the results of susceptibility testing are available; alternatively, cloxacillin PLUS ceftriaxone in the regimen above can be replaced with piperacillin+tazobactam.

Modify therapy based on the results of cultures and susceptibility testing. Switch to oral antibiotic therapy once the patient has improved significantly and is clinically stable (usually after 2 to 3 days). Treatment duration depends on patient response and the results of microbiological investigations. Generally, a total treatment duration of a minimum of 7 days (IV + oral) is adequate, though longer therapy (up to 14 days) is recommended for infection caused by *S. aureus* or some Gram negative bacilli. Ongoing management may require adjustment if complications are present.

Management of community-acquired pneumonia (CAP) in adults [NB1][NB2][NB3] (Figure 7.1)

Figure 7.1, part A



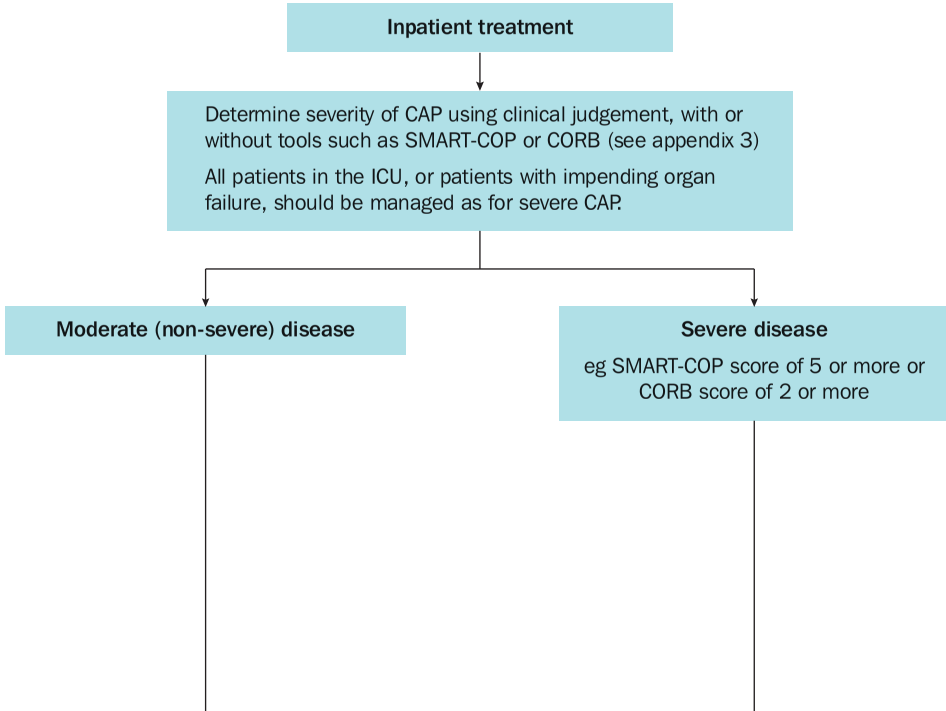
NB1: See text for treatment in patients with penicillin hypersensitivity

NB2: **Seek specialist advice** if antibiotics recommended are unavailable.

NB3: See text for dosing in children over 5 years.

NB4: If doxycycline is not appropriate (eg in pregnant women or children less than 8 years) or poorly tolerated, **replace** it in the above regimen with erythromycin 500 mg orally, 6-hourly or clarithromycin 500 mg orally, 12-hourly.

Figure 7.1, part B: inpatient treatment



benzylpenicillin 2 million units IV, 6-hourly until improved, then amoxicillin 1 g orally, 8-hourly for a total of 5 to 7 days (IV + oral)

PLUS

doxycycline 100 mg orally, 12-hourly for 5 to 7 days [NB4]

ceftriaxone 2 g IV, daily

PLUS

cloxacillin 2 g IV, 6-hourly

PLUS

azithromycin 500 mg IV OR 1 g orally, daily for 5 days [NB5]

For oral stepdown (total of 7 to 14 days (IV + oral):

amoxicillin+clavulanate 500+125mg orally, 8-hourly

OR where staphylococcal pneumonia is unlikely:

amoxicillin 1 g orally 8-hourly

PLUS

doxycycline 100 mg orally 12-hourly [NB4]

NB1: See text for treatment in patients with penicillin hypersensitivity

NB2: **Seek specialist advice** if antibiotics recommended are unavailable.

NB3: See text for dosing in children over 5 years.

NB4: If doxycycline is not appropriate (eg in pregnant women or children less than 8 years) or poorly tolerated, **replace** it in the above regimen with erythromycin 500 mg orally, 6-hourly or clarithromycin 500 mg orally, 12-hourly.

NB5: If azithromycin is not available, **replace** it with erythromycin 1 g IV 6-hourly until significant improvement, then 500 my orally, 6-hourly for a total of 10-14 days (IV + oral)

Community-acquired pneumonia in infants and children up to 5 years

In neonates, most early onset (in the first 3 days of life) pneumonia is acquired from the maternal perineal flora; common pathogens include *Streptococcus agalactiae* (group B streptococcus) and *Escherichia coli*.

After the neonatal period, up to 70% of community-acquired pneumonia (CAP) in children is viral, with influenza A virus, respiratory syncytial virus (RSV) and parainfluenza viruses the most commonly identified. Bacterial pneumonia in children is predominantly caused by *Streptococcus pneumoniae*. *Mycoplasma pneumoniae* can cause CAP, especially in school-aged children, though it may also cause CAP in younger children. Other bacterial causes of CAP (see below) are less common.

Chlamydia trachomatis is uncommon but should be considered in infants up to 3 months of age, particularly infants who are afebrile, have a 'staccato' cough (single coughs separated by inspiration) with a subacute onset, and diffuse crackles on auscultation. As many as 50% of infants with *C. trachomatis* pneumonia also have conjunctivitis (see chlamydial conjunctivitis page 155).

Bordetella pertussis is also an uncommon cause of CAP in children, though infants with pertussis may develop pneumonia. *B. pertussis* should be suspected in infants who present with paroxysmal cough associated with colour change or apnoea.

Although uncommon, *Staphylococcus aureus* can cause severe pneumonia in children of all ages. Staphylococcal pneumonia is characterised by systemic symptoms as well as pneumatoceles and/or lung abscesses on chest X-ray. Empirical therapy should include anti-staphylococcal drugs, and methicillin-resistant *S. aureus* (MRSA) should be considered as a cause of pneumonia based on epidemiology, and in all severely ill infants.

Typical clinical features of CAP in children include cough, tachypnoea and increased work of breathing. Fever is usually, but not always, present. Clinical features do not reliably distinguish between viral and bacterial (including atypical) pathogens. However, infants or children who have widespread pulmonary wheeze and/or crackles but no focal changes on chest X-ray are likely to have a viral infection, and symptomatic treatment

may be sufficient. Acute viral bronchiolitis is the most likely diagnosis in an infant younger than 18 months who presents with cough and respiratory distress.

Oral antibiotic therapy is preferred in mild disease; children with severe pneumonia usually require IV therapy initially. Infants and children with pre-existing cardiac or pulmonary disease require prompt and intensive treatment for CAP.

Classification of the severity of pneumonia in infants and children

Classification of the severity of pneumonia in infants and children (Table 7.1)

Sign or symptom	Classification	Treatment
Cough or difficulty in breathing with: • Oxygen saturation < 90% or central cyanosis • Severe respiratory distress (eg grunting, very severe chest indrawing) • Signs of pneumonia with a general danger sign (inability to breastfeed or drink, lethargy or reduced level of consciousness, convulsions)	**Severe pneumonia**	• Admit to hospital • Give oxygen if saturation < 90% • Manage airway as appropriate • Give recommended antibiotic regimen • Treat high fever if present
• Fast breathing: – ≥ 50 breaths/min in a child aged 3-11 months – ≥ 40 breaths/min in a child aged 1-5 years • Chest indrawing	**Pneumonia**	• Home care • Give recommended antibiotic regimen • Advise the mother to return immediately if symptoms of severe pneumonia • Follow up after 3 days

• No signs of pneumonia or severe pneumonia	**No pneumonia: cough or cold**	• Home care • Symptomatic relief eg paracetamol • Advise the mother when to return • Follow up after 5 days if not improving • If coughing for more than 14 days, seek expert advice from a paediatrician.

Adapted from WHO *Pocket Book of Hospital Care for Children*, 2013.

All pneumonia in infants under 3 months of age is considered severe.

All children treated in the community or in a sub-divisional hospital for mild to moderate pneumonia who are not improving after 3 days should be referred to a divisional hospital.

Management CAP in infants 0 to 1 months

All pneumonia is considered **severe** and management should therefore include hospital admission and **discussion with a specialist paediatrician**.

Use:

ampicillin 50 mg/kg IV for 7 to 10 days

First week of life: 12 hourly

Week 2-4 of life: 6-hourly

PLUS

gentamicin 5 mg/kg IV for up to 5 days; see appendix for dosing intervals and monitoring

Chlamydia trachomatis is an uncommon cause of pneumonia in children between 2-4 weeks of age, consider in the setting of untreated maternal sexually transmitted infection. If indicated, ADD to the above regimen:

azithromycin 10 mg/kg IV [Non-EML] or orally, daily on day 1 and 2 followed by 5 mg/kg daily for 3 more days

OR

erythromycin 10 mg/kg orally, daily on day 1 and 2 followed by 5 mg/kg daily for 3 more days

Management CAP in infants 1 to 3 months

Use:

gentamicin 7.5 mg/kg up to 350 mg IV, daily; see appendix for administration and monitoring

PLUS

benzylpenicillin 50,000 units/kg (30 mg/kg) IV 4 to 6-hourly

OR

ampicillin 50 mg/kg IV 6-hourly

If staphylococcal pneumonia is suspected, switch ampicillin or benzylpenicillin to cloxacillin. Continue gentamicin unless **confirmed** *Staphylococcus*. Use:

cloxacillin 50 mg/kg IV, 6-hourly for 14 days

If first line treatment fails, discuss with consultant and use:

cefotaxime 50 mg/kg IV, 6-hourly

PLUS

cloxacillin 50 mg/kg IV, 6-hourly

The total duration of treatment depends on the clinical response. Consider the need for MRSA cover with vancomycin for infants with septic shock, those who do not respond to initial therapy or with risk factors for MRSA.

In children aged 1 to 3 months, consider pneumonia caused by *Chlamydia trachomatis*, - particularly if there is afebrile pneumonia or staccato cough or a history of atypical neonatal conjunctivitis. Add:

azithromycin 10 mg/kg IV [Non-EML] or orally once daily on day 1 and 2, followed by 5 mg/kg orally daily for 3 more days

If azithromycin is unavailable use erythromycin 10 mg/kg IV once daily for 10-14 days, however, there is a risk of pyloric stenosis with the use of erythromycin in neonates.

Management CAP in children aged 3 months to 5 years

> Viruses are the most common cause of CAP in children 3 months and older – antibiotics are not required to treat viral infections.

Non-severe pneumonia (children 3 months to 5 years)

Usually managed as an outpatient. Use:

amoxicillin 40 mg/kg up to 1 g orally, 12-hourly for 3 days

Advise the patient's carer of **danger signs** and always review the patient after 3 days.

Alternatively, if worried about compliance, use:

procaine penicillin 50,000 units/kg up to 1.5 million units IM, daily for 5 days

For patients hypersensitive to penicillins, use:

azithromycin 10 mg/kg up to 500 mg orally once daily on days 1 and 2 followed by 5 mg/kg orally daily for 3 more days

OR if not available:

erythromycin 10 mg/kg up to 500 mg orally, 6-hourly for 5 days

OR, only if the first two options not available, use

trimethoprim+sulfamethoxazole 4+20 mg/kg (maximum 160+800 mg) orally, 12-hourly for 5 days

Severe pneumonia (children 3 months to 5 years)

For further information on treatment of severe pneumonia in children, see the *PICU Clinical Practice Guidelines*. Use:

benzylpenicillin 100 000 units/kg (60 mg/kg) up to 4 million units IV, 6-hourly

PLUS

gentamicin 7.5 mg/kg up to 350 mg IV, daily; see appendix for administration and monitoring

Once clinically stable, step down to oral amoxicillin as for mild pneumonia above to complete 7 days total (IV + oral) therapy

If staphylococcal pneumonia is suspected, add:

cloxacillin 50 mg/kg up to 2 g IV, 6-hourly

Once clinically stable, step down to oral flucloxacillin 50 mg/kg up to 1 g orally, 6-hourly to complete 14 days of treatment.

If MRSA suspected or proven or not improving on above therapy, instead of cloxacillin, use:

vancomycin IV infusion: 15 mg/kg actual body weight up to 750 mg 6-hourly; see appendix for additional dosing information

If child not responding in 48 hours or if severe systemic toxicity discuss with paediatrician

For **delayed nonsevere** penicillin hypersensitivity or for complicated pneumonia (including loculated parapenumonic effusion, empyema, pneumothorax, necrotising pneumonia or lung abscess) or for pneumonia that does not respond to first line therapy above, **discuss with consultant** and use:

ceftriaxone 50 mg/kg up to 2 g IV, once daily

For **immediate** or **delayed severe** penicillin hypersensitivity, use

azithromycin 10 mg/kg IV [Non-EML] or orally on day 1 and 2 followed by 5 mg/kg daily for 3 more days

OR, if not available, use

erythromycin 10 mg/kg up to 500 mg IV, 6-hourly until significant improvement, followed by 10 mg/kg up to 500 mg orally, 6-hourly for a total of 7 days (IV + oral)

Atypical pneumonia (non-viral) in infants and children

Mycoplasma pneumoniae can cause pneumonia in children, particularly in children aged 5 years and over. The onset of disease is more gradual. If the

patient is **afebrile** and only **mildly unwell**, C. trachomatis may be the cause of infection. If bacterial pneumonia is suspected clinically or on chest X-ray, and acute bronchiolitis is not present, use:

azithromycin 10 mg/kg up to 500 mg orally, daily on day 1 and 2 followed by 5 mg/kg orally daily for 3 more days

OR

erythromycin 10 mg/kg up to 500 mg orally, 6-hourly for 7 days

Pneumonia in immunosuppressed adults and children

Immunosuppressed patients (eg patients on long-term steroid use ≥ the equivalent of 20 mg daily of prednisolone for more than 1 month) with severe CAP may have recurrent infection and/or infection caused by atypical organisms. Consider:

- influenza
- *Pseudomonas* species. in patients with chronic suppurative lung disease
- *Pneumocystis jirovecii* pneumonia (PJP) in HIV-positive patients

Pneumocystis jirovecii pneumonia (PJP)

Pneumocystis jirovecii usually causes pneumonia in immunocompromised patients (eg patients with HIV infection, organ transplant recipients and patients with malignancy). If an apparently immunocompetent patient develops *P. jirovecii* pneumonia (PJP), investigations for an immune system disorder are recommended.

Parameters of severe *P. jirovecii* pneumonia are:

- Dyspnoea without exertion
- Severe hypoxia (oxygen saturation less than 94% on room air)

Trimethoprim+sulfamethoxazole is the most effective treatment for *P. jirovecii* pneumonia.

Use:

trimethoprim+sulfamethoxazole (adult and child 1 month or older) 5+25 mg/kg orally, 8-hourly for 21 days

For severe PJP use the regimen above. However, for clinically unstable patients, 6-hourly dosing is preferred for initial therapy. Once clinically improved, reduce to 8-hourly therapy. Consider adjunctive corticosteroid therapy for patients with severe PJP (see below).

For patients who have **nonsevere** hypersensitivity to trimethoprim+sulfamethoxazole, use:

> dapsone 100 mg (child: 2 mg/kg up to 100 mg) orally, daily for 21 days
>
> PLUS
>
> trimethoprim 5 mg/kg orally, 8-hourly for 21 days

For patients with **severe** hypersensitivity to trimethoprim+sulfamethoxazole (eg anaphylaxis, DRESS, SJS/TEN), do not give dapsone because there is a possibility of cross-reactivity between dapsone and sulfamethoxazole. Seek specialist advice.

After completing 21 days of therapy, maintenance therapy (secondary prophylaxis) for *P. jirovecii* pneumonia may be required for immunocompromised patients.

Corticosteroid therapy for severe PJP

Use adjunctive corticosteroid therapy in addition to antimicrobial therapy for patients with HIV infection who have severe *P. jirovecii* pneumonia. Although evidence is lacking, corticosteroids are also often used for patients without HIV infection.

When indicated, start corticosteroids as soon as possible:

> prednisolone 40 mg orally, 12-hourly for 5 days, then 40 mg daily for 5 days, then 20 mg daily for 11 days or until antibiotic therapy is completed

For children, use:

> prednisolone 1 mg/kg up to 40 mg orally, 12-hourly for 5 days, then 1 mg/kg up to 40 mg daily for 5 days, then 0.5 mg/kg up to 20 mg daily for 11 days or until antibiotic therapy is completed

Hospital-acquired pneumonia in adults and children

For hospital-acquired pneumonia in neonates, refer to neonatal sepsis page 83.

Hospital-acquired pneumonia (HAP) refers to pneumonia not present at the time of admission and developing in patients after 48 hours of hospitalisation. The spectrum of pathogens causing HAP differs from that of CAP. Hospitalised patients are more likely to have colonisation of the oropharynx with aerobic Gram negative bacteria and *Staphylococcus aureus,* with subsequent pneumonia secondary to microaspiration. They may also have been exposed to, and colonised with, multi-drug-resistant pathogens (MDR). The risk of MDR infection depends upon a number of variables, including the hospital ward (especially ICU), length of hospital stay (increased risk with recurrent or prolonged hospitalisation), preceding antibiotic exposure and immunosuppression.

Diagnosis of HAP is difficult and there are no universally accepted diagnostic criteria. The isolation of bacteria from expectorated sputum or lower respiratory tract secretion cultures often represents colonisation, and is not sufficient to diagnose HAP or ventilator-associated pneumonia (VAP). HAP, including VAP, is more likely in patients who have a new, progressive or persistent infiltrate on chest X-ray, plus two or more of the following features:

- fever above 38°C
- total white cell count above or below the normal range
- presence, or increased amount, of purulent sputum or lower respiratory tract secretions
- worsening gas exchange (eg desaturation, increased oxygen requirement or increased ventilator demand)

> The isolation of bacteria from expectorated sputum or lower respiratory tract secretion cultures alone is not sufficient to diagnose HAP or VAP.

Defining severe disease in this setting is imprecise, but any of the following features can indicate severe disease:

- hypotension
- need for intubation

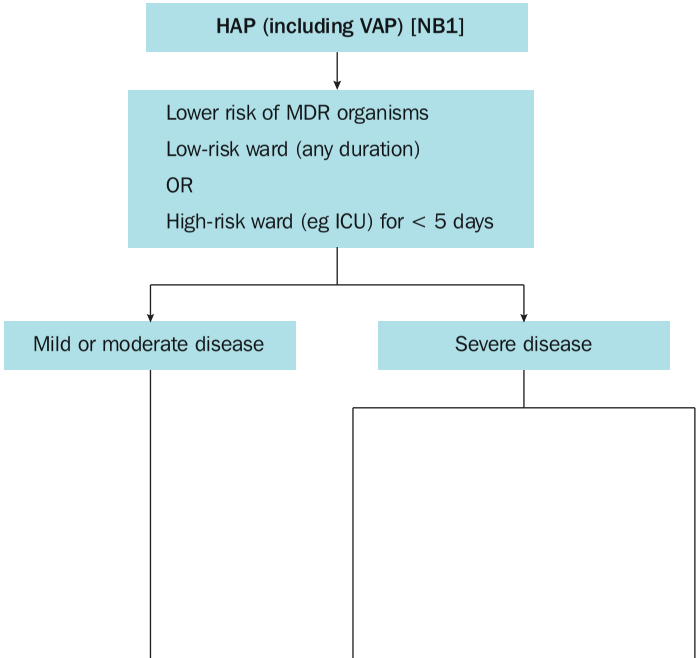
- severe sepsis
- rapid progression of infiltrates

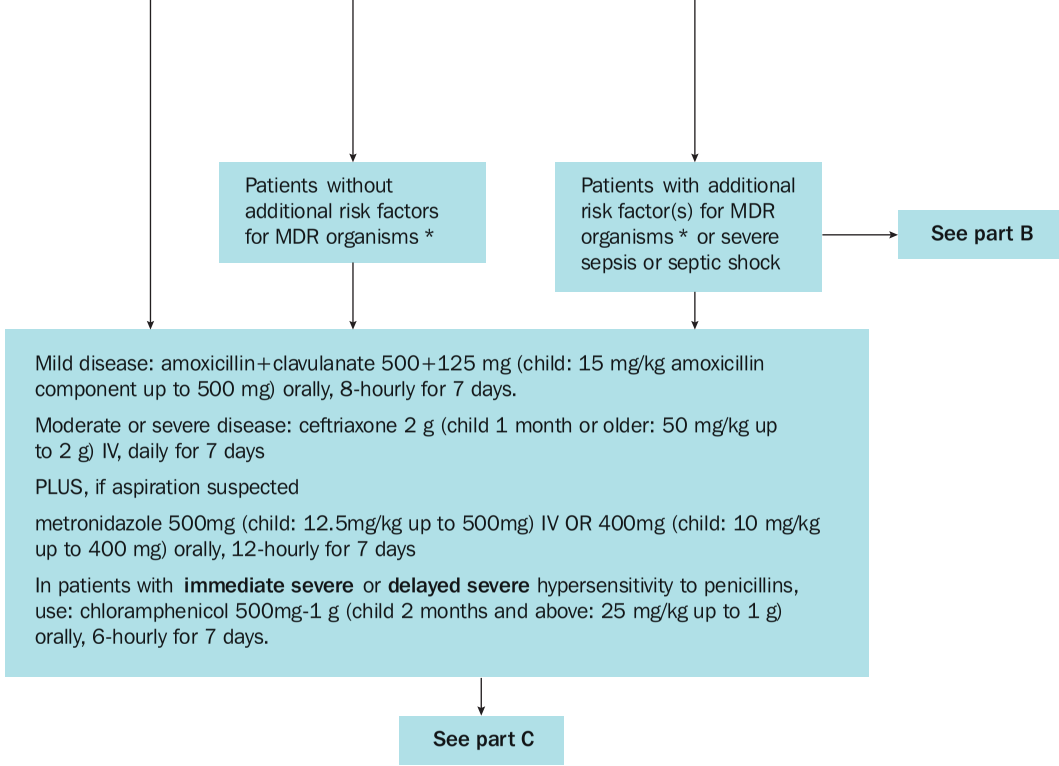
The algorithm on the next page provides recommendations for the management of HAP according to severity and risk of MDR infection.

Management of hospital-acquired pneumonia (HAP) in children and adults (Figure 7.2)

Stratify treatment according to the severity of disease

Figure 7.2, part A: Lower risk of MDR organisms





* Additional risk factors for MDR organisms include recent treatment with antibiotics, recurrent or prolonged hospitalisation, or immunosuppression

Figure 7.2, part B: higher risk of MDR organisms

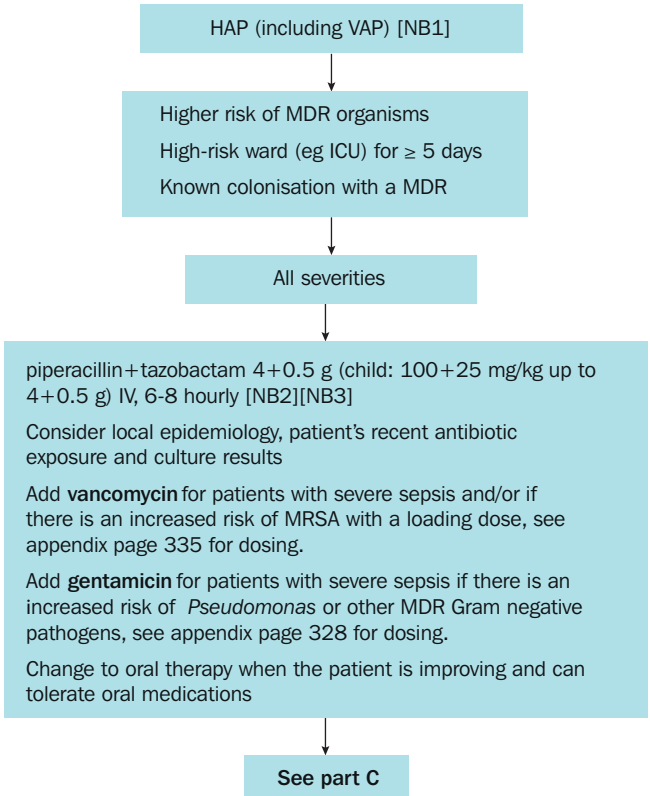
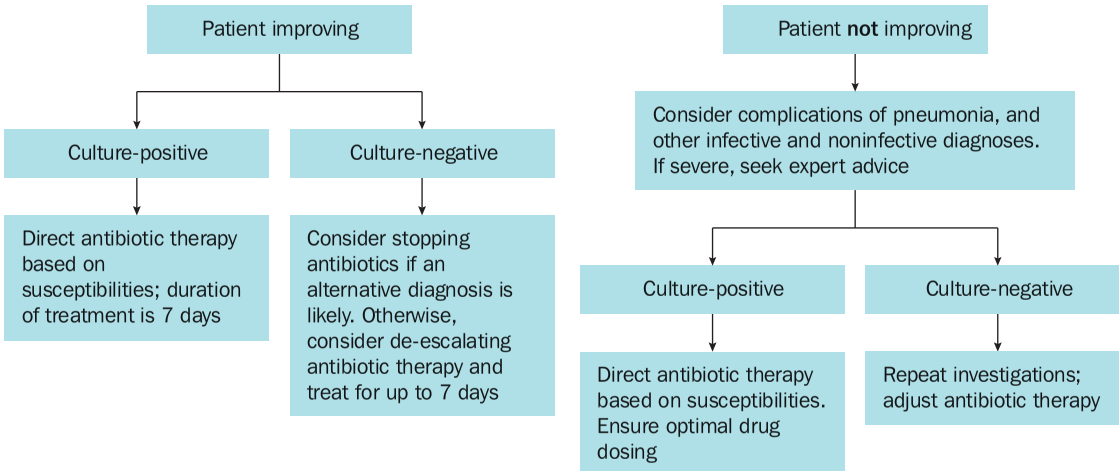


Figure 7.2, part C: treatment review



ICU = intensive care unit; MDR = multidrug-resistant; MRSA = methicillin-resistant *Staphylococcus aureus*; VAP = ventilator-associated pneumonia

Figure 7.3 notes

NB1: For patients with recent colonisation or infection with MDR organisms, or recent hospitalisation in a country with high rates of MDR organisms, seek expert advice.

NB2: If piperacillin+tazobactam is not available, use:

ceftriaxone 2 g (child 1 month or older: 50 mg/kg up to 2 g) IV, daily[19]

PLUS

cloxacillin 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly

PLUS

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

PLUS

metronidazole 500 mg (child:12.5 mg/kg up to 500 mg) IV, 12-hourly OR 400 mg (child: 10 mg/kg up to 400 mg) orally, 12-hourly

NB3: For patients with **delayed nonsevere** hypersensitivity to penicillins, replace cloxacillin in the above regimen with:

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, give:

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

PLUS

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

PLUS

metronidazole 500 mg (child:12.5 mg/kg up to 500 mg) IV, 12-hourly OR 400 mg (child: 10 mg/kg up to 400 mg) orally, 12-hourly

[21] If ceftriaxone not available, use cefotaxime 1 g (child: 50 mg/kg up to 1 g) 8-hourly

Modify therapy based on the results of cultures and susceptibility testing. Switch to an oral regimen once there is significant clinical improvement and oral intake is tolerated.

For patients who are not improving after 48 hours, or where MDR pathogens are suspected or confirmed, **seek expert advice**.

Aspiration pneumonia

Aspiration pneumonia is a bacterial infection that occurs in the days following 'macro-aspiration' of organisms from the oropharynx. It is frequently associated with risk factors such as bulbar dysfunction and impaired consciousness eg post stroke.

Aspiration pneumonitis is an important differential diagnosis for aspiration pneumonia; it is characterised by acute lung inflammation within several hours of aspiration of acidic gastric contents. Antibacterial therapy is not required for the classical aspiration pneumonitis syndrome because acidic gastric contents are normally sterile, however, aspiration pneumonia can develop following aspiration pneumonitis.

Bacteria such as *Streptococcus pneumoniae*, which can cause community-acquired pneumonia, are also a frequent cause of aspiration pneumonia, but additional pathogens potentially colonising the oropharynx need to be considered including other streptococci, staphylococci, aerobic Gram negative bacilli and anaerobes. Cultures are important to guide treatment.

The role of anaerobic organisms in aspiration pneumonia is frequently overestimated. In mild disease, penicillin effectively treats anaerobic organisms aspirated from the oropharynx, and the addition of metronidazole is not required. The addition of metronidazole to treat anaerobic organisms may be indicated in patients with moderate disease who:

- have putrid sputum, severe periodontal disease or a history of chronic hazardous alcohol consumption
- develop lung abscess, empyema or necrotising pneumonia
- do not respond to initial empirical therapy.

When a pathogen is identified, use directed therapy. If oral therapy is not tolerated, consider whether medications can be administered enterally eg via nasogastric tube.

Initial management of aspiration pneumonia

If the patient has had an aspiration event, try to exclude aspiration pneumonitis before starting antibiotic therapy for pneumonia.

> Manage aspiration pneumonia as community- or hospital-acquired pneumonia initially.

For initial management of aspiration pneumonia in a patient from the community, or a patient who has been in hospital for less than 48 hours, see community-acquired pneumonia, page 112.

For initial management of aspiration pneumonia in a patient who has been in hospital for more than 48 hours, see hospital-acquired pneumonia, page 130.

Review the patient within 24 to 48 hours of starting antibiotic therapy. Consider stopping antibiotic therapy if aspiration pneumonitis is a more likely diagnosis based on the results of investigations or the speed of recovery (symptoms of aspiration pneumonitis usually improve within 24 to 48 hours).

> Consider stopping antibiotic therapy if the patient has improved and aspiration pneumonitis is a more likely diagnosis.

Management of aspiration pneumonia in patients who are not improving on empirical therapy for CAP or HAP

If oral or enteral therapy is tolerated, change to:

amoxicillin 1 g (child: 25 mg/kg up to 1 g) orally, 8-hourly

PLUS

metronidazole 400 mg (child: 10 mg/kg up to 400 mg) orally, 12-hourly

Alternatively, if a single drug regimen is preferred (eg to reduce toxicity or improve adherence), use:

amoxicillin+clavulanate 500+125 mg (child: 15 mg/kg amoxicillin component up to 500 mg) orally, 8-hourly

OR

clindamycin 450 mg (child: 10 mg/kg up to 450 mg) orally, 8-hourly Non-EML

For patients hypersensitive to penicillins, use clindamycin (see dosages above).

If the patient cannot tolerate oral (or enteral) therapy, change to:

benzylpenicillin 2 million units (1.2 g) (child: 50,000 units/kg up to 2 million units) IV, 6-hourly

PLUS

metronidazole 500 mg (child: 12.5 mg/kg up to 500 mg) IV, 12-hourly

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

ceftriaxone 2 g (child 1 month or older: 50 mg/kg up to 2 g) IV, daily[22]

PLUS

metronidazole 500 mg (child: 12.5 mg/kg up to 500 mg) IV, 12-hourly

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

clindamycin 600 mg (child: 15 mg/kg up to 600 mg) IV, 8-hourly

OR

chloramphenicol 1 g (child: 25 mg/kg up to 1 g) IV, 6-hourly

Intravenous to oral switch: Once the patient improves, switch to an oral regimen as above. The duration of therapy for aspiration pneumonia is guided by the setting. For community-acquired aspiration pneumonia, the total duration of therapy is 5 to 7 days (IV + oral). For hospital-acquired aspiration pneumonia, treat for 7 to 14 days (IV + oral).

Lung abscess and empyema

Lung abscesses may present acutely, eg as a complication of pneumonia caused by organisms such as *Klebsiella pneumoniae*, or secondary to

[22] If ceftriaxone is not available, substitute cefotaxime 1 g (child: 50 mg/kg up to 1 g) IV 8-hourly

haematogenous spread of *Staphylococcus aureus*, or more commonly subacutely secondary to aspiration of oral organisms, eg in association with periodontal disease. They are frequently polymicrobial, with organisms including anaerobes. Sputum should be collected for culture, ideally before starting antibiotics.

Empyema usually develops as a complication of a parapneumonic effusion. When complicating community-acquired pneumonia, the most common pathogen is *Streptococcus pneumoniae*, however the *"Streptococcus milleri"* group, *Staphylococcus aureus*, aerobic enteric Gram negatives and frequently anaerobes may also be implicated. Fungi are occasionally seen. Adequate surgical drainage is required in addition to antibiotic therapy. Fluid should be sent for microscopy and culture (where history is suggestive, TB should be excluded).

Patients with lung abscess or empyema require hospital admission for management. If the patient is not systemically unwell, empirical antibiotic therapy may be given orally. If the patient is systemically unwell, use intravenous therapy until the patient is afebrile and clinically improved, then switch to oral antibiotic therapy. Where possible, therapy should be guided by microbiology results. If not available, use:

Mild disease

amoxicillin+clavulanate 500+125 mg (child: 15 mg/kg amoxicillin component up to 500 mg) orally, 8-hourly

OR

clindamycin 450 mg (child: 10 mg/kg up to 450 mg) orally, 8-hourly[Non-EML]

OR

chloramphenicol 500 mg (child 2 months or older: 25 mg/kg up to 500 mg) orally, 6-hourly

Moderate to severe disease

In moderate to severe disease, or if Gram negative infection is clinically suspected, use:

ceftriaxone 2 g (child: 50 mg/kg up to 2 g) IV, daily[23]

[23] If ceftriaxone is not available, substitute cefotaxime 1 g (child: 50 mg/kg up to 1 g) IV 8-hourly

PLUS

cloxacillin 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly

PLUS

metronidazole 400 mg (child: 10 mg/kg up to 400 mg) orally, 12-hourly
OR metronidazole 500 mg (child: 12.5 mg/kg up to 500 mg) IV, 12-hourly

Alternatively, as a single agent, use:

piperacillin+tazobactam 4+0.5 g (child: 100+12.5 mg/kg up to 4+0.5 g) IV, 8-hourly

For patients hypersensitive to penicillins, use:

clindamycin 450 mg (child: 10 mg/kg up to 450 mg) orally, 8-hourly OR 600 mg (child: 15 mg/kg up to 600 mg) IV, 8-hourly Non-EML

PLUS

ciprofloxacin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 12-hourly
OR 400 mg (child: 10mg/kg up to 400mg) IV, 8-12 hourly

Alternatively, use:

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

PLUS

ciprofloxacin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 12-hourly
OR 400 mg (child: 10mg/kg up to 400mg) IV, 8-12 hourly

PLUS

metronidazole 400 mg (child: 10 mg/kg up to 400 mg) orally, 12-hourly
OR metronidazole 500 mg (child: 12.5 mg/kg up to 500 mg) IV, 12-hourly

Modify therapy based on the results of cultures and susceptibility testing. In lung abscess, continue antibiotics until the sputum is not purulent and the abscess cavity is free of fluid; a minimum of 3 to 4 weeks in total (IV + oral) is generally required. The duration of antibiotic therapy in empyema depends on a number of factors including clinical response, organisms(s) involved and the adequacy of drainage of the pleural space; radiological improvement is often incomplete.

A minimum of 3 to 4 weeks in total (IV and oral) is generally required.

Note: Aminoglycosides (including gentamicin) should NOT be used for empyema as they may be inactivated at the low pleural fluid pH.

Bronchiectasis with infection

Patients with bronchiectasis often have chronically purulent sputum which if cultured grows organisms. If the patient is clinically stable, it is not appropriate to treat colonising organisms as this will promote the emergence of antibiotic resistance. If antibiotic therapy is required for acute exacerbations, generally presenting as increased sputum volume and/or purulence, with or without dyspnoea and fever, treat as for community-acquired pneumonia.

Mild exacerbations:

amoxicillin 1 g (child: 25 mg/kg up to 1 g) orally, 8-hourly

OR

doxycycline 100 mg (child over 8 years: 2 mg/kg up to 100 mg) orally, 12-hourly

Moderate exacerbations:

benzylpenicillin 2 million units (1.2 g) (child: 50,000 units/kg up to 2 million units) IV, 6-hourly until significant improvement,
then switch to amoxicillin 1 g (child: 25 mg/kg up to 1 g) orally, 8-hourly

PLUS

doxycycline 100 mg (child over 8 years: 2 mg/kg up to 100 mg) orally, 12- hourly

If doxycycline is not appropriate (eg in pregnant women or children younger than 8 years) or poorly tolerated, **replace** it in the above regimen with:

erythromycin 500 mg (child: 10 mg/kg up to 500 mg) orally 6-hourly

OR

clarithromycin 500 mg (child: 15 mg/kg up to 500 mg) orally, 12-hourly[Non-EML]

For patients with **delayed nonsevere** hypersensitivity to penicillins, replace the penicillin in the above regimen with:

ceftriaxone[24] 2 g (child: 50 mg/kg) IV, daily until significant improvement, ***then switch to*** cefaclor[25] 500 mg (child: 15 mg/kg up to 500 mg) orally, 8-hourly

OR

chloramphenicol 1 g (child: 25 mg/kg up to 1 g) oral/IV 6-hourly until improved,
then switch to 500 mg (child: 25 mg/kg up to 500 mg) orally, 6-hourly

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

chloramphenicol 1 g (child: 25 mg/kg up to 1 g) oral/IV 6-hourly until improved,
then switch to 500 mg (child: 25 mg/kg up to 500 mg) orally 6-hourly

PLUS

doxycycline 100 mg (child over 8 years: 2 mg/kg up to 100 mg) orally, 12-hourly

Treat for a total of 10 to 14 days (IV + oral).

Empirical treatment regimens for mild to moderate bronchiectasis do NOT routinely require the addition of antimicrobial cover for *Pseudomonas*, even in the presence of known prior colonisation. Modify therapy based on the results of cultures and susceptibility testing, however if the patient is improving, do not escalate therapy.

Anti-pseudomonal cover (gentamicin, ciprofloxacin or piperacillin-tazobactam) should be given empirically for **severe** acute exacerbations, and considered for patients with less severe exacerbations who fail to respond to initial antimicrobial therapy, particularly where *Pseudomonas* has been isolated on culture. Where ciprofloxacin is added, use:

ciprofloxacin 500 mg (small weight patient) to 750 mg (child: 20 mg/kg

[24] If ceftriaxone is not available, substitute cefotaxime 1 g (child: 50 mg/kg up to 1 g) IV 8-hourly

[25] Cefuroxime is preferred to cefaclor, but is more expensive. Where available, use cefuroxime 500 mg (child 3 months or older: 15 mg/kg up to 500 mg) orally, 12-hourly

up to 750 mg) orally, 12-hourly for 14 days[26]

Severe exacerbations

piperacillin+tazobactam 4+0.5 g (child: 100+12.5 mg/kg up to 4+0.5 g) IV, 8-hourly

PLUS

ciprofloxacin 400 mg (child: 10 mg/kg up to 400 mg) IV, 8-hourly OR 500 mg (small weight patient) to 750 mg (child: 20 mg/kg up to 750 mg) orally, 12-hourly

OR for a maximum of three days

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

Alternatively, where piperacillin+tazobactam is not available, use:

ceftriaxone 2 g (child: 50 mg/kg up to 2 g) IV, daily[27]

PLUS

ciprofloxacin 400 mg (child: 10 mg/kg up to 400 mg) IV, 8-hourly OR 500 mg (small weight patient) to 750 mg (child: 20 mg/kg up to 750 mg) orally, 12-hourly

PLUS for a maximum of three days:

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

Once significant improvement occurs, change to oral therapy with:

amoxicillin+clavulanate 500+125mg orally (child: 15 mg/kg amoxicillin component up to 500 mg), 8-hourly

PLUS

[26] where 750mg dosing is not practical (i.e. if tablet not scored), and higher doses are required, ciprofloxacin can be given as 500mg 8-hourly

[27] If ceftriaxone is not available, substitute cefotaxime 1 g (child: 50 mg/kg up to 1 g) IV 8-hourly

ciprofloxacin 500 mg (small weight patient) -750 mg (child: 20 mg/kg up to 750 mg) orally, 12-hourly[28]

If sputum culture results are available and show **no** *Pseudomonas*, use amoxicillin+clavulanate alone.

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

PLUS

ciprofloxacin 400mg (child: 10 mg/kg up to 400 mg) IV 8-hourly

Once significant improvement occurs, switch to:

trimethoprim+sulfamethoxazole 160+800 mg (child 1 month or older: 4+20 mg/kg up to 160+800 mg) orally, 12-hourly for 14 days

PLUS

ciprofloxacin 500 (small weight patient) to 750 mg (child: 20 mg/kg up to 750 mg) orally, 12-hourly for 14 days[25]

Treat for a total of 14 days (IV + oral).

Influenza

Influenza is caused by influenza A and B viruses. These viruses cause minor or major epidemics of seasonal influenza in most years.

The influenza virus is spread through droplets and contact with fomites (virus-contaminated objects), so infection control precautions (eg hand hygiene, patient isolation, use of personal protective equipment) are essential, particularly for hospitalised patients.

The available evidence shows that treatment with a neuraminidase inhibitor reduces duration of symptoms of influenza by only 1 day, on average, when treatment is started within 48 hours of the onset of symptoms (though

[28] where 750mg dosing is not practical (i.e. if tablet not scored), and higher doses are required, ciprofloxacin can be given as 500mg 8-hourly

the earlier that treatment is given, the greater the benefit). Such limited benefit must be balanced against the potential adverse effects of antiviral treatment, such as nausea and vomiting.

Consider treatment for individuals at high risk of poor outcomes from influenza:

Individuals at high risk of poor outcomes (eg hospitalisations or death) from influenza (Box 7.2)

- adults aged 65 years or older
- people with the following conditions:
- pregnancy
- heart disease
- Down syndrome
- obesity (body mass index [BMI] 30 kg/m^2 or more)
- chronic respiratory conditions
- severe neurological conditions
- immunocompromise
- other chronic illnesses
- children aged 5 years or younger
- homeless people.

In addition, regardless of the duration of symptoms, offer treatment to all individuals with established complications or to patients requiring admission to hospital for management of influenza.

If treatment is indicated, use:

> oseltamivir 75 mg (child 1 year or older and less than 15 kg: 30 mg; 15 to 23 kg: 45 mg; 23 to 40 kg: 60 mg; more than 40 kg: 75 mg) orally, 12-hourly for 5 days Non-EML

For treatment in children less than one year, refer to the *PICU Clinical Practice Guidelines 2019*.

8. Eye infections

Eyelid, orbital and peri-orbital infections

Blepharitis

Blepharitis is an inflammation of the lid margins. Blepharitis (anterior and posterior) is usually caused by *Staphylococcus* species.

Eyelid hygiene and gentle eyelid scrubbing are the mainstay of therapy. Warm compresses, applied to both eyes daily for 2-5 minutes, followed by gentle scrubbing of the lashes with either sodium bicarbonate solution (1 teaspoon in 500 mL of freshly boiled and cooled water), baby shampoo solution (5 drops in 100ml freshly boiled and cooled water), or proprietary eyelid solutions or wipes may be helpful. Topical antibiotics are not indicated as initial therapy. If symptoms of anterior blepharitis are not controlled despite adequate lid hygiene, consider adding:

> chloramphenicol 1% eye ointment applied to the lid margin of both eyes, once or twice daily for 1 week

Occasionally up to 3 weeks of treatment is required. Short-term topical steroid ointments may also help.

For resistant cases, use:

> doxycycline 50 to 100 mg (child 8 years or older: 1 to 2 mg/kg up to 50 to 100 mg, respectively) orally, 12-hourly for 3 to 4 weeks, then taper to 50 mg daily as necessary based on clinical response

In children younger than 8 years, or in pregnancy and breastfeeding, use:

> erythromycin 250 mg (child 1 month or older: 10 mg/kg up to 250 mg) orally, once or twice daily for 8 weeks
>
> OR
>
> azithromycin 500 mg (child: 10 mg/kg up to 500 mg) orally, daily for 3 days for 3 cycles at 1 week intervals

Stye

A stye is an abscess of the sebaceous gland associated with an eyelash, usually caused by *Staphylococcus aureus*. Antibiotics are usually not recommended; use warm compresses. Removal of the associated eyelash often aids resolution of external styes.

In the presence of cellulitis and/or a visible abscess treat as preseptal (periorbital) cellulitis below.

Herpes zoster ophthalmicus

Herpes zoster virus (HSV) reactivation (shingles) involving the ophthalmic division of the trigeminal nerve may be complicated by ocular involvement (eg keratitis, uveitis) with sight-threatening complications. Warning signs include a red eye, discharge, visual loss, photophobia or the presence of vesicular lesions on the side or tip of the nose. Systemic therapy is required. Oral antiviral treatment, optimally given within 72 hours of rash onset, reduces the severity and duration of the acute episode and the risk of post-herpetic neuralgia. Use:

aciclovir 800 mg orally, 5 times daily for 7 days.

An ophthalmologist should be consulted in all cases of trigeminal nerve shingles.

Dacryocystitis

Dacryocystitis is an infection of the lacrimal sac, usually associated with obstruction of the nasolacrimal duct. It can be acute or chronic.

Acute dacryocystitis

Acute dacryocystitis is characterised by pain, redness and swelling. It is usually caused by *Staphylococcus aureus*, *Streptococcus pyogenes* (group A streptococcus) or Gram negative bacteria. It may be associated with periorbital (preseptal) cellulitis. Systemic antibiotic therapy is required and choice is directed by results of Gram stain and culture.

For initial empirical therapy of acute dacryocystitis, use:

cefalexin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly Non-EML

OR

amoxicillin+clavulanate 500+125 mg (child: 15 mg/kg amoxicillin component up to 500 mg) orally, 8-hourly

Cefalexin can be used in most patients with **delayed nonsevere** penicillin hypersensitivity. For patients with **immediate** or **delayed severe** hypersensitivity to penicillins or those at increased risk of infection with **methicillin-resistant *Staphylococcus aureus*** (**MRSA**) or if MRSA is isolated from culture, seek expert advice.

If the patient is in significant pain, refer to an ophthalmologist because surgical drainage may be indicated.

Chronic dacryocystitis is characterised by recurring episodes of epiphora or mucopurulent discharge, which may be associated with a non-tender mass (or a mucocoele). Pressure over the lacrimal sac may express mucopurulent material from the punctum. There is no role for antibiotics in cases of chronic dacryocystitis and surgical management is usually required. Acute dacryocystitis may be superimposed on chronic dacryocystitis, and should be treated as for acute dacryocystitis above.

Consider using a topical antibiotic if associated bacterial conjunctivitis is present.

Preseptal (periorbital) cellulitis

Preseptal cellulitis is a soft tissue infection of the eyelid, originating anterior to the orbital septum (the anatomical barrier separating the eyelids from the orbit), usually caused by local trauma or infection of the surrounding skin. Common pathogens are *Staphylococcus aureus* and *Streptococcus* species. Use:

flucloxacillin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly for 7 days

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefalexin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly for 7 days Non-EML

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

clindamycin 450 mg (child: 10 mg/kg up to 450 mg) orally, 8-hourly for 7 days Non-EML

OR

erythromycin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly for 7 days

Consider IV antibiotics for more severe infections.

Orbital (postseptal) cellulitis

Orbital cellulitis is an infection involving the contents of the orbit (fat and ocular muscles) usually arising from paranasal sinus infection or orbital trauma. It is usually caused by *Staphylococcus aureus*, *Streptococcus* species, *Haemophilus influenza*e (in unvaccinated patients) and anaerobic bacteria. Clinical symptoms are more pronounced; patients are generally unwell and may have reduced vision, pain with eye movements, ophthalmoplegia with diplopia or proptosis. This is a serious infection requiring urgent referral to an ophthalmologist and hospital admission. Drainage of an orbital abscess should be considered at an early stage. CT scan should be considered after 72 hours if not improving. For initial empirical therapy, use:

cloxacillin 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly until improved

PLUS

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefazolin 2 g (child: 50mg/kg up to 2g) IV, 8-hourly[29]

PLUS

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese

[29] If cefazolin is unavailable, use cefalotin 2 g (child: 50 mg/kg up to 2 g) IV 6-hourly

patients, and dosing in children

Where superinfection with anaerobes is suspected, ADD:

metronidazole 400 mg (child: 10 mg/kg up to 400 mg) orally, 12-hourly for 7-10 days

If there is no improvement after 48 hours of therapy OR if the patient is improving but IV therapy is required for more than 72 hours, change gentamicin in the above regimen to:

ceftriaxone 2 g (child 1 month or older: 50 mg/kg up to 2 g) IV, daily

Once clinical improvement (usual minimum duration IV therapy 3 days), change to oral therapy for a further 10 days with:

amoxicillin+clavulanate 500+125 mg (child: 15 mg/kg amoxicillin component up to 500 mg) orally, 8-hourly

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefalexin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly for a further 10 days Non-EML

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, seek expert advice; commence treatment with:

clindamycin 600 mg (child: 15 mg/kg up to 600 mg) IV or oral, 8-hourly Non-EML

PLUS

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

Conjunctival infections

Conjunctivitis is inflammation of the conjunctiva. There are no specific clinical signs to differentiate bacterial and viral.

Pain, loss of vision or photophobia, or failure to respond to initial therapy, require prompt referral to an ophthalmologist, as this may suggest acute keratitis or another serious disorder.

Comparative features of allergic, viral and bacterial conjunctivitis (Table 8.1)

	Allergic	Viral	Bacterial [NB1]
Age	Children or adults	More common in adults	More common in children
Aetiology	Local response to an allergen, including: • seasonal (typically spring and autumn) • perennial • contact hypersensitivity reactions (eg preservatives in eye drops, contact lens solutions).	Frequently associated with a viral upper respiratory tract infection and preauricular lymphadenopathy. Most commonly caused by adenovirus.	Can be primary or secondary (eg to nasolacrimal duct obstruction). Pathogens include *S. aureus*, *S. pneumonia*, *H. influenzae*.
Clinical features	In seasonal and perennial conjunctivitis, symptoms are usually bilateral. Common symptoms: • itch • watery or mucoid discharge.	Symptoms are initially unilateral but often become bilateral within days. Common symptoms: • conjunctival injection (red eye) • watery or mucoid discharge • irritation.	Symptoms have a rapid onset. Usually unilateral but may be bilateral. Common symptoms: • conjunctival injection (red eye) • purulent discharge • crusting of the eyelids.
NB1: Excluding chlamydial conjunctivitis and gonococcal conjunctivitis			

Viral conjunctivitis

Viral conjunctivitis begins as a unilateral red eye with a watery discharge and dense follicles; it may transfer to the other eye after 2-3 days. It is usually caused by adenovirus and is frequently associated with upper respiratory tract symptoms.

Antibiotics are not indicated if there is no secondary infection. Viral conjunctivitis is highly contagious; transmission may be reduced with meticulous personal hygiene and avoiding eye rubbing and towel sharing. There should be scrupulous disinfection (eg with sodium hypochlorite or povidone-iodine) of instruments and clinical surfaces after examination of an infected patient. Sometimes symptomatic and supportive treatment may be needed, including cold compresses several times a day and lubricant eye drops. Inform patients of hygiene measures to reduce the spread of infection. Spontaneous resolution of adenoviral infection usually occurs within 2 to 3 weeks, so specific treatment is typically unnecessary.

Bacterial conjunctivitis

Bacterial conjunctivitis begins as a unilateral red eye with a purulent discharge; it may transfer to the other eye after 1 to 2 days. Common pathogens include *Haemophilus influenzae* (especially in children younger than 5 years, often causing 'conjunctivitis-otitis media syndrome'), *Streptococcus pneumoniae*, *Streptococcus pyogenes* and *Staphylococcus aureus*. About 60% of cases resolve within 5 days without treatment. If treatment is required, choice of topical antibiotic depends on severity.

For mild infection, use:

> chloramphenicol 0.5% eye drops 1 to 2 drops into the affected eye, 2- to 4-hourly for 7 days. (chloramphenicol 1% eye ointment may be used at bedtime instead of chloramphenicol drops)

For severe infection seek specialist advice (refer to Pacific Eye Centre).

Gonococcal conjunctivitis

> Gonococcal conjunctivitis is an ophthalmic emergency – seek advice from an ophthalmologist urgently

Conjunctivitis caused by *Neisseria gonorrhoeae* can also cause ulceration and perforation of the cornea, leading to blindness. Treatment involves copious irrigation with topical saline eye drops or artificial tears every 30 to 60 minutes until excessive discharge resolves, and systemic antibiotic therapy in addition to topical therapy. Use:

ciprofloxacin 0.3% (or ofloxacin 0.3%) eye drops 1 to 2 drops into the affected eye, 2- to 4-hourly for 7 days Non-EML

PLUS

ceftriaxone 1 g (infant > 1 month and child: 50 mg/kg up to 1 g) IM or IV, as a single dose

OR

cefotaxime 1 g (infant > 1 month and child: 50 mg/kg up to 1 g) IM or IV, as a single dose

If corneal ulceration is present, use:

ceftriaxone 1 g (infant > 1 month and child: 50 mg/kg up to 1 g) IV, 12-hourly for 3 days

OR

cefotaxime 2 g (infant > 1 month and child: 50 mg/kg up to 2 g) IV, 8-hourly for 3 days

Consider addition of azithromycin for chlamydial conjunctivitis as coinfection with *N. gonorrhoeae* and *C. trachomatis* is common.

Neonatal gonococcal conjunctivitis

Gonococcal conjunctivitis in neonates usually presents in the first 2 to 5 days of life, and sometimes at birth, with acute, severe, hyperpurulent conjunctivitis. It is highly contagious and can lead rapidly to perforation of the cornea and blindness.

Use:

cefotaxime 100 mg/kg IM or IV as a single dose

PLUS

azithromycin 20 mg/kg orally, daily for 3 days

Irrigate the eye with saline several times daily until purulence subsides. Immediately refer to an ophthalmologist if corneal opacity develops.

The mother of the neonate (and her sexual contacts) should be treated for gonorrhoea.

Chlamydial conjunctivitis and trachoma

Acute *Chlamydia trachomatis* conjunctivitis resembles acute bacterial or viral conjunctivitis but usually occurs in neonates or in patients with other sexually transmitted infections. Trachoma is a form of chronic *C. trachomatis* conjunctivitis. It is the leading cause of preventable infectious blindness in the world. In areas where trachoma is prevalent, regular face washing and the treatment of all household contacts is recommended. Community-wide treatment may be required in areas where prevalence is high. Systemic treatment is recommended; use:

azithromycin 1 g (child: 20 mg/kg up to 1 g) orally, as a single dose

For neonates, use:

azithromycin 20 mg/kg orally, daily for 3 days

If azithromycin is unavailable, use as a less preferred option:

doxycycline 100 mg (child 8 years or older: 2 mg/kg up to 100 mg) orally, twice daily for 14 days

OR

tetracycline 1% eye ointment applied to both eyes, twice daily for a minimum of 6 weeks. Repeat for another 6 weeks after an interval of 6 months if necessary.

OR

erythromycin 500 mg (child 1 month or older: 10 mg/kg up to 500 mg) orally, twice daily for 14 days

Treat the mother (and her sexual contacts) of an infected neonate for *C. trachomatis* infection.

Corneal infections

Corneal abrasion

Chloramphenicol eye ointment has been used as prophylaxis in corneal abrasion, despite no proven benefit. Consider:

chloramphenicol 1% eye drops or ointment topically, 4 times daily until healed

Keratitis

Infective keratitis involves infection and inflammation of the cornea and is a sight-threatening emergency.

> Urgent referral to an ophthalmologist is essential.

Causes include bacteria such as *Staphylococcus aureus*, *Streptococcus pyogenes*, *Streptococcus pneumoniae*, Enterobacteriaceae and *Pseudomonas aeruginosa* (in contact lens wearers) and viruses such as herpes simplex virus (HSV). Keratitis caused by fungi, mycobacteria or *Acanthamoeba* is rarer but more difficult to treat. Take corneal scraping (ophthalmologist only) and/or pus swab and commence empirical topical antimicrobials immediately.

Bacterial keratitis

For non-severe (small peripheral) bacterial keratitis, consider monotherapy with:

chloramphenicol 0.5% eye drops 1 to 2 drops into the affected eye, 1- to 2-hourly for the first 48 hours, then taper according to clinical response. Chloramphenicol 1% eye ointment may be used at bedtime

For severe bacterial keratitis (including contact lens related keratitis), under the guidance of an ophthalmologist only, use dual therapy:

gentamicin 0.9% or 1.4% eye drops 1 to 2 drops into the affected eye, 1- to 2-hourly for the first 48 hours, then taper according to clinical response

PLUS

ciprofloxacin 0.3% (or ofloxacin 0.3%) eye drops 1 to 2 drops into the affected eye, 1- to 2-hourly for the first 48 hours, then taper according to clinical response Non-EML

Oral or IV antibiotic therapy does not have a role in the management of uncomplicated bacterial keratitis.

Fungal keratitis

For *Candida* infection, use:

natamycin 5% eye drops 1 to 2 drops into the affected eye, 1- to 2-hourly for the first 48 hours, then taper according to clinical response and continue for at least 12 weeks Non-EML

OR

voriconazole 1% or 2% eye drops 1 to 2 drops into the affected eye, 1- to 2-hourly for the first 48 hours, then taper according to clinical response and continue for at least 12 weeks Non-EML

If neither or the above are available, as a less preferred option, use:

amphotericin B 0.15% eye drops 1 to 2 drops into the affected eye, 1- to 2-hourly for the first 48 hours, then taper according to clinical response and continue for at least 12 weeks Non-EML

For filamentous infection, use:

natamycin 5% eye drops 1 to 2 drops into the affected eye, 1- to 2-hourly for the first 48 hours, then taper according to clinical response and continue for at least 12 weeks Non-EML

Systemic antifungals (usually oral fluconazole) may be required for severe infections; consult an ophthalmologist for expert advice.

Tetracyclines (eg doxycycline 100 mg orally, twice daily) may be given for their anticollagenase effect in cases of significant thinning of the cornea.

Viral keratitis

Herpes simplex keratitis

Herpes simplex keratitis is often treated with a combination of topical and oral antiviral therapy. Use:

aciclovir 3% eye ointment 5 times per day for 10 to 14 days, or at least 3 days after healing

Where oral therapy is required (eg necrotising stromal keratitis) use:

aciclovir 400 mg orally 5 times per day for 7-10 days

Herpes zoster keratitis

See herpes zoster ophthalmicus.

Intraocular infections

Opportunistic infections

Ocular toxoplasmosis, cytomegalovirus (CMV) and tuberculosis may occur in immunocompromised patients, particularly those who are HIV-positive. Management of these conditions should be undertaken by an ophthalmologist only.

Endophthalmitis

Post-operative bacterial endophthalmitis is a serious but uncommon complication of cataract surgery. Any suspected cases require urgent management by an ophthalmologist. Treatment includes a combination of intravitreal, topical and systemic antibiotics.

Endogenous endophthalmitis may rarely occur as a result of metastatic bacterial or fungal infection, and treatment is based on the focus and microbiology of the primary infection. All cases require systemic therapy. Intravitreal injection is indicated in cases with vitreous involvement and sight-threatening choroidal lesions. Consult an ophthalmologist for expert advice.

9. Central nervous system infections

Acute bacterial meningitis

In adults, *Streptococcus pneumoniae* is the mostly likely organism. *Haemophilus influenzae* and *Neisseria meningitidis* are less common. *Listeria monocytogenes* is more common in adults older than 50 years and immunocompromised patients.

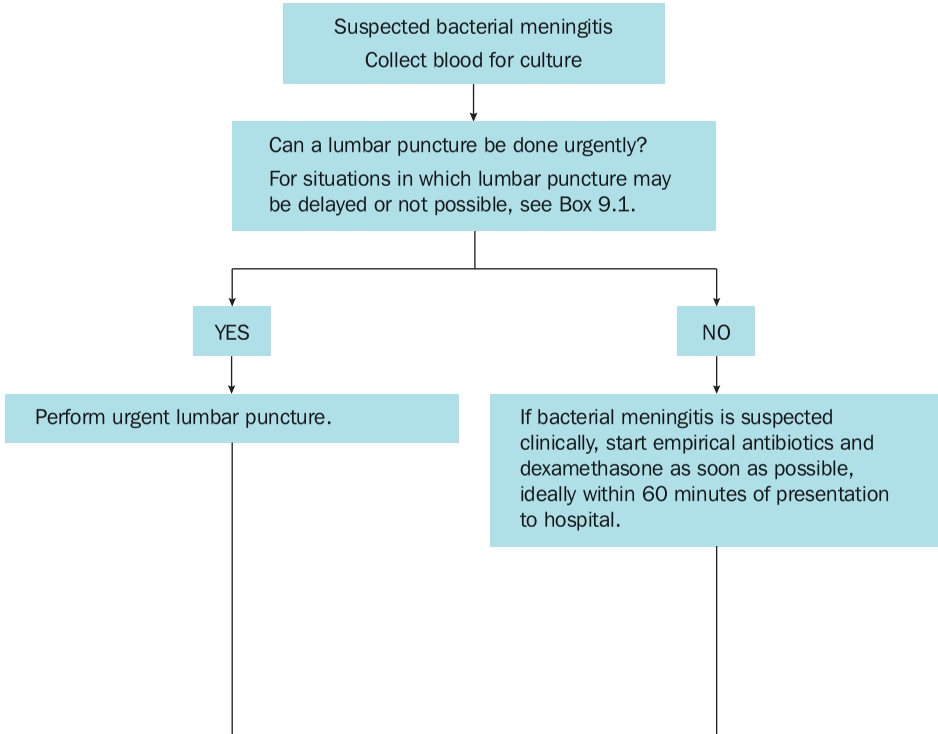
CSF microscopy and culture are vital in directing antibiotic therapy. Therefore, a lumbar puncture and blood culture should be performed urgently, if possible before antibiotic treatment is commenced. Lumbar puncture may be contraindicated in certain patients, and caution is required if the patient has a reduced conscious state, signs of increased intracranial pressure or has focal neurological signs (see Figure 9.1). A CT scan of the head is preferred before lumbar puncture in such cases if facilities are available. Where CT scan is not available, or where patients are on clopidogrel or warfarin therapy, specialist advice should be sought. Where a lumbar puncture cannot be performed, empirical therapy should be used.

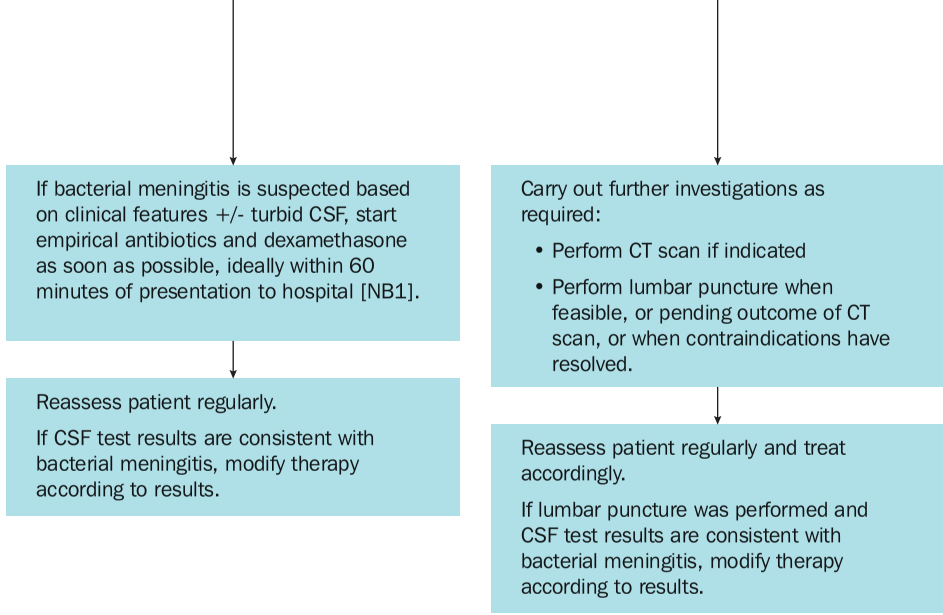
> Bacterial meningitis is a medical emergency and antibiotic therapy should be commenced as soon as possible, ideally within 60 minutes of presentation to medical care.

Do not delay treatment if there is difficulty in obtaining a CSF sample, or while awaiting a CT scan. In such cases, a blood culture should be taken and empirical therapy should be started immediately.

Chemoprophylaxis of meningitis, or other infections caused by *Neisseria meningitidis* (meningococcus) and *Haemophilus influenzae* type b (Hib) is offered to close (usually household) contacts of the index case (see page 63 for further information).

Management of suspected bacterial meningitis in adults and children (Figure 9.1)





CSF = cerebrospinal fluid; CT = computerised tomography

NB1: If clinical suspicion of bacterial meningitis is high, do not delay therapy to await CSF findings.

Can a lumbar puncture be done urgently? (Box 9.1)

Situations in which lumbar puncture may be delayed or not possible:

1. Logistical delay

2. Contraindication to lumbar puncture

- anticoagulant therapy [NB1]
- bleeding diathesis
- suspected disseminated intravascular coagulation (including evolving petechial/purpuric rash)
- localised infection overlying the lumbar region
- Chiari malformation
- significant cardiorespiratory compromise that may further deteriorate with positioning for lumbar puncture

3. CT scan indicated before considering lumbar puncture

Possible raised ICP:

- focal neurological signs
- papilloedema
- new-onset seizures (within last 7 days)
- rapidly deteriorating conscious state

Possible alternative diagnosis:

- suspected focal CNS disease
- subarachnoid haemorrhage
- immunocompromised (including HIV infection)—increased risk of mass lesions

CT = computed tomography; ICP = intracranial pressure

NB1: If available, consider use of a reversal agent in consultation with a haematologist.

Resistance to penicillin and ceftriaxone/cefotaxime have been increasingly reported in *S. pneumoniae*, and to penicillin in *N. meningitidis*. Measure the minimum inhibitory concentrations (MIC) if these organisms are isolated.

Chloramphenicol achieves good CSF penetration when taken orally, but most other drugs need to be given IV in a relatively high dose.

Early treatment with dexamethasone improves outcomes in Hib and pneumococcal meningitis. Dexamethasone should be given before or with the first dose of antibiotic; the benefit is lost if given **more than 4 hours after the first dose** of antibiotic. However, do not delay antibiotics if dexamethasone is not available.

Empirical therapy

If the organism or susceptibility is unknown, use dexamethasone and empirical antibiotic therapy to cover the most common pathogens.

For neonates and infants younger than 2 months, refer to neonatal sepsis page 83.

For adults and children 2 months or older, use:

dexamethasone 10 mg (child: 0.15 mg/kg up to 10 mg) IV, preferably starting before or with the first dose of antibiotic, then 6-hourly for 4 days [30]

PLUS EITHER

ceftriaxone 2 g (child: 50 mg/kg up to 2 g) IV, 12-hourly

OR

cefotaxime 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly

Do not delay administration of antibiotics if corticosteroids are not available. Corticosteroids can be administered up to 4 hours after starting antibiotic therapy.

[30] If dexamethasone is not available, hydrocortisone (200 mg [child: 4 mg/kg up to 200 mg] IV) may be used for the initial dose.

Where IV access is not available (eg prior to hospitalisation), treatment may be initiated with:

ceftriaxone 2 g (child 1 month or older: 50 mg/kg up to 2 g) IM[31]

OR

cefotaxime 2 g (child: 50 mg/kg up to 2 g) IM

Where ceftriaxone or cefotaxime are not available, use:

chloramphenicol 1 g (child > 1 month: 12.5 mg/kg up to 1 g) IV, 6-hourly

Where IV access is not available (eg prior to hospitalisation), chloramphenicol may be given via the IM route (same dosing applies), although this is not preferred as the preparation available in Fiji has slow and unpredictable absorption.

Listeria monocytogenes is intrinsically resistant to cephalosporins. In immunocompromised patients, adults older than 50 years, patients with a history of hazardous alcohol consumption, or patients who are pregnant or debilitated, to cover *Listeria*, **add** to the above regimen:

ampicillin 2 g IV 4-hourly (infants > 2 months and children: 75 mg/kg up to 2 g IV 6 hourly)

OR

benzylpenicillin 4 million units (2.4 g) (child: 100 000 units/kg up to 4 million units) IV, 4-hourly

OR, for patients with hypersensitivity to penicillins, use

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

For the empirical management of patients with suspected/confirmed acute bacterial meningitis with **immediate** or **delayed severe** hypersensitivity to penicillins, use

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults);

[31] Intramuscular injection of ceftriaxone is painful; consider reconstituting with lignocaine 1%. Split large intramuscular doses into two injections

see appendix for dose intervals and dosing in children

PLUS

ciprofloxacin 400 mg (child: 10 mg/kg up to 400 mg) IV 8-hourly

Where the above combination is not available, use:

chloramphenicol 1 g (child > 1 month: 25 mg/kg up to 1 g) IV 6-hourly

Once the organism has been identified and the results of susceptibility testing are available, choose the appropriate directed regimen, see directed therapy (organism and susceptibility known). If no pathogen is isolated, continue the empirical antibiotic regimen for a minimum of 10 days, depending on response.

Consider stopping antibiotics and dexamethasone if the CSF examination is consistent with viral meningitis. Stop dexamethasone if a cause other than *H. influenzae* type b (Hib) or *S. pneumoniae* is confirmed.

Directed therapy (organism and susceptibility known)

Neisseria meningitidis (meningococcal meningitis)

For meningitis caused by *Neisseria meningitidis* (meningococcal meningitis), including in patients with **delayed nonsevere** hypersensitivity to penicillins, use:

ceftriaxone 2 g (child 1 month or older: 50 mg/kg up to 2 g) IV, 12-hourly for 5 days (child: 5 to 7 days)

OR

cefotaxime 2 g (child: 50 mg/kg up to 2 g) IV, 4-6-hourly for 5 days (child: 5 to 7 days)

If susceptibility to benzylpenicillin is confirmed and the patient is **not** hypersensitive to penicillin, de-escalate therapy and use:

benzylpenicillin 4 million units (2.4 g) (child: 100 000 units/kg up to 4 million units) IV, 4-hourly for 5 days

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

ciprofloxacin 400 mg (child: 10 mg/kg up to 400 mg) IV, 8-hourly for 5 days

OR

chloramphenicol 1 g (child: 25 mg/kg up to 1 g) IV, 6-hourly for 5 days (5-7 days for children)

When *N. meningitidis* infection is confirmed, **stop** dexamethasone therapy because it is of unproven benefit.

> Prophylaxis is essential for certain close contacts and for patients who only received benzylpenicillin (see chapter 4: prevention of infection: medical, page 63).

Streptococcus pneumoniae (pneumococcal meningitis)

Test all *Streptococcus pneumoniae* isolates for susceptibility to penicillin and ceftriaxone.

For meningitis caused by *Streptococcus pneumoniae* (pneumococcal meningitis), including in patients with **delayed nonsevere** hypersensitivity to penicillins, use:

ceftriaxone 2 g (child 1 month or older: 50 mg/kg up to 2 g) IV, 12-hourly for 10 to 14 days

OR

cefotaxime 2 g (child: 50mg/kg up to 2 g) IV, 6-hourly for 10-14 days

If susceptibility to benzylpenicillin is confirmed and the patient is **not** hypersensitive to penicillin, de-escalate therapy and use:

benzylpenicillin 4 million units (2.4 g) (child: 100 000 units/kg up to 4 million units) IV, 4-hourly for 10 to 14 days

For strains resistant to penicillin and ceftriaxone, or for patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to

2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

PLUS

ciprofloxacin 400 mg (child: 10 mg/kg up to 400 mg) IV 8-hourly

Where the above combination is not available, for patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

chloramphenicol 1 g (child: 25 mg/kg up to 1 g) IV 6-hourly

Strains with resistance to penicillin are associated with high rates of failure of chloramphenicol treatment.

Haemophilus influenzae type b

For meningitis caused by *Haemophilus influenzae* type b (Hib), including in patients with **delayed nonsevere** hypersensitivity to penicillins, use:

ceftriaxone 2 g (child 1 month or older: 50 mg/kg up to 2 g) IV, 12-hourly for 7 days

OR

cefotaxime 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly for 7 days

If susceptibility to benzylpenicillin is confirmed and the patient is **not** hypersensitive to penicillin, de-escalate therapy and use:

benzylpenicillin 4 million units (2.4 g) (child: 100 000 units/kg up to 4 million units) IV, 4-hourly for 7 days

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

ciprofloxacin 400 mg (child: 10 mg/kg up to 400 mg) IV, 8-hourly for 7 days

OR

chloramphenicol 1 g (child: 25 mg/kg up to 1 g) IV, 6-hourly for 7 days

Prophylaxis is essential for certain close contacts (see chapter 4: prevention of infection: medical, page 65).

In patients younger than 5 years who have not been immunised, give age-appropriate catch-up Hib vaccination after recovery.

Listeria monocytogenes

For meningitis caused by *Listeria monocytogenes*, the preferred agent is:

> ampicillin 2 g IV 4-hourly (infants > 2 months and children: 75 mg/kg up to 2 g IV 6 hourly)
>
> OR
>
> benzylpenicillin 4 million units (2.4 g) (child: 100 000 units/kg up to 4 million units) IV, 4-hourly

For patients hypersensitive to penicillins, international guidelines recommend IV trimethoprim- sulfamethoxazole, however this is not currently available in Fiji. The role of oral trimethoprim-sulfamethoxazole is uncertain. Both vancomycin and meropenem have some activity, but their use in listeria meningitis are prone to treatment failure. Seek expert advice.

When listeria infection is confirmed, **stop** dexamethasone therapy because it is of unproven benefit.

The usual duration of therapy is 3 weeks, extended to 6 weeks in immunocompromised patients. For treatment extending beyond 3 weeks, oral therapy with trimethoprim+sulfamethoxazole can be used to complete the course if clinical features of infection have resolved and the patient is able to tolerate oral medication. Use:

> trimethoprim+sulfamethoxazole 160+800 mg (child 1 month or older: 4+20 mg/kg up to 160+800 mg) oral, 6-hourly

Healthcare-associated meningitis (including CSF shunt infection)

Meningitis and/or ventriculitis can follow cranial trauma, neurosurgery, spinal surgery, or insertion of an intracranial device, or can occur spontaneously in patients with ventricular shunts. Intracranial shunts and other devices should usually be removed. The presence of white cells in cerebrospinal fluid (CSF), especially following surgery, in the absence of other clinical features

of bacterial infection does not always indicate healthcare-associated meningitis—consider alternative diagnoses.

For empirical therapy, use:

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

PLUS

ceftazidime 2 g (child 50 mg/kg up to 2 g) IV, 8-hourly Non-EML

OR, where ceftazidime is not available, as a less preferred option **add** to vancomycin:

cetriaxone 2 g (child: 50 mg/kg up to 2 g) IV 12-hourly[32]

Ceftriaxone will cover most Gram negative pathogens, but has no cover against *Pseudomonas* or multidrug-resistant organisms (MROs).

Alternatively, where there is a high risk of multi-resistant Gram negative infection (eg known colonisation with an MRO) use meropenem (adult: 2 g [child: 40 mg/kg up to 2 g] IV 8-hourly) in addition to vancomycin.

> Blood and CSF cultures should be taken prior to antibiotic therapy wherever possible, and culture and susceptibility results followed promptly.

Modify therapy according to Gram stain and the results of CSF cultures and susceptibility testing. Increasing numbers of hospital-acquired infections are associated with MROs and antibiotic choice is complicated by the need to select antimicrobials with reliable CNS penetration—seek expert advice.

If CSF cultures remain negative after 5 to 7 days, stop empirical antibiotics and monitor the patient.

For culture-positive cases, the duration of therapy usually ranges from 10 to 21 days, depending on the:

- pathogen—shorter duration for coagulase-negative staphylococci or *Cutibacterium acnes* (formerly *Propionibacterium acnes*); longer duration

[32] If ceftriaxone is not available, substitute cefotaxime 2 g (child: 50 mg/kg up to 2 g) IV 6-hourly

- for *Staphylococcus aureus* and Gram negative bacilli
- clinical findings—shorter duration if few systemic features
- CSF findings—shorter duration if minimal CSF pleocytosis or normal CSF glucose concentration.

Temporary external ventricular catheters (used for drainage and management of intracranial pressure) that become infected should be removed.

If retention of the catheter is essential for the management of raised intracranial pressure, or an intracranial shunt cannot be removed immediately, intraventricular antimicrobial therapy can be used. The choice of antibiotic depends on Gram stain and the results of CSF cultures and susceptibility testing. Daily doses for intraventricular administration (using preservative-free preparations) that are reported in the literature for adults are: vancomycin 10 to 20 mg, gentamicin 4 to 8 mg, amikacin 30 mg. Seek expert advice.

Brain abscess and subdural empyema

Most brain abscesses are polymicrobial and can include streptococci and anaerobic bacteria. When the origin of infection is the ear, enteric Gram negative bacilli are commonly involved; after trauma or surgery *Staphylococcus aureus* is the predominant cause.

Seek a surgical opinion because aspiration or biopsy is helpful to guide antimicrobial therapy, and subdural empyema requires urgent surgical drainage. Consultation with a specialist is also advised.

For empirical therapy, use:

metronidazole 500 mg (child: 12.5 mg/kg up to 500 mg) IV, 8-hourly

PLUS

ceftriaxone 2 g (child 1 month or older: 50 mg/kg up to 2 g) IV, 12-hourly

OR

cefotaxime 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly

If clinically or bacteriologically indicated (ie suspected *Staphylococcus aureus* infection), add:

cloxacillin 2 g (child: 50 mg/kg up to 2 g) IV 6-hourly

For patients hypersensitive to penicillins instead of cloxacillin, add:

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

For brain abscess after neurosurgery or trauma, use:

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

PLUS

ceftazidime 2 g (child 50 mg/kg up to 2 g) IV, 8-hourly Non-EML

Where ceftazidime is not available, as a less preferred option **add** to vancomycin:

ceftriaxone 2 g (child 1 month or older: 50 mg/kg up to 2 g) IV, 12-hourly

OR

cefotaxime 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly

Ceftriaxone will cover most Gram negative pathogens, but has no cover against *Pseudomonas* or multidrug-resistant organisms (MROs). Alternatively, where there is a high risk of multi-resistant Gram negative infection (eg known colonisation with an MRO) use meropenem (adult: 2g IV 8-hourly) in addition to vancomycin.

Modify therapy according to Gram stain and the results of cultures and susceptibility testing. The duration of therapy is usually 4 to 8 weeks, with a minimum of 2 weeks of intravenous treatment, depending on whether surgical drainage was performed, the clinical response and radiological evidence of resolution.

In patients who show prompt clinical improvement, particularly those who have had surgical drainage of the abscess, and after a minimum of 2 weeks of intravenous therapy, a switch to oral antibiotics may be appropriate to complete a total of 4 to 8 weeks of therapy (IV + oral). Only oral antibiotics active against the pathogen and with high bioavailability and adequate cerebrospinal fluid (CSF) penetration are suitable (eg

trimethoprim+sulfamethoxazole, chloramphenicol), and the patient must be able to adhere to oral therapy. Do not use oral beta-lactams because these have only moderate bioavailability and poor CSF penetration in the absence of meningeal inflammation. Seek expert advice.

Epidural abscess

Spinal epidural abscess in adults

This is generally due to *Staphylococcus aureus*; streptococci and Gram negative bacilli are also occasionally implicated. Magnetic resonance imaging (MRI) should be used for diagnosis where available because abscesses may be missed with CT scan. Urgent surgical assessment is essential as the condition may be complicated by spinal cord compression and permanent paralysis. Antibiotics should be started as soon as the diagnosis is strongly suspected, following the collection of blood cultures (where available). For initial empirical therapy, use:

> cloxacillin 2 g (child: 50 mg/kg up to 2 g) IV, 4-6-hourly
>
> PLUS
>
> gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

For patients with hypersensitivity to penicillins, use:

> vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals
>
> PLUS
>
> gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

Due to their poor CNS penetration, cefazolin/cefalotin are not generally recommended for this indication as an alternative to cloxacillin in penicillin hypersensitivity, however they may be used as a less preferred alternative in non-immediate penicillin hypersensitivity where vancomycin is not available.

Modify therapy based on the results of Gram stain and culture of blood culture and/or operative material. If the organism is proven to be *S. aureus*, stop the gentamicin.

If no organism is identified by 72 hours, continue empiric therapy but change gentamicin to:

ceftriaxone 2 g (child: 50 mg up to 2 g) IV, 12-hourly

For **immediate** or **delayed severe** penicillin hypersensitivity, change gentamicin to:

ciprofloxacin 400 mg IV, 8-hourly OR ciprofloxacin 750 mg orally, 12-hourly

Continue therapy for at least 6 weeks, with a minimum of 2 weeks of intravenous treatment. The duration depends on whether the abscess was surgically drained, the clinical response, normalisation of inflammatory markers, susceptibility of the pathogen, presence of implanted material and radiological evidence of improvement or resolution. It may be appropriate to switch to oral therapy in patients who are clinically improving, and after a minimum of 2 weeks of intravenous therapy—this depends on the availability of suitable oral antibiotics (active against the pathogen, good bioavailability, adequate tissue penetration and patient adherence); seek expert advice.

Empirical therapy for spinal epidural abscess in children

Spinal epidural abscess is usually caused by *Staphylococcus aureus* in children. Take blood for culture before starting antibiotic therapy.

Start empirical therapy for spinal epidural abscess as soon as possible, but do not delay surgery. For children, use:

cloxacillin 50 mg/kg up to 2 g IV, 6-hourly

Use a 4-hourly cloxacillin dosing interval (ie 50 mg/kg up to 2 g IV, 4-hourly) for critically ill children.

For children with **delayed nonsevere** hypersensitivity to penicillins, use:

cefazolin 50 mg/kg up to 2 g IV, 8-hourly [33] Non-EML

[33] If cefazolin is unavailable, use cefalotin 2 g (child: 50 mg/kg up to 2 g) IV 6-hourly

For children with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

> vancomycin 15 mg/kg as an IV infusion; see appendix for dosing intervals and administration

If there is an increased risk of methicillin-resistant *S. aureus* (MRSA) (see Box 6.1 page 83), **add** to the cloxacillin or cefazolin:

> vancomycin IV infusion: 15 mg/kg actual body weight up to 750 mg 6-hourly; see appendix for additional dosing information

Continue therapy for at least 6 weeks, with a minimum of 2 weeks of intravenous treatment. The duration depends on whether the abscess was surgically drained, the clinical response, normalisation of inflammatory markers, susceptibility of the pathogen, presence of implanted material and radiological evidence of improvement or resolution. It may be appropriate to switch to oral therapy in patients who are clinically improving, and after a minimum of 2 weeks of intravenous therapy—this depends on the availability of suitable oral antibiotics (active against the pathogen, good bioavailability, adequate tissue penetration and patient adherence); seek expert advice.

Herpes simplex encephalitis

Encephalitis often presents with symptoms similar to those of acute meningitis, in particular acute onset of fever and headache. Encephalitis should be suspected if focal neurological symptoms and signs are present, including seizures, behavioural changes, focal neurological deficits and coma. A mild CSF pleocytosis is usually present, so encephalitis can be difficult to distinguish from bacterial or viral meningitis. Start aciclovir therapy in all patients with suspected acute encephalitis while further investigations are underway, because herpes simplex is the most common treatable cause.

Use:

> aciclovir 10 mg/kg (child: 500 mg/m^2 [approximately 20 mg/kg for child 5 years or younger; 15 mg/kg for child 5-12 years]) IV, 8-hourly for 14 to 21 days

If bacterial meningitis is also possible, add empirical treatment with

antibiotics (see above) until results of CSF are available.

Ongoing empirical therapy for *Listeria* infection, in addition to aciclovir, should be considered in those at risk (includes neonates and patients who are older than 50 years, immunocompromised, pregnant or debilitated, or those with a history of hazardous alcohol consumption) due to the difficulties in distinguishing the two conditions clinically and on lumbar puncture.

Toxoplasma encephalitis

In AIDS cerebral infection with *Toxoplasma gondii* is not uncommon. Ideally therapy is with sulfadiazine and pyrimethamine, which are currently unavailable in Fiji. An alternative regimen is:

> trimethoprim+sulfamethoxazole 5+25 mg/kg orally, 12-hourly for a minimum of 6 weeks

Secondary prophylaxis is often required; seek expert advice.

10. Cardiovascular system infections

Bacterial endocarditis

It is strongly recommended that the diagnosis of infective endocarditis should be based on the modified Duke diagnostic criteria. All patients with suspected endocarditis should have three samples taken for blood cultures (no more than one from each venipuncture) before initiating therapy. This should be possible even in fulminant infections, when prompt empirical use of antimicrobials is essential. A transthoracic echocardiography (TTE) or transoesophageal echocardiography (TOE) should be done in all patients with suspected endocarditis. Given the relative insensitivity of TTE, a negative scan does not exclude endocarditis where the clinical suspicion is high.

The important principles of management include:

- Intravenous treatment for the entire course, to ensure adequate drug concentrations
- Prolonged treatment – usually 4 -6 weeks

All patients with suspected endocarditis should be referred to a divisional hospital with consultant input for appropriate diagnostic tests and treatment. Surgical consultation should be considered especially in cases where infections are fulminant, complicated or slow to respond.

Once-daily dosing of gentamicin is recommended for the empirical treatment of endocarditis to cover the possibility of Gram negative sepsis. This is only an interim regimen pending the results of blood cultures. In confirmed streptococcal or enterococcal endocarditis, 8-hourly administration of gentamicin is recommended for synergistic therapy with benzylpenicillin.

In patients with proven infective endocarditis, blood cultures should be performed following initiation of antibiotic therapy to ensure clearance of bacteraemia. A single set of blood cultures should be taken after 48-72 hours of antibiotic therapy and second daily thereafter until negative.

Empirical therapy

For empirical treatment of **native valve endocarditis**, after taking three sets of blood for culture (from separate venipuncture sites), as a three-drug regimen, use:

benzylpenicillin 3 million units (1.8 g) (child: 75 000 units/kg up to 3 million units) IV, 4-hourly

PLUS

cloxacillin 2 g (child: 50 mg/kg up to 2 g) IV, 4-hourly

PLUS

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefazolin 2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly[34]

PLUS

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins use vancomycin PLUS gentamicin (see doses below).

For empirical therapy of **fulminant hospital-acquired** endocarditis, **replace** benzylpenicillin in the above regimen with vancomycin. Use:

cloxacillin 2 g (child: 50 mg/kg up to 2 g) IV, 4-hourly

PLUS

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

PLUS

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to

[34] If cefazolin is unavailable, use cefalotin 2 g (child: 50 mg/kg up to 2 g) IV 6-hourly

2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefazolin 2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly[35] Non-EML

PLUS

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

PLUS

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins use vancomycin PLUS gentamicin in doses as above.

Modify therapy based on the results of culture and susceptibility testing.

Specific therapy

Streptococcal endocarditis

Streptococcus viridans and *Streptococcus bovis* are generally highly sensitive to benzylpenicillin however, it is important to confirm sensitivities. Where susceptible, for **native valve endocarditis**, use:

benzylpenicillin 3 million units (1.8 g) (child: 75 000 units/kg up to 3 million units) IV, 4-hourly for 4 weeks

Where gentamicin therapeutic drug monitoring is available, an alternative regimen is:

benzylpenicillin 3 million units (1.8 g) (child: 75 000 units/kg up to 3 million units) IV 4-hourly for 2 weeks

PLUS

gentamicin **1 mg/kg** IV **8-hourly** for 2 weeks

[35] If cefazolin is unavailable, use cefalotin 2 g (child: 50 mg/kg up to 2 g) IV 6-hourly

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

ceftriaxone 2 g (child: 50 mg/kg up to 2 g) IV, daily for 4 weeks

Where gentamicin therapeutic drug monitoring is available, an alternative regimen is:

ceftriaxone 2 g (child: 50 mg/kg up to 2 g) IV, daily for 2 weeks

PLUS

gentamicin ***1 mg/kg*** IV ***8-hourly*** for 2 weeks

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children, for ***4 weeks***

For isolates with reduced susceptibility to penicillin, or for complicated endocarditis (large vegetation, perivalvular abscess, multiple emboli, or secondary septic events) seek expert advice. A longer course of 4-6 weeks of benzylpenicillin in combination with 2-4 weeks of synergistic gentamicin therapy is frequently required.

For **prosthetic valve endocarditis** seek expert advice. Use:

benzylpenicillin 3 million units (1.8 g) (child: 75 000 units/kg up to 3 million units) IV, 4-hourly for 6 weeks

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

ceftriaxone 2 g (child: 50 mg/kg up to 2 g) IV, daily for 6 weeks

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children, for ***6 weeks***

In complicated endocarditis, the addition of gentamicin for the first 2 weeks of therapy may be considered.

Enterococcal endocarditis

Test all enterococcal isolates for sensitivity to penicillin and gentamicin. Where susceptible, use:

benzylpenicillin 4 million units (2.4 g) (child: 100 000 units/kg up to 4 million units) IV, 4-hourly for 4-6 weeks

OR

ampicillin 2 g (child: 50mg/kg up to 2g) IV 4-hourly for 4-6 weeks

PLUS EITHER

ceftriaxone 2 g (child: 50mg/kg up to 2 g) IV 12-hourly for 6 weeks

OR (if gentamicin drug level monitoring is available)

gentamicin ***1 mg/kg*** IV, ***8-hourly*** for 4-6 weeks (adjust dose according to plasma levels)

For most patients the duration of therapy is 6 weeks; patients with uncomplicated native valve endocarditis who respond well to treatment may be treated for 4 weeks only.

For penicillin-resistant isolates, OR for patients with hypersensitivity to penicillins, use:

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children, for ***6 weeks***

PLUS (if gentamicin drug level monitoring is available)

gentamicin ***1 mg/kg*** IV, ***8-hourly*** for 4- 6 weeks (adjust dose according to plasma levels)

If gentamicin levels are not available, use vancomycin alone.

For gentamicin or vancomycin-resistant isolates, seek expert advice.

Staphylococcal endocarditis

Cloxacillin is more effective than vancomycin for methicillin-susceptible *Staphylococcus aureus* (MSSA).

For MSSA endocarditis, use:

cloxacillin 2 g (child: 50 mg/kg up to 2 g) IV, 4-hourly for 4-6 weeks

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefazolin 2 g (child: 50mg/kg up to 2 g) IV 8-hourly, for 4-6 weeks[36] Non-EML

Cefazolin does not reliably penetrate the blood–brain barrier; if spread of infection to the central nervous system is suspected, **add** vancomycin (see below) to cefazolin.

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children, for ***4-6 weeks***

For patients with complicated native valve MSSA infective endocarditis, or with prosthetic valve MSSA endocarditis, 6 weeks of therapy should be used.

Do not add gentamicin to the treatment regimen for native valve staphylococcal endocarditis because it does not improve outcomes.

For patients with methicillin-resistant *Staphylococcus aureus* (MRSA) endocarditis, use:

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children, for ***6 weeks***

Culture-negative endocarditis

The HACEK group of oral Gram negative bacilli (*Haemophilus parainfluenzae, Haemophilus aphrophilus, Aggregatibacter* [formerly *Haemophilus* or *Actinobacillus*] species, *Cardiobacterium* species, *Eikenella corrodens*, and *Kingella* species) are slow to grow in traditional culture media and their isolation may require specialised microbiological techniques currently not available in Fiji. HACEK group organisms cause fewer than 5% of cases of endocarditis and approximately one-third of these cases have prosthetic valves. Treat as per culture and sensitivity results if available.

Culture-negative endocarditis may be due to previous antibiotic use (most commonly), or unusual microorganisms. Patients with culture-negative

[36] Where cefazolin not available, use cefalotin 2 g (child: 50mg/kg up to 2 g) IV 6-hourly

endocarditis should be treated empirically with benzylpenicillin PLUS ceftriaxone as for enterococcal endocarditis, for a period of 6 weeks.

Prosthetic valve and pacemaker lead endocarditis

May be due to low-virulence members of normal flora (eg coagulase-negative staphylococci) that may be resistant to penicillin or cloxacillin. Prosthetic valve endocarditis is harder to diagnose on TTE than native valve disease. Eradication of infection may be more difficult and surgery to replace the valve, where available, is more commonly indicated.

For empirical therapy, use:

cloxacillin 2 g (child: 50 mg/kg up to 2 g) IV, 4-hourly

PLUS

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

PLUS

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

For patients with **delayed nonsevere** hypersensitivity to penicillins, use

cefazolin 2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly[37]

PLUS

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

PLUS

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins use gentamicin PLUS vancomycin in doses as above.

[37] Where cefazolin not available, use cefalotin 2 g (child: 50mg/kg up to 2 g) IV 6-hourly

Modify therapy based on the results of culture and susceptibility testing; specific therapy is given as for native valve endocarditis above.

Monitoring antibiotic therapy

Particular attention should be given to therapeutic drug monitoring (TDM) in endocarditis. Recommended doses are for the commencement of treatment only and may need to be modified according to plasma levels attained.

Gentamicin

Gentamicin levels and renal function should ideally be monitored if therapy is expected to continue for more than 48 hours. This is to ensure adequate dosing and avoid drug toxicity. Doses are lower, dosing is more frequent and synergy is the objective; monitoring hinges on trough levels. Patients should be clinically monitored for vestibular and auditory ototoxicity.

Vancomycin

Vancomycin peak and troughs concentration should be first measured at 48 to 72 hours, although a steady state may not have been reached at this time.

Note: Therapeutic drug monitoring currently has very limited availability in Fiji.

11. Intra-abdominal infections

Introduction

Intra-abdominal infections are generally polymicrobial and caused by intestinal flora. Empirical treatment of intra-abdominal infections should include antibiotics with activity against enteric aerobic Gram negative organisms (eg *Escherichia coli*). Activity against enteric anaerobic organisms is also required if the distal small bowel, appendix or colon is involved, and for more proximal gastrointestinal perforations in the presence of obstruction or paralytic ileus. Empirical treatment need not necessarily have activity against enterococci; however, treatment should be modified if enterococci are isolated from diagnostic specimens.

Gentamicin is preferred to broad-spectrum penicillins or cephalosporins (eg ceftriaxone) for empirical therapy, because gentamicin is likely to treat a greater percentage of Enterobacteriaceae, and is more rapidly bactericidal. In addition, gentamicin is less likely to contribute to the development of *Clostridioides (Clostridium) difficile* infection and the selection of antibiotic-resistant organisms.

> If amoxicillin+clavulanate or piperacillin+tazobactam are used, additional anaerobic treatment (eg metronidazole) is ***not*** required.

For patients with specific cardiac conditions (see Box 4.1 page 54) who have an intra-abdominal infection, the empirical treatment regimen should include an antibiotic active against enterococci.

Adequate drainage and debridement, to control the source of infection, are the greatest contributors to cure.

Acute appendicitis

Appendicitis begins as inflammation of the appendiceal wall, and may be followed by localised ischaemia, perforation and the development of an appendiceal abscess or generalised peritonitis.

Surgical drainage and appendicectomy are the mainstays of treatment of appendicitis.

For empirical antibiotic therapy for acute appendicitis, see peritonitis due to perforated viscus below. Following successful surgery, IV therapy can be rapidly switched to oral therapy. However, in cases of acute nonperforated appendicitis, antibiotic therapy can be discontinued after appendicectomy. For patients with a perforated appendix or an appendiceal abscess, the total duration of therapy is 5 days (IV + oral) after adequate surgical control of the source of infection has been achieved.

Diverticulitis

Diverticulitis occurs when a colonic diverticulum becomes inflamed. Diverticulitis usually presents with abdominal pain in the left lower quadrant and fever, often with an alteration in bowel habit.

Surgery should be considered if there is peritonitis associated with perforation, an abscess that is not amenable to percutaneous drainage, or bowel obstruction.

Mild diverticulitis

Antibiotic therapy may not be required for patients with mild abdominal pain and tenderness who do not have significant systemic signs or symptoms.

Antibiotics should be considered in patients with signs of diverticulitis who have markers of systemic involvement (eg fever, elevated white cell count), or in patients who have failed to respond to conservative management. See peritonitis due to perforated viscus below for appropriate oral antibiotic regimens. Continue antibiotic treatment for 5 days.

Severe or complicated diverticulitis

Patients with peritonism, or those who have signs of diverticulitis and significant systemic signs or symptoms (eg fever, elevated white cell count), should be evaluated for severe or complicated diverticulitis.

Severe or complicated diverticulitis is managed with bowel rest, IV fluids and IV antibiotics. See peritonitis due to perforated viscus for appropriate

antibiotic regimens.

For patients who have **not** undergone surgery, the total duration of therapy is 7 to 10 days (IV + oral).

For patients who have undergone surgery, the total duration of therapy is 5 days (IV + oral) after adequate surgical control of the source of infection has been achieved.

Acute cholecystitis

Acute cholecystitis is usually caused by enteric Gram negative bacilli (eg *E. coli* and *Klebsiella* species) and, less commonly, *Enterococcus faecalis*. Infrequently, infection is caused by anaerobic bacteria. A laparoscopic cholecystectomy should be considered early in the acute presentation.

For empirical therapy, use:

> gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children
>
> PLUS
>
> ampicillin 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly

If IV therapy is required beyond 72 hours, cease the gentamicin-containing regimen and use:

> ceftriaxone 2 g (child 1 month or older: 50 mg/kg up to 2 g) IV, daily[38]

For patients with **delayed nonsevere** hypersensitivity to penicillins use ceftriaxone as above. For patients with **immediate** or **delayed severe** hypersensitivity to penicillins gentamicin as a single drug is usually adequate. Seek specialist advice if intravenous therapy is required beyond 72 hours.

If oral continuation is required, use:

> amoxicillin+clavulanate 500+125 mg (child: 15 mg/kg amoxicillin component up to 500 mg) orally, 8-hourly

[38] If ceftriaxone is not available, use cefotaxime 1 g (child: 50 mg/kg up to 1 g) IV 8-hourly

For patients with hypersensitivity to penicillins, use

trimethoprim+sulfamethoxazole 160+800 mg (child 1 month or older: 4+20 mg/kg up to 160+800 mg) orally, 12-hourly

For acute cholecystitis, stop antibiotic therapy immediately after cholecystectomy. Otherwise the total duration of therapy should not exceed 7 days (IV + oral).

Acute acalculous cholecystitis is an uncommon variant of cholecystitis. For empirical therapy, **add** metronidazole to the gentamicin-containing or ceftriaxone regimen:

metronidazole 500 mg (child: 12.5 mg/kg up to 500 mg) IV, 12-hourly

For patients with hypersensitivity to penicillins, as a two-drug regimen, use:

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

PLUS

clindamycin 600 mg (child: 15 mg/kg up to 600 mg), IV, 8-hourly Non-EML

Seek expert advice for an appropriate oral step down regimen. For acute acalculous cholecystitis, the total duration of therapy is 5 days (IV + oral) after adequate surgical control of the source of infection has been achieved.

Ascending cholangitis

Ascending cholangitis is a medical emergency; it is usually associated with Gram negative bacteraemia. Anaerobic bacteria are more commonly involved where there is a history of chronic biliary obstruction. Urgent relief of biliary obstruction and prompt antibiotic treatment is required. Take blood samples for cultures before administering antibiotics.

For empirical therapy, use:

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

PLUS

ampicillin 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly

To treat anaerobic organisms in patients with ascending cholangitis in the context of chronic biliary obstruction add:

metronidazole 500 mg (child: 12.5 mg/kg up to 500 mg) IV, 12-hourly

If gentamicin is contraindicated or if IV therapy is required beyond 72 hours, cease the gentamicin-containing regimen and use:

ceftriaxone 2 g (child 1 month or older: 50 mg/kg up to 2 g) IV, daily[39]

OR

piperacillin+tazobactam 4+0.5 g (child: 100+12.5 mg/kg up to 4+0.5 g) IV, 8-hourly

If anaerobic cover is required, **add** metronidazole to ceftriaxone. Metronidazole is not required if piperacillin+tazobactam is used.

For patients with **delayed nonsevere** hypersensitivity to penicillins, use ceftriaxone as above. For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, gentamicin (with metronidazole if anaerobic cover is required) as a single drug is usually adequate. Seek specialist advice if intravenous therapy is required beyond 72 hours.

After clinical improvement, switch to oral therapy. Use:

amoxicillin+clavulanate 500+125 mg (child: 15 mg/kg amoxicillin component up to 500 mg) orally, 8-hourly

For patients hypersensitive to penicillins, for oral continuation therapy, use:

trimethoprim+sulfamethoxazole 160+800 mg (child 1 month or older: 4+20 mg/kg up to 160+800 mg) orally, 12-hourly

PLUS in patients with chronic biliary obstruction

metronidazole 400 mg (child: 10 mg/kg up to 400 mg) orally, 12-hourly

Metronidazole is not required if amoxicillin+clavulanate is used.

For cholangitis, for patients who have **not** undergone biliary drainage, the total duration of therapy is 7 to 10 days (IV + oral).

[39] If ceftriaxone is not available, substitute cefotaxime 1 g (child: 50 mg/kg up to 1 g) IV 8-hourly

For patients who have undergone biliary drainage, the total duration of therapy is 5 days (IV + oral) after drainage.

Prevention of recurrent cholangitis

In patients with recurrent cholangitis associated with ongoing bile duct disease, long-term suppressive antibiotic therapy may reduce the frequency of recurrences. Seek expert advice.

Acute peritonitis

Peritonitis due to perforated viscus

Peritonitis due to perforated viscus is usually a polymicrobial infection with aerobic and anaerobic bowel flora. Surgery is usually required.

For empirical therapy, use:

> gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children
>
> PLUS
>
> ampicillin 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly
>
> PLUS
>
> metronidazole 500 mg (child: 12.5 mg/kg up to 500 mg) IV, 12-hourly

If gentamicin is contraindicated or relevant precautions preclude its use (see appendix 1), OR if the results of susceptibility testing are not available by 72 hours and empirical IV therapy is still required, **replace** the gentamicin in the above regimen with:

> ceftriaxone 2 g (child: 50 mg/kg up to 2 g) IV, daily

Alternatively, as a single agent, use:

> piperacillin+tazobactam 4+0.5 g (child: 100+12.5 mg/kg up to 4+0.5 g) IV, 8-hourly

For patients with **delayed nonsevere** hypersensitivity to penicillins, as a two-drug regimen, use:

ceftriaxone 2 g (child 1 month or older: 50 mg/kg up to 2 g) IV, daily[40]

PLUS

metronidazole 500 mg (child: 12.5 mg/kg up to 500 mg) IV, 12-hourly

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

PLUS

clindamycin 600 mg (child: 15 mg/kg up to 600 mg) IV, 8-hourly Non-EML

Alternatively, as a single agent, use:

chloramphenicol 1 g (child: 25 mg/kg up to 1 g) IV 6-hourly

Empirical antifungal therapy is not usually required; however, consider antifungal therapy if yeasts are identified in specimens from deep surgical sites.

Use the results of susceptibility testing to guide ongoing therapy, and after clinical improvement, switch to oral therapy. If the results of susceptibility testing are not available, use:

amoxicillin+clavulanate 500+125 mg (child: 15 mg/kg up amoxicillin component up to 500 mg) orally, 8-hourly

For patients hypersensitive to penicillins, for oral continuation therapy, use:

trimethoprim+sulfamethoxazole 160+800 mg (child 1 month or older: 4+20 mg/kg up to 160+800 mg) orally, 12-hourly

PLUS

metronidazole 400 mg (child: 10 mg/kg up to 400 mg) orally, 12-hourly

The total duration of therapy is 5 days (IV + oral) after adequate control of the source of infection has been achieved.

[40] If ceftriaxone is unavailable, use cefotaxime 2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly

Patients with residual undrained intra-abdominal collections or abscesses often require a longer duration of therapy (up to 4 to 6 weeks depending on clinical and radiological progress).

Spontaneous bacterial peritonitis

Diagnosis

Spontaneous bacterial peritonitis (SBP) is usually a complication of large volume ascites in patients with severe chronic liver disease. SBP should be considered in any patient with ascites whose clinical state deteriorates. An ascitic tap is typically used to collect samples for analysis. Ascitic fluid microscopy, and cultures of ascitic fluid directly inoculated into blood culture bottles, should be performed. Total white cell count greater than 500/mm3 or neutrophil count greater than 250/mm3 is considered diagnostic. The most likely pathogens are enteric Gram negative bacilli, such as *Escherichia coli* and *Klebsiella* species. *Streptococcus pneumoniae*, other streptococci and enterococci occasionally cause infection. Anaerobic bacteria are uncommon.

In children, SBP may also occur as a primary phenomenon (without prior pathology) or as a complication of nephrotic syndrome, and in both cases *S. pneumoniae* is the most common cause.

Treatment

For empirical therapy, use:

ceftriaxone 2 g (child 1 month or older: 50 mg/kg up to 2 g) IV, daily[41]

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, ciprofloxacin is an alternative treatment option—seek expert advice.

Streptococcal or enterococcal infection is more common in patients who develop SBP while receiving prophylaxis with trimethoprim+sulfamethoxazole or norfloxacin. In these patients use piperacillin+tazobactam (4+0.5 g [child: 100+12.5 mg/kg up to 4+0.5 g] IV, 8-hourly), because cephalosporins are not active against enterococci.

[41] If ceftriaxone is unavailable, use cefotaxime 2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly

Modify antibiotic therapy according to the results of cultures and susceptibility testing. If signs and symptoms of infection resolve rapidly, treat for 5 days.

Patients with SBP and chronic liver disease who have renal impairment or jaundice are at high risk of developing hepatorenal syndrome. Albumin reduces the rate of kidney failure and improves survival.

Seek expert advice about the use of albumin in children.

Prophylaxis

Antibiotic prophylaxis to prevent SBP is indicated under certain circumstances; seek expert advice.

Acute infected pancreatitis

Introduction

The role of antibiotic therapy in the management of acute pancreatitis is limited to the treatment of infected pancreatic necrosis or pancreatic abscess. A Cochrane review found that the use of antibiotics to prevent pancreatic infection does not reduce mortality and prophylaxis is not recommended.

Infected pancreatic necrosis and pancreatic abscess

Patients with severe pancreatitis can intermittently appear septic during a prolonged hospitalisation; however, this may not necessarily indicate infection. Before giving antibiotics, every effort should be made to perform image-guided percutaneous aspiration of any pancreatic collection, with Gram stain and cultures of the aspirate.

Treatment for infected pancreatic necrosis is a step-up approach using percutaneous drainage, minimally invasive surgery and, if necessary, open surgical debridement. In pancreatic abscess, prompt percutaneous or surgical drainage is important.

For empirical treatment, use:

piperacillin+tazobactam 4+0.5 g (child: 100+12.5 mg/kg up to 4+0.5 g)

IV, 8-hourly

For patients **delayed nonsevere** hypersensitivity to penicillins, as a two-drug regimen, use:

ceftriaxone 2 g (child 1 month or older: 50 mg/kg up to 2 g) IV, daily

PLUS

metronidazole 500 mg (child: 12.5 mg/kg up to 500 mg) IV, 12-hourly

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, seek expert advice.

Data to support the use of carbapenems as the preferred agent in empirical treatment are lacking.

Modify therapy according to the results of cultures and susceptibility testing. Reserve carbapenems for infections caused by resistant pathogens.

The optimal duration of treatment is uncertain, so duration should be based on clinical response and resolution of signs of sepsis. An initial treatment course of 7 days is commonly used. The decision to prolong treatment should be based on a careful review of the patient's clinical status, and radiology and pathology results.

In severe and prolonged cases, consider secondary infection with *Candida* species or multidrug-resistant organisms, such as vancomycin-resistant enterococci and carbapenem-resistant Enterobacteriaceae. Antibiotic therapy should be directed by the results of cultures and susceptibility testing of specimens from a deep site—seek expert advice.

Liver abscess

Empirical therapy

Liver abscesses are usually bacterial (pyogenic) or amoebic. Bacterial liver abscess can be a primary infection (eg caused by *Klebsiella pneumoniae*) or a secondary infection (eg following spread from an intra-abdominal source, such as diverticulitis or biliary tract infection, or seeding from a bacteraemia).

Secondary infection is often polymicrobial, caused by aerobic and anaerobic bowel flora. Occasionally an organism of the *Streptococcus* 'milleri' group (*S. anginosus, S. constellatus, S. intermedius*) may be the sole pathogen.

The presentation of bacterial and amoebic liver abscess can be identical, so both blood cultures (for bacterial causes) and stool microscopy (for *Entamoeba histolytica*) should be performed in all cases. Ultrasound- or computerised tomography (CT)–guided needle aspiration of the abscess, together with microbiological examination of the aspirate, is usually necessary for diagnosis.

> For the treatment of bacterial liver abscess, drainage (percutaneous or open surgical) remains the mainstay of therapy; drainage is not usually necessary for the treatment of amoebic liver abscess.

The empirical antibiotic regimen must contain metronidazole to treat potential *E. histolytica* infection until the aetiology of the abscess is confirmed.

For empirical therapy, while awaiting the results of cultures and susceptibility testing, use:

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

PLUS

ampicillin 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly

PLUS

metronidazole 750 mg (child: 15 mg/kg up to 750 mg) IV, 8-hourly

OR

metronidazole 800 mg (child 15mg/kg up to 800 mg) orally, 8-hourly

If the results of susceptibility testing are not available by 72 hours and empirical IV therapy is still required, cease the gentamicin-containing regimen and use metronidazole plus ceftriaxone as below.

If gentamicin is contraindicated or relevant precautions preclude its use

(see appendix 1) or for patients with **delayed nonsevere** hypersensitivity to penicillins, as a two-drug regimen, use:

ceftriaxone 2 g (child 1 month or older: 50 mg/kg up to 2 g) IV, daily[42]

PLUS

metronidazole 750 mg (child: 15 mg/kg up to 750 mg) IV, 8-hourly.

OR

metronidazole 800 mg (child 15mg/kg up to 800 mg) orally, 8-hourly

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, metronidazole in combination with either gentamicin or ciprofloxacin are alternative treatment options—seek expert advice.

Use the results of susceptibility testing to guide ongoing therapy. If pyogenic liver abscess is confirmed, the dose of metronidazole can be decreased to standard.

The optimal treatment duration for bacterial liver abscess is unclear; a total treatment duration of 4 to 6 weeks (IV + oral) is often adequate. Clinical parameters (eg temperature and pain), inflammatory markers (eg WCC) and serial liver ultrasounds may help to assess the response to therapy. Patients with more extensive infection and/or difficult to drain abscesses may require longer courses. If there is adequate clinical improvement, consider a switch to oral therapy, especially if oral antibiotics that are as effective as parenteral antibiotics are used—seek expert advice. If results of culture and susceptibility testing are not available a reasonable oral option is amoxicillin + clavulanate.

For a confirmed *Entamoeba histolytica* liver abscess, use:

metronidazole 800 mg (child: 15 mg/kg up to 800 mg) orally, 8-hourly for 7 days

OR

tinidazole 2 g (child: 50 mg/kg up to 2 g) orally, daily for 5 days Non-EML

OR, if the patient is unable to tolerate oral therapy:

[42] If ceftriaxone is unavailable, use cefotaxime 2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly

metronidazole 750 mg (child: 15 mg/kg up to 750 mg) IV, 8-hourly for 7 days

Where available, co-administer a luminal amoebicide to eradicate cysts in the gut to prevent relapse. Use:

paromomycin 500 mg (child: 10 mg/kg up to 500 mg) orally, 8-hourly for 7 days Non-EML

12. Gastrointestinal tract infections

Candida oesophagitis

Candida oesophagitis is uncommon in Fiji's population, and most likely in immunocompromised (HIV) patients.

In patients with mild oesophageal candidiasis who are not immunosuppressed, use:

> nystatin 100 000 units/mL suspension 1 mL orally, 6-hourly for 10-14 days

In patients with more severe oesophageal candidiasis, or in patients who are immunosuppressed, use:

> fluconazole 300 mg (child: 6 mg/kg up to 300 mg) orally for the first dose, then 150 mg (child: 3 mg/kg up to 150 mg) daily for 14 to 21 days [43]

Acute gastroenteritis (diarrhoeal diseases)

Most diarrhoeal diseases are self-limiting and do not require antibiotic therapy. Oral rehydration is all that is required. Anti-motility agents such as loperamide can be used for symptomatic relief in adults, provided that there is no evidence to suggest invasive disease (eg high-grade fever or diarrhoea with blood or mucus) or obstruction. **These agents should NOT be used in children.**

Acute gastroenteritis (symptoms < 14 days) is most commonly caused by viral or bacterial pathogens. Viral gastroenteritis is typically acute and resolves spontaneously within 24 to 48 hours. Treatment is supportive; rehydration is the mainstay of therapy.

The presence of systemic symptoms (eg fever) and/or bloody diarrhoea increases the likelihood of a bacterial cause. *Campylobacter*, *Salmonella* and *Escherichia coli* are the most common pathogens. Invasive amoebiasis

[43] Only 150 mg are capsules available in Fiji, therefore doses must be in multiples of 150 mg

should be considered.

Features of viral, bacterial and toxin-mediated acute diarrhoea (Table 12.1)

Viral	Bacterial	Toxin-mediated
Prominent upper gastrointestinal symptoms such as vomiting and nausea. Typically acute, and resolves within 24 to 48 hours. Often history of contact with a person who has acute infectious diarrhoea (person-to-person transmission). May be part of an outbreak with secondary cases.	Fever, tenesmus and bloody stool. Returned travellers and immunocompromised patients at greater risk. May be associated with recent antibiotic use or hospital admission, which should prompt investigation for *Clostridioides (Clostridium) difficile*.	Vomiting, nausea and abdominal pain are usually prominent symptoms, and diarrhoea, if present, occurs later in the course of illness. Short incubation period (typically several hours only). Closely clustered cases. Infections arise from a single point source.

Antibiotics are not required, or appropriate, for many cases of bacterial diarrhoea. However, empirical antibiotic therapy is generally indicated in patients who have clinical features suggesting severe disease (eg high fever +/- rigors, tachycardia, leukocytosis, marked abdominal pain or tenderness, high-volume diarrhoea with hypovolaemia, or blood in stool), or in immunocompromised patients. Where antibiotic therapy is being given, faecal microbiological testing should be performed where practical. For empirical treatment, use:

chloramphenicol 500 mg (child 2 months or older: 12.5 mg/kg up to 500 mg) orally 6-hourly for 5 days

OR

ciprofloxacin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 12-hourly for 3 days

For more severe cases, or where oral therapy is not feasible (eg vomiting or impaired absorption), use:

ceftriaxone 2 g (child: 1 month or older: 50 mg/kg up to 2 g) IV, daily

OR

cefotaxime 2 g (child 50mg/kg up to 2 g) IV, 8-hourly

OR

ciprofloxacin 400 mg (child: 10 mg/kg up to 400 mg) IV, 12-hourly

Once improved, switch to one of the oral regimens above, using the same dose and total duration (IV + oral).

Patients who have been hospitalised for ≥48 hours who develop diarrhoea with features suggestive of severe disease should be empirically treated for *Clostridioides (Clostridium) difficile* infection.

Hydration status should be carefully assessed; oral rehydration is generally appropriate unless dehydration is severe when IV therapy is necessary.

Specific bacterial pathogens

Even when a specific bacterial pathogen is identified, not all patients require antibiotic therapy.

Shigellosis

Antimicrobial therapy is generally indicated only for patients with moderate or severe dysentery, or immunocompromised patients; it is not required for patients with mild disease or where symptoms have settled prior to identification. Treatment reduces disease transmission and may therefore also be considered for public health reasons in certain groups eg food handlers or the institutionalised. Treatment should be guided by sensitivity results where available.

For moderate cases, use:

chloramphenicol 500 mg (child 2 months or older: 12.5 mg/kg up to 500 mg) orally 6-hourly, or 1g IV 6-hourly for 5 days

OR

trimethoprim+sulfamethoxazole 160+800 mg (child 1 month or older: 4+20 mg/kg up to 160+800 mg) orally, 12-hourly for 5 days

OR

ciprofloxacin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 12-hourly for 5 days

For severe cases, use:

ciprofloxacin 400 mg (child: 10 mg/kg up to 400 mg) IV, 12-hourly

OR

ceftriaxone 2 g (child: 1 month or older: 50 mg/kg up to 2 g) IV, daily

OR

cefotaxime 2g (child 50mg/kg up to 2g) IV, 8-hourly

Once improved, switch to oral therapy as above for a total of 5 days (IV + oral).

Salmonella (non-typhoidal) enteritis

Antibiotic therapy is not generally advisable in otherwise healthy patients without risk factors for complications, as it does not improve outcome and can prolong excretion of pathogenic organisms. It is indicated in the following patient groups:

- age 65 years or older
- immunocompromised
- severe illness, sepsis or bacteraemia
- neonates and children < 3 months, or children 3-12 months who are febrile or toxic

If antibiotics are required, treat as for typhoid fever (see page 203) or based on antibiotic susceptibility, for 5 days.

Campylobacter enteritis

Antibiotics are unnecessary in most cases. In severe or prolonged (> 1 week) cases, or in frail elderly, pregnant or immunocompromised patients, use:

azithromycin 500 mg (child: 10 mg/kg up to 500 mg) orally, daily for 3 days

OR

erythromycin 500mg (child: 10 mg/kg up to 500 mg) orally 6-hourly for 5 days

OR

ciprofloxacin 500 mg (child: 12.5 mg/kg up to 500mg) orally, 12-hourly for 3 days

Parasitic infections

Intestinal amoebiasis (*Entamoeba histolytica*)

For acute amoebic colitis (dysentery), use:

metronidazole 600 mg (child: 15 mg/kg up to 600 mg) orally, 8-hourly for 7 days

For severe amoebic colitis, or with hepatic involvement (liver abscess), use:

metronidazole 800mg (child: 15 mg/kg up to 800 mg) orally, 8-hourly for 7 days

Or, if the patient is unable to tolerate oral therapy:

metronidazole 750 mg (child: 15 mg/kg up to 750 mg) IV, 8-hourly for 7 days

In order to prevent relapse, eradicate cysts in the gut with a luminal amoebicide. Where available, follow metronidazole therapy with:

paromomycin 500 mg (child: 10 mg/kg up to 500 mg) orally, 8-hourly for 7 days Non-EML

Giardiasis (*G. intestinalis, G. duodenalis, G. lamblia*)

Treatment of asymptomatic passage of giardia cysts is unwarranted. For symptomatic patients, use:

metronidazole 400 mg (child: 10 mg/kg up to 400 mg) orally, 8-hourly for 5 days

Antibiotic-associated diarrhoea

In most cases of antibiotic-associated diarrhoea, a pathogen is not identified. *Clostridioides (Clostridium) difficile* is the cause in a significant minority of cases; it is usually responsible for the more severe cases,

including pseudomembranous colitis and toxic megacolon. Infection can occur at any time during, or for some months after, a course of antibiotics. In Fiji currently, no specific diagnostic test is available, hence a high index of suspicion is required, particularly in patients developing diarrhoea in association with current or recent antimicrobial therapy, or while hospitalised for > 48 hours.

Unless ongoing antibiotic treatment is mandatory, cease treatment with any antibiotic likely to be causing the symptoms. For mild cases, observe patients for symptom resolution after stopping antibiotics. For more severe cases consider:

> metronidazole 400 mg (child: 10 mg/kg up to 400 mg) orally, 8-hourly for 10 days

For severe and/or relapsing cases seek expert advice; use:

> vancomycin 125 mg (child: 5 mg/kg up to 125 mg) ***orally***, 6-hourly for 10 days (vancomycin for injection may be made up into a solution for oral administration)

Where oral intake cannot be tolerated, metronidazole may be given IV. Use:

> metronidazole 500 mg (child: 12.5 mg/kg up to 500 mg) IV, 8-hourly until improved, then switch to
>
> metronidazole 400 mg (child: 10 mg/kg up to 400 mg) orally, 8-hourly for a total of 10 days (IV + oral)

The emergence of vancomycin-resistant enterococci (VRE) makes it essential to reserve vancomycin for severe cases of *Clostridioides (Clostridium) difficile* infection unresponsive to metronidazole. Contact the Pharmacy department regarding preparation of oral vancomycin. Intravenous vancomycin is not effective against *C. difficile* infection due to inadequate penetration of the drug into the lumen of the colon.

Early surgical referral is indicated in patients with severe disease; colectomy may occasionally be required, particularly if toxic megacolon develops.

For recurrent disease seek specialist advice; treatment strategies include use of pulse-tapered vancomycin regimens, fidaxomicin or faecal microbiota transplantation.

Typhoid and paratyphoid fevers (enteric fever)

Strains of *Salmonella* Typhi and Paratyphi (A, B and C) acquired within Fiji remain in general widely susceptible to first line agents (amoxicillin, chloramphenicol and trimethoprim-sulfamethoxazole) and second-line agents (ciprofloxacin, ceftriaxone and azithromycin). However, resistance is widespread globally, including in infections acquired on the Indian subcontinent and in Southeast Asia, and local patterns must be monitored.

For mild to moderate disease in males and non-pregnant females, where oral intake can be tolerated use:

ciprofloxacin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 12-hourly for 5-7 days

Where ciprofloxacin is not available, alternative less preferred agents include:

amoxicillin 500 mg - 1 g (child: 25-30 mg/kg up to 1 g) orally, 8-hourly for 14 days[44]

OR

trimethoprim+sulfamethoxazole 160+800 mg (child: 4 mg/kg trimethoprim component up to 160+800 mg) orally, 12-hourly for 14 days

OR

chloramphenicol 500 mg (child: 12.5-25 mg/kg up to 500 mg) orally, 6-hourly for 14 to 21 days

Sensitivities should be confirmed where possible.

For more severe disease (eg systemic toxicity, altered conscious state or organ dysfunction, prolonged fever or other need for hospitalisation), or where oral therapy is not tolerated/absorbed, use:

ciprofloxacin 400 mg (child: 10 mg/kg up to 400 mg) IV, 12-hourly

OR

ceftriaxone 2 g (child 1 month or older: 50 mg/kg up to 2 g) IV, daily [45]

[44] Amoxicillin is the preferred oral treatment for typhoid in pregnant women

[45] If ceftriaxone is unavailable, use cefotaxime 2g (child 50mg/kg up to 2g) IV, 8-hourly

Once improved, switch to oral ciprofloxacin as above for a total of 10 -14 days (IV + oral).

An alternative, but more expensive option, which may be appropriate where multidrug resistance is anticipated or proven, is:

azithromycin 1 g (child 20 mg/kg up to 1 g) orally, daily for 7 days

It is essential the patient completes the full course of treatment, even if they have fully recovered.

Despite the limited evidence base, patients with suspected/proven enteric fever and severe systemic illness with delirium, obtundation, stupor, coma or shock, should receive adjuvant corticosteroid therapy; use:

dexamethasone 3 mg/kg IV stat, followed by 1 mg/kg 6-hourly, for a total of 48 hours

Symptom resolution with successful therapy frequently takes several days; slow defervescence does not indicate treatment failure.

Following treatment, stool samples should be taken to ensure clearance of *S. typhi*; if these remain positive, or if the patient has clinical relapse, repeat treatment should be given with close attention to compliance.

Some patients may become chronic carriers of *S. typhi*, continuing to shed the organism in their stool for greater than 1 year following acute infection. For treatment of chronic carriers use:

ciprofloxacin 750 mg (child: 20 mg/kg up to 750 mg) orally, 12-hourly for 28 days

If gallstones are present, consider their removal.

Helicobacter pylori infection

Most people with *Helicobacter pylori* infection are asymptomatic, but infection confers a lifetime risk of peptic ulcer disease of 15-20% and of gastric cancer of up to 2%. *H. pylori* eradication therapy may improve dyspepsia symptoms in some patients with *H. pylori* gastritis and may reduce the risk of ulcer disease, and of gastric cancer in high risk individuals. In *H. pylori*-associated peptic ulcer disease, eradication speeds ulcer healing

and greatly reduces the chance of relapse. Indications for treatment of *H. pylori* infection include:

- all patients with duodenal ulcer, or proven *H. pylori* associated gastric ulcer (past or present)
- following resection of gastric cancer, or in *H. pylori* positive patients with first degree relatives with gastric cancer
- gastric-mucosa associated lymphoid tissue (MALT) lymphoma
- *H. pylori* positive non-ulcer dyspepsia
- *H. pylori* positive atrophic gastritis.

Eradication of *H. pylori* in asymptomatic patients may also be considered according to patient's wishes.

Eradication therapy for *H. pylori* infection requires a combination of drugs; a variety of regimens are available but vary in efficacy, compliance and cost. Where available, use:

omeprazole 20 mg orally, 12-hourly for 7 days

PLUS

clarithromycin 500 mg orally, 12-hourly for 7 days [Non-EML]

PLUS

amoxicillin 1 g orally, 12-hourly for 7 days

For patients hypersensitive to penicillins, substitute amoxicillin with:

metronidazole 400 mg orally, 12-hourly for 7 days

An alternative equally effective regimen available commercially in Fiji is Pylokit® (lansoprazole/clarithromycin/amoxicillin).

Where cost or availability is an issue, as a less preferred option, use:

ranitidine 300mg orally, once daily at night for 14 days

PLUS

amoxicillin 500mg orally, 8-hourly for 14 days

PLUS

metronidazole 400mg orally, 8-hourly for 14 days

Worms (helminths)

Hookworm infection

mebendazole 100 mg (child 10 kg or less: 50 mg) orally, 12-hourly for 3 days

Or, in pregnancy or children under 6 months

pyrantel (adult and child) 10 mg/kg up to 1 g orally, daily for 3 days

Roundworm infection

mebendazole 100 mg (child 10 kg or less: 50 mg) orally, 12-hourly for 3 days

Or, in pregnancy or children under 6 months

pyrantel (adult and child) 10 mg/kg up to 1 g orally, as a single dose (repeat after 7 days if heavy infection)

Threadworm infection

mebendazole 100 mg (child 10 kg or less: 50 mg) orally, as a single dose

Or, in pregnancy or children under 6 months

pyrantel (adult and child) 10 mg/kg up to 1 g orally, as a single dose

Due to the frequency of re-infection and autoinfection, consider repeating the dose after 2 weeks. Treat household contacts and carers at the same time to reduce the risk of re-infection. Provide advice on hygiene measures to reduce the risk of re-infection and spread of infection: wash hands regularly, avoid scratching around the anus, keep fingernails short, take a shower or bath daily, and wash clothing, towels and bed linen in hot water.

Whipworm infection

mebendazole 100 mg (child 10 kg or less: 50 mg) orally, 12-hourly for 3 days

Treatment with albendazole or mebendazole reduces worm burden but is often not curative, and re-infection is common in communities where

whipworm is endemic. Worm burden correlates with associated morbidity, such as anaemia, gastrointestinal disturbance, stunted growth and, rarely, rectal prolapse.

Strongyloidiasis

To treat strongyloidiasis in immunocompetent patients, use:

ivermectin (adult and child 15 kg or more) 200 micrograms/kg orally with fatty food, on day 1; repeat after 7 to 14 days Non-EML

OR alternatively, a less preferred option is:

albendazole 400 mg (child 10 kg or less: 200 mg) orally with fatty food, 12-hourly for 3 days; repeat course after 7 to 14 days Non-EML

In immunocompromised patients, to reduce the risk of relapse, use:

ivermectin (adult and child 15 kg or more) 200 micrograms/kg orally with fatty food, on days 1, 2, 15 and 16 Non-EML

13. Skin, muscle, bone and joint infections

Skin and soft tissue infections

Impetigo

Impetigo is most commonly caused by streptococcus species (predominantly *Streptococcus pyogenes*) and *Staphylococcus aureus*.

Many children with impetigo have dry sores as well as sores with pus or crusts. In general, only sores with pus or surrounding redness or multiple crusts require treatment with an antibiotic. Mild impetigo can be managed with simple skin hygiene methods.

First line treatment, as per the *Fiji Skin and Sore Throat Guidelines* 2018, is:

benzathine penicillin IM as a single dose

Age in months	Weight in kg	Dose in units	Volume in mL
0 up to 3	2.5 – 5.9	300 000	1.3
4 – 12	6 - 10	450 000	1.9
13 – 36	11 - 14	600 000	2.5
37 – 60	15 – 18	900 000	3.8
> 60	> 18	1 200 000	5.0
Benzathine penicillin 2.4 million units per vial. Mix with 8 mL of water for injection to make 10 mL			

OR as second line treatment or for penicillin hypersensitivity, use:

trimethoprim+sulfamethoxazole 160+800 mg (child 1 month or older: 4+20 mg/kg up to 160+800 mg) orally, 12-hourly for 5 days

If present, treat dermatosis (eg scabies, dermatitis).

Folliculitis, boils, carbuncles and skin abscesses

Usually caused by *Staphylococcus aureus* and/or *Streptococcus pyogenes*.

If the infection is mild and the patient is not diabetic or immunosuppressed,

antibiotics are not usually required. If the lesions are small and few in number they may be managed by local antiseptics and hot compresses, with incision and drainage if appropriate.

If the infection is more severe (eg spreading cellulitis or systemic symptoms, or larger abscess), or the patient is diabetic or immunosuppressed, in addition to incision and drainage (if appropriate), use:

flucloxacillin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly for 5 days

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefalexin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly for 5 days[46] Non-EML

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

trimethoprim+sulfamethoxazole 160+800 mg (child 1 month or older: 4+20 mg/kg up to 160+800 mg) orally, 12-hourly for 5 days

OR

clindamycin 450 mg (child: 10 mg/kg up to 450 mg) orally, 8-hourly for 5 days Non-EML

Where cost is a consideration, as a less preferred option, use:

erythromycin 500 mg (child: 10 mg/kg up to 500 mg) orally, 6-hourly for 5 days

Large, deep-seated abscesses may require admission to hospital for intravenous antibiotics and surgical drainage; use:

cloxacillin 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefazolin 2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly[47] Non-EML

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

[46] For mild skin infection, administering the total daily dose of cefalexin in two 12-hourly doses is also effective (cefalexin 1 g [child 25 mg/kg up to 1 g] orally, 12-hourly).
[47] If cefazolin is unavailable, use cefalotin 2 g (child: 50 mg/kg up to 2 g) IV 6-hourly

clindamycin 600 mg (child: 15 mg/kg up to 600 mg) IV, 8-hourly Non-EML

OR

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

When clinically improved, switch to oral therapy as above.

Recurrent staphylococcal skin infection

Boils (furuncles) are usually self-limiting. Decolonisation regimens are used for some patients with recurrent boils or other recurrent staphylococcal skin infections. However, successful eradication of staphylococcal carriage is only achieved in around half of patients who are treated.

Treat acute lesions (eg boils, carbuncles, folliculitis or impetigo) as above. Collect nasal and/or perineal swabs to determine antibiotic susceptibilities of *Staphylococcus aureus* before starting a decolonisation regimen. Successful eradication is unlikely if the strain is resistant to mupirocin.

Routine decolonisation of household contacts of patients with staphylococcal skin infection is not recommended. However, decolonisation of household contacts should be considered if the measures below fail to prevent recurrence in the index case. Alternatively, if household contacts of patients with staphylococcal skin infection have a history of recurrent boils or other recurrent staphylococcal skin infection, they should be decolonised concurrently with the index case.

For eradication of staphylococcal carriage (decolonisation), once all acute lesions have healed, use:

mupirocin 2% ointment inside each nostril, twice daily for 5 days Non-EML

PLUS, EITHER

for use in showers—an antiseptic wash or soap containing chlorhexidine 2% or triclosan 1%, wash once daily for at least 5 days; pay particular attention to areas of hairy skin Non-EML

OR

for use in baths—60 mL of sodium hypochlorite solution per bathtub or

triclosan 2% bath oil (diluted according to manufacturer's instructions), wash once daily for at least 5 days Non-EML

Using hot water, wash bed linen initially and then at least weekly, and wash towels after each use.

If lesions recur despite adherence to the above regimen, seek specialist advice.

Cellulitis and erysipelas

Cellulitis and erysipelas present as diffuse, spreading areas of skin erythema. Lymphangitis and lymphadenopathy, fever and systemic toxicity may be present.

> Many conditions can present similarly to cellulitis—always consider differential diagnoses.

Erysipelas is usually caused by *S. pyogenes*. Cellulitis is usually due to *S. aureus*, or beta-haemolytic streptococci eg *S. pyogenes*. Many other organisms can cause cellulitis under specific circumstances (eg *Aeromonas* following fresh water exposure, and *Vibrio* species following salt water exposure; see water-immersed wound infections page 221. In immunocompromised patients, a broad range of organisms can cause infection including Gram negative bacteria, fungi and mycobacteria.

Rest and elevation of the affected area improves clinical response. If the skin has eroded, use nonadherent dressings.

Mild early cellulitis and erysipelas

For empirical therapy to cover *Staphylococcus aureus* or *Streptococcus pyogenes* infection, use:

flucloxacillin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly for 5 days

If *S. pyogenes* is isolated from cultures, or suspected based on clinical presentation, use:

phenoxymethylpenicillin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly for 5 days

OR

procaine penicillin 1.5 million units (1.5 g) (child: 50,000 units/kg up to 1.5 million units) IM, daily for at least 3 days

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefalexin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly for 5 days[48] Non-EML

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

clindamycin 450 mg (child: 10 mg/kg up to 450 mg) orally, 8-hourly for 5 days Non-EML

Where cost is a consideration, as a less preferred option, use:

erythromycin 500 mg orally (child: 10 mg/kg up to 500 mg), 6-hourly for 5 days

Severe cellulitis

If the patient has significant systemic features or is not improving after 48 hours of oral therapy, start IV therapy. For patients with significant systemic symptoms, assess for necrotising fasciitis or underlying myonecrosis, see necrotising skin and soft tissue infections page 227. If there is associated bacteraemia, see dose modification in severe sepsis page 90.

For empirical treatment, use:

cloxacillin 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly

This dose of cloxacillin will provide sufficient cover for Group A Streptococci (GAS). There is no need to add benzylpenicillin.

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefazolin 2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly[49] Non-EML

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

[48] For mild skin infection, administering the total daily dose of cefalexin in two 12-hourly doses is also effective (cefalexin 1 g [child 25 mg/kg up to 1 g] orally, 12-hourly).
[49] If cefazolin is unavailable, use cefalotin 2 g (child: 50 mg/kg up to 2 g) IV 6-hourly

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

OR

clindamycin 600 mg (child: 15 mg/kg up to 600 mg) IV, 8-hourly

Ceftriaxone/cefotaxime have poor activity against *S. aureus* and therefore are not advisable for the treatment of cellulitis.

Even with effective therapy, local symptoms (eg erythematous rash) can worsen for 48 hours after initiation of therapy while systemic features improve.

Switch to oral therapy when systemic features have improved as for mild early cellulitis and erysipelas. The total treatment duration depends on clinical response: 5-10 days (IV + oral) is recommended.

Examine patients for skin conditions predisposing to cellulitis (via damage to the cutaneous barrier) eg tinea of the feet or scabies and treat if necessary.

Where cellulitis occurs as a complication of an ulcer, consider the need for Gram negative and / or anaerobic cover.

Acute wound infections

Traumatic wound infections (restricted to skin and soft tissues)

Antibiotic prophylaxis is not routinely required for traumatic wounds that do not require surgical management and are not significantly contaminated. Careful cleaning and debridement is the mainstay of therapy for these wounds. Consider tetanus prophylaxis. For wounds that require prophylaxis, administer as soon as possible. Likely pathogens in post-traumatic wound infection include *Staphylococcus aureus* and *Streptococcus pyogenes*; anaerobes including *Clostridium perfringens* should be considered in heavily contaminated wounds. For penetrating abdominal wounds and chest trauma other pathogens may be implicated; seek expert advice.

For significantly contaminated wounds not requiring surgical management, use as prophylaxis:

flucloxacillin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly for 5 days

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefalexin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly for 5 days[50] Non-EML

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

clindamycin 450 mg (child: 10 mg/kg up to 450 mg) orally, 8-hourly for 5 days Non-EML

These regimens are also suitable for localised wound infections where there are no systemic symptoms and no deep tissue involvement.

For wounds requiring surgical management, use as prophylaxis:

cefazolin 2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly[51] Non-EML

Where heavily contaminated (eg severe agricultural injuries), ADD:

metronidazole 500 mg (child: 12.5 mg/kg up to 500 mg) IV, OR 400 mg (child 10 mg/kg up to 400 mg) orally, 12-hourly

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use as a single agent:

clindamycin 600mg (child: 15mg/kg up to 600mg) IV, 8-hourly Non-EML

These regimens are also appropriate for wound infections associated with systemic features or involving deeper tissues.

For patients with sepsis or septic shock associated with a traumatic wound, treat as for necrotising skin and soft tissue infection.

Surgical site infections

Antibiotics may not be necessary in mild infections; surgical drainage and irrigation may be adequate. Where antibiotics are indicated, eg for associated cellulitis or deeper tissue infection, take samples for culture and susceptibility testing before starting antibiotics and adjust therapy. Surgical

[50] For mild skin infection, administering the total daily dose of cefalexin in two 12-hourly doses is also effective (cefalexin 1 g [child 25 mg/kg up to 1 g] orally, 12-hourly).
[51] If cefazolin is unavailable, use cefalotin 2 g (child: 50 mg/kg up to 2 g) IV 6-hourly

exploration, drainage, irrigation and debridement may be required for more severe infections.

Superficial surgical site infection

If antibiotics are indicated for mild to moderate infection eg cellulitis or infection of the subcutaneous tissues, where Gram positive bacteria only are suspected following a procedure which did not enter the gastrointestinal, respiratory or genitourinary tracts, use:

flucloxacillin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefalexin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly Non-EML

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

clindamycin 450 mg (child: 10 mg/kg up to 450 mg) orally, 8-hourly Non-EML

If Gram negative or anaerobic bacteria are suspected in addition to Gram positive skin flora (eg the procedure entered the gastrointestinal, respiratory or genitourinary tracts), use:

amoxicillin+clavulanate 500+125 mg (child: 15 mg/kg amoxicillin component up to 500 mg) orally, 8-hourly

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefalexin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly Non-EML

PLUS

metronidazole 400 mg (child 10 mg/kg up to 400 mg) orally, 12-hourly

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

trimethoprim+sulfamethoxazole 160+800mg (child 1 month or older: 4+20mg/kg up to 160+800mg) orally, 12-hourly

PLUS

metronidazole 400 mg (child: 10 mg/kg up to 400 mg) orally, 12-hourly

Continue antibiotic therapy for 5 days; a longer duration may be required

depending on clinical response. If there is a poor response to empirical therapy, review whether the pathogen is adequately treated and re-evaluate the wound for evidence of deeper tissue involvement.

Severe surgical site infection

For incisional surgical site infection associated with systemic features or involving deeper tissues (eg fascia or muscle), where Gram positive skin flora only are suspected following procedures which did not enter the gastrointestinal, respiratory or genitourinary tracts, use:

cloxacillin 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly

OR

cefazolin 2 g (child: 50mg/kg up to 2g) IV, 8-hourly[52] Non-EML

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

If Gram negative or anaerobic bacteria are suspected in addition to Gram positive skin flora (eg the procedure entered the gastrointestinal, respiratory or genitourinary tracts), use as a three-drug regimen:

cloxacillin 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly

OR

cefazolin 2 g (child: 50mg/kg up to 2g) IV, 8-hourly[46] Non-EML

PLUS

metronidazole 500 mg (child: 12.5 mg/kg up to 500 mg) IV, OR 400 mg (child 10 mg/kg up to 400 mg) orally, 12-hourly

PLUS

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

[52] If cefazolin is unavailable, use cefalotin 2 g (child: 50 mg/kg up to 2 g) IV 6-hourly

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use initially:

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

PLUS

clindamycin 600 mg (child: 15 mg/kg up to 600 mg) IV, 8-hourly Non-EML

If the patient is at increased risk of MRSA infection (see Box 6.1 page 83) **add** vancomycin to any of the above regimens.

Switch to oral therapy as for mild wounds as soon as possible (eg following surgery at 48 hours). Seek expert advice if MRSA is suspected or proven. The total duration of treatment (IV + oral) depends on the clinical response.

For surgical site infections associated with sepsis or septic shock, it is usually necessary to combine antibiotic therapy with source control (eg drainage, irrigation, debridement). Use vancomycin plus piperacillin+tazobactam and seek expert advice.

Bites and clenched fist injuries

General considerations

Bites and clenched fist injuries (in which the hand is lacerated by contact with another person's teeth), often become infected. The organisms associated with **human bites** and clenched fist injuries are *Staphylococcus aureus*, *Eikenella corrodens*, *Streptococcus* species and beta-lactamase–producing anaerobic bacteria. The organisms associated with **animal bites** are *Pasteurella* species, *S. aureus*, *Capnocytophaga canimorsus*, *Streptococcus* species and anaerobic bacteria. Cat bites have a higher incidence of deep infection than dog bites.

In all cases, the patient's tetanus immunisation status must be ascertained. Tetanus toxoid should be administered if the patient is not immune.

The recommended management of clenched fist injuries, and human and animal bites, is thorough cleaning, debridement, irrigation, elevation and immobilisation.

Infection not established (presumptive therapy)

For otherwise healthy individuals, antibiotic therapy is usually not necessary for bites and clenched fist injuries with a low risk of infection (eg small wounds not involving tendons or joints that present within 8 hours and that can be adequately debrided and irrigated).

Antibiotic therapy is necessary for bites and clenched fist injuries with a high risk of infection. These include:

- wounds with delayed presentation (8 hours or more)
- puncture wounds that cannot be debrided adequately
- wounds on the hand, feet or face
- wounds involving deeper tissues (eg bones, joints, tendons)
- wounds in immunocompromised patients.

If antibiotic therapy is necessary, use:

> amoxicillin+clavulanate 500+125 mg (child: 15 mg/kg amoxicillin component up to 500 mg) orally, 8-hourly for 3 days.

If there is a delay in accessing amoxicillin+clavulanate, give:

> procaine penicillin 1.5 million units (child: 50,000 units/kg up to 1.5 million units) IM, as a single dose

Start continuation therapy with oral amoxicillin+clavulanate as soon as it is available or use one of the oral regimens recommended for established infection for 2 further days.

For patients hypersensitive to penicillins, use one of the oral regimens recommended for established infection, for 3 days.

Established infection

Collect infected tissue for cultures before starting antibiotic therapy. Delaying primary wound closure should also be considered. For wounds to the hand or face, seek prompt specialist surgical consultation.

Mild infection

> amoxicillin+clavulanate 500+125 mg (child: 15 mg/kg amoxicillin

component up to 500 mg) orally, 8-hourly

For patients hypersensitive to penicillins, use:

metronidazole 400 mg (child: 10 mg/kg up to 400 mg) orally, 12-hourly

PLUS either

doxycycline 100 mg (child 8 years or older: 2 mg/kg up to 100 mg) orally, 12-hourly

OR

trimethoprim+sulfamethoxazole 160+800 mg (child 1 month or older: 4+20 mg/kg up to 160+800 mg) orally, 12-hourly

Usual treatment duration is 5 days, but a longer duration may be required depending upon clinical response.

Moderate to severe infection

piperacillin+tazobactam 4+0.5 g (child: 100+12.5 mg/kg up to 4+0.5 g) IV, 8-hourly

Where piperacillin+tazobactam is not available, use:

cloxacillin 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly

PLUS

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

PLUS

metronidazole 500mg (child: 12.5 mg/kg up to 500mg) IV, OR 400 mg (child 10 mg/kg up to 400 mg) orally, 12-hourly

Alternatively, including in patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

clindamycin 600 mg (child: 15 mg/kg up to 450 mg) IV, 8-hourly Non-EML

PLUS

ciprofloxacin 400 mg (child: 10 mg/kg up to 400 mg) IV OR if injection unavailable use 500 mg (child: 12.5 mg up to 500 mg), orally 12-hourly

Modify therapy based on the results of Gram stain, cultures and susceptibility testing. Switch to oral therapy once the patient is stable. If the pathogen is unknown, use oral antibiotic therapy as for mild infection, above.

For severe and penetrating wounds, total treatment duration is usually 14 days (IV + oral). A longer duration of directed therapy is needed for injuries involving bones, joints and/or tendons; see osteomyelitis (page 233) or septic arthritis (page 240).

Water-immersed wound infections

Aetiology of water-immersed wound infections

Skin infection or sepsis following immersion of a wound in water (eg in fishermen, swimmers, or with a marine animal bite or coral cut) may involve less typical organisms such as *Aeromonas* species and *Vibrio* species as well as the more classical wound infection pathogens such as *Staphylococcus aureus* and *Streptococcus pyogenes* (particularly from coral cuts).

Principles of management of water-immersed wounds

Careful cleaning, and debridement if necessary, of wounds that have been immersed in water is important to prevent infection.

For patients with traumatic water-immersed wounds, ensure that tetanus immunisation is up to date.

Preventive antibiotics are not routinely required for wounds that have been immersed in water. Prophylaxis is required for traumatic water-immersed wounds that require surgical management or are significantly contaminated. Presumptive therapy is required for marine animal bite wounds.

Consider early empirical therapy for patients with risk factors for developing severe infections (eg immunocompromised or diabetes).

Water-immersed wound infections can progress rapidly and even localised infections require close monitoring. Combined medical and surgical management is often required. Seek expert advice if infection is associated with systemic symptoms or involves deeper tissues (such as bones, joints or tendons), or if localised infection progresses.

The appropriate antibiotic regimen for definitive therapy depends on the pathogen. Collect samples of infected tissue or wound exudate for Gram stain, culture and susceptibility testing before antibiotic therapy is started. Modify therapy based on the results.

Empirical therapy for localised water-immersed wound infections

Seawater-immersed wounds

For empirical therapy for **localised** infection of seawater-immersed wounds (including coral cuts), use:

doxycycline 100 mg (child 8 years or older: 2 mg/kg up to 100 mg) orally, 12-hourly

PLUS

flucloxacillin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly

OR

cefalexin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly Non-EML

If an alternative to doxycycline is required for **children younger than 8 years**, replace in one of the above regimens with:

ciprofloxacin (child younger than 8 years) 12.5 mg/kg up to 500 mg orally, 12-hourly

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins replace flucloxacillin or cefalexin with:

clindamycin 450 mg (child: 10 mg/kg up to 450 mg) orally, 8-hourly Non-EML

Modify therapy based on the results of culture and susceptibility testing. The duration of therapy is determined by clinical response. A duration of 5 days is likely to be appropriate.

Fresh, brackish or soil- or sewage-contaminated water-immersed wounds

For empirical therapy for localised infection of **fresh** or **brackish water**-immersed wounds, use:

trimethoprim+sulfamethoxazole 320+1600 mg (child 1 month or over:

8+40 mg/kg up to 320+1600 mg) orally, 12-hourly

OR, as a two-drug regimen (for patients not hypersensitive to penicillins)

ciprofloxacin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 12-hourly

PLUS

flucloxacillin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly

For empirical therapy for localised infection of wounds immersed in **soil**- or **sewage-contaminated water** (eg following a flood or natural disaster) not associated with systemic features or involving deeper tissues, **add** metronidazole to the above regimens:

metronidazole 400 mg (child: 10 mg/kg up to 400 mg) orally, 12-hourly

Modify therapy based on the results of culture and susceptibility testing. The duration of therapy is determined by clinical response. A duration of 5 days is likely to be appropriate.

Empirical therapy for water-immersed wound infections associated with systemic features or deeper tissues

For empirical therapy for patients with sepsis or septic shock treat as for necrotising skin or soft tissue infection (see page 227).

Wounds not associated with significant trauma and not exposed to soil- or sewage-contaminated water

For empirical therapy, use:

cloxacillin 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly

PLUS

ciprofloxacin 400 mg (child: 10 mg/kg up to 400 mg) IV 8-hourly OR if injection not available 750 mg (child: 20 mg/kg up to 750 mg) orally, 12-hourly

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefazolin 2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly[53] Non-EML

PLUS

ciprofloxacin 400 mg (child: 10 mg/kg up to 400 mg) IV 8-hourly OR if

[53] If cefazolin is unavailable, use cefalotin 2 g (child: 50 mg/kg up to 2 g) IV 6-hourly

injection not available 750 mg (child: 20 mg/kg up to 750 mg) orally, 12-hourly

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

clindamycin 600 mg (child: 15 mg/kg up to 600 mg) IV, 8-hourly Non-EML

PLUS

ciprofloxacin 400 mg (child: 10 mg/kg up to 400 mg) IV 8-hourly OR if injection not available 750 mg (child: 20 mg/kg up to 750 mg) orally, 12-hourly

Modify therapy based on the results of culture and susceptibility testing. Switch to oral therapy (as for localised infection) as soon as possible. A total duration of therapy (IV + oral) of 5 to 7 days is likely to be appropriate; however, a longer duration of therapy is needed for wounds involving the deeper tissues (such as bones, joints or tendons).

Wounds associated with significant trauma or exposed to soil- or sewage-contaminated water

For empirical therapy for patients whose wounds are associated with **significant trauma** (including shark bites) or have been exposed to **soil**- or **sewage-contaminated water** (eg following a flood or natural disaster), seek specialist advice.

Diabetic foot infections

Diabetic foot infections may involve the skin and soft tissue as well as underlying muscle and bone, and should always be regarded as serious. They are often caused by polymicrobial (mixed) infection with aerobes and anaerobes, Gram positive and Gram negative organisms. Surgical debridement is often necessary. Surgical advice should be sought (this may not be necessary in mild cases).

Proper dressings and wound care are also extremely important. Good glycaemic control aids healing.

Adjust drug dosage (especially gentamicin) according to renal function (for drugs excreted via the kidneys), as renal impairment is common in diabetic patients. See appendix for dosing of antimicrobials in renal impairment page 357.

Renal impairment is common in diabetic patients; adjust drug dosage according to renal function (see appendix page 357)

Mild infections

For mild infections with no evidence of osteomyelitis or septic arthritis which can be managed as an outpatient, use:

amoxicillin+clavulanate 500+125 mg orally, 8-hourly for at least 5 days

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

metronidazole 400 mg orally, 12-hourly for at least 5 days

PLUS

cefalexin 500 mg orally, 6-hourly for at least 5 days Non-EML

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

chloramphenicol 500 mg orally, 6-hourly for at least 5 days

Moderate infections (requiring hospitalisation)

Empirical broad-spectrum intravenous therapy and early surgical referral is required. Use:

cloxacillin 2 g IV, 6-hourly

PLUS

metronidazole 500mg IV 12-hourly OR metronidazole 400 mg orally, 12-hourly

PLUS

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

After the first dose of gentamicin, if ongoing gentamicin therapy is not appropriate (or after a maximum of 3 days), replace in above regimen with:

ceftriaxone 2g IV daily[54]

For patients with **delayed nonsevere** hypersensitivity to penicillins, **replace** cloxacillin in the above regimen with:

cefazolin 2 g IV, 8-hourly[55] Non-EML

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

clindamycin 600 mg IV, 8-hourly Non-EML

PLUS

ciprofloxacin 400 mg IV, 12-hourly OR ciprofloxacin 500mg orally, 12-hourly

Modify therapy based on the results of culture and susceptibility testing. Switch to oral therapy once there is significant clinical improvement; where culture and susceptibility testing are not available. See mild diabetic foot infection for antibiotic choices. Continue antibiotic therapy until the infection has resolved, but not necessarily until the wound has healed. Typically a total duration of 1 to 2 weeks (IV + oral) is sufficient, however a longer duration is required for infection involving deeper tissues.

Severe infections

Early surgical referral is critical

Empirical broad-spectrum intravenous therapy is required, including cover for Pseudomonas infection, use:

piperacillin+tazobactam 4-0.5 g IV, 6-hourly

Alternatively, use the combination of:

ciprofloxacin 400 mg IV, 12-hourly OR if injection unavailable 500 mg orally 12-hourly

PLUS

[54] If ceftriaxone is not available, substitute cefotaxime 1 g IV 8-hourly
[55] If cefazolin is unavailable, use cefalotin 2 g IV 6-hourly

metronidazole 500 mg IV 12-hourly OR 400 mg orally, 12-hourly

PLUS

cloxacillin 2 g IV, 6-hourly

If ciprofloxacin is not available, such as in a peripheral centre, gentamicin can be substituted while transferring the patient or obtaining ciprofloxacin. However, do **not** use ceftriaxone / cefotaxime (unless gentamicin is also unavailable) as these do not have Pseudomonal cover.

For patients hypersensitive to penicillins, use:

clindamycin 900mg IV, 8-hourly Non-EML

PLUS

ciprofloxacin 400 mg IV, 12- hourly OR if injection unavailable 750mg orally 12-hourly

Alternatively, use:

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

PLUS

ciprofloxacin 400 mg IV, 12- hourly OR if injection unavailable 750mg orally 12-hourly Non-EML

PLUS

metronidazole 500mg IV 12-hourly OR 400 mg orally, 12-hourly

Depending on the organisms isolated from cultures of deep tissue specimens, other antibiotic combinations may be required.

Modify therapy based on the results of culture and susceptibility testing. Switch to oral therapy once there is significant clinical improvement; where culture and susceptibility testing are not available see mild diabetic foot infection for antibiotic choices. Continue antibiotic therapy until the infection has resolved, but not necessarily until the wound has healed. Typically, a total duration of 3 weeks (IV + oral) is sufficient, however a longer duration is required for infection involving deeper tissues (eg osteomyelitis or septic arthritis).

Antibiotic therapy should be ceased 2 to 5 days after amputation if the infected bone is entirely removed.

Necrotising skin and soft tissue infections (including necrotising fasciitis)

Introduction

Patients who are critically ill with skin and soft tissue infections may have necrosis of the soft tissues (necrotising fasciitis) or muscle (myonecrosis). Extensive necrosis is referred to as gangrene. These infections can be monomicrobial (eg *Streptococcus pyogenes* or *Clostridium perfringens*) or polymicrobial, when infection involves mixed aerobe–anaerobe bacterial flora (eg *Escherichia coli*, *Bacteroides fragilis*, streptococci and staphylococci).

Clinical features that suggest a necrotising infection of the skin and deeper tissues include:

- constant severe pain, even if skin inflammation is initially limited
- bullae
- skin necrosis or bruising
- the subcutaneous tissue is hard ('wooden') and painful to touch
- oedema beyond the margin of erythema
- cutaneous anaesthesia
- gas in the soft tissues (detected by palpation or imaging)
- systemic toxicity, including fever, leucocytosis, delirium or kidney failure
- rapidly spreading infection.

> The cornerstone of treatment is surgical removal of devitalised tissue (this reduces mortality and assists in diagnosis), with prompt antibiotic therapy

If available, hyperbaric oxygen therapy can be considered as an adjunct to surgical debridement for clostridial gas gangrene, but it should not delay surgery or administration of antibiotics. Intravenous immunoglobulin (IVIG) may play a role in the treatment of proven streptococcal necrotising fasciitis; seek expert advice.

Empirical therapy

For empirical therapy, if diagnosis is uncertain, until the results of tissue and blood cultures are available, use:

piperacillin+tazobactam 4+0.5 g (child: 100+12.5 mg up to 4+0.5 g) IV, 6-hourly

OR

meropenem 1 g (child: 20 mg/kg up to 1 g) IV, 8-hourly

PLUS with either of the above regimens

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

PLUS

clindamycin 600 mg (child: 15 mg/kg up to 600 mg) IV, 8-hourly Non-EML

If the above antibiotics are not available, use broad-spectrum antibiotics such as the combination of:

benzylpenicillin 3 million units (1.8 g) (child: 75 000 units/kg up to 3 million units) IV, 4-hourly

PLUS

clindamycin 600 mg (child: 15 mg/kg up to 600 mg) IV, 8-hourly

PLUS

cloxacillin 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly

PLUS

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

If clindamycin is not available, for anaerobic cover **replace** clindamycin in the above regimen with:

metronidazole 500 mg IV 12-hourly OR, if injection unavailable, 400 mg orally, 12-hourly

For penicillin hypersensitivity, seek expert advice.

Modify therapy and de-escalate antibiotic therapy based on the results of cultures and susceptibility testing of a surgical deep tissue specimen (see relevant section below). The duration of IV treatment depends on the patient's response and the ongoing need for surgery but is usually a minimum of 5 days.

Switch to oral therapy after significant improvement. If a specific cause of monomicrobial infection is not found and if methicillin-resistant *S. aureus* is not isolated from cultures, use oral antibiotics as for mild diabetic foot infection. Continue antibiotic therapy until the infection has resolved, but not necessarily until the wound has healed.

Streptococcus pyogenes necrotising fasciitis

For *S. pyogenes* necrotising fasciitis, in combination with surgical debridement, use:

benzylpenicillin 3 million units (1.8 g) (child: 75 000 units/kg up to 3 million units) IV, 4-hourly

PLUS

clindamycin 600 mg (child: 15 mg/kg up to 600 mg) IV, 8-hourly Non-EML

PLUS (consider after expert advice)

normal immunoglobulin (adult and child) 2 g/kg IV, as a single dose as soon as possible but not later than 72 hours. It is reasonable to give the dose in divided doses if it is not possible to give a single dose.

For patients with **delayed nonsevere** hypersensitivity to penicillins, **replace** benzylpenicillin in the above regimen with:

cefazolin 2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly[56] Non-EML

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, seek expert advice.

The duration of IV treatment depends on the patient's response and the ongoing need for surgery, but is usually a minimum of 7 days. Switch to oral therapy after significant clinical improvement and when no further debridement is necessary; use:

[56] If cefazolin is unavailable, use cefalotin 2 g (child: 50 mg/kg up to 2 g) IV 6-hourly

amoxicillin 1 g (child: 25mg/kg up to 1 g) orally 8-hourly.

For patients with hypersensitivity to penicillins, use:

clindamycin 450 mg (child: 10 mg/kg up to 450 mg) orally, 6-hourly Non-EML

Consider prophylaxis for close contacts of patients with *S. pyogenes* necrotising fasciitis (see prevention of infection: medical, page 65).

Clostridium perfringens myonecrosis

Myonecrosis (gas gangrene) is usually caused by *C. perfringens* and is a surgical emergency. In severe infection, hyperbaric oxygen therapy should be considered if available. Use:

benzylpenicillin 3 million units (1.8 g) (child: 75 000 units/kg up to 3 million units) IV, 4-hourly

PLUS

clindamycin 600 mg (child: 15 mg/kg up to 600 mg) IV, 8-hourly Non-EML

For patients hypersensitive to penicillin, use:

clindamycin 600 mg (child: 15 mg/kg up to 600 mg) IV, 8-hourly Non-EML

PLUS

metronidazole 500 mg (child: 12.5 mg/kg up to 500 mg) IV, ***8-hourly***

Change to oral treatment once significant clinical improvement, afebrile for 48-72 hours and no further debridement is necessary. Continue oral therapy until infection has resolved, but not necessarily until wound has healed.

Burns

For minor burns use sterilised gauze dressing impregnated with white soft paraffin.

For severe burns or if there is evidence of infection, use:

topical 1 % silver sulfadiazine + 0.2 % chlorhexidine cream (eg Silvazine®)

OR

silver-impregnated dressing Non-EML

Silver sulfadiazine cream is active against most Gram positive organisms and Gram negative bacteria and yeasts. It can be used with or without a light dressing. It does not penetrate eschar.

Systemic antibiotic treatment should not be used routinely but only to treat infections based on microbiological testing.

A single dose of an antibiotic may be given before surgical debridement (see Table 3.1, page 45).

Pyomyositis

Staphylococcus aureus is the most common organism. Surgical intervention is usually necessary. Use:

cloxacillin 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly until improved

then flucloxacillin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefazolin 2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly until improved[57] Non-EML

then cefalexin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly Non-EML

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

then clindamycin 450 mg (child: 10 mg/kg up to 450 mg) orally, 6-hourly

Treat for a total of 14 to 21 days (IV + oral).

Mastitis

Acute mastitis is usually associated with lactation and is frequently due to *Staphylococcus aureus*. Milk stasis is to be avoided; breastfeeding or expressing milk (manually or via a pump) from the infected breast is safe

[57] If cefazolin is unavailable, use cefalotin 2 g (child: 50 mg/kg up to 2 g) IV 6-hourly

and should be continued. In the absence of systemic symptoms in early mastitis these measures are adequate.

If systemic symptoms develop, use:

flucloxacillin 500 mg orally, 6-hourly

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefalexin 500 mg orally, 6-hourly Non-EML

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

erythromycin 500 mg orally, 6-hourly

OR

clindamycin 450 mg orally, 8-hourly Non-EML

For severe infection, use:

cloxacillin 2 g IV, 6-hourly

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefazolin 2 g IV, 8-hourly[58] Non-EML

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals

OR

clindamycin 600 mg IV, 8-hourly Non-EML

Switch to oral therapy as for mild infection when symptoms are resolving.

Generally, 5 days of therapy is sufficient, treatment may be required for up to 10 days. If infection does not resolve with antibiotic therapy, consider whether infection is caused by another pathogen or the presence of an abscess (which requires review, surgical drainage and microbiological examination of the pus).

[58] If cefazolin is unavailable, use cefalotin 2 g (child: 50 mg/kg up to 2 g) IV 6-hourly

Bone and joint infections

Bone infections (osteomyelitis)

Osteomyelitis is best classified by its anatomical location (long-bone or vertebral), its time course (acute or chronic) and patient factors (child or adult, and the presence or absence of vascular compromise).

Acute osteomyelitis refers to symptoms present for less than 14 days. Chronic osteomyelitis refers to a relapsed or long-standing bone infection. It is characterised pathologically by low-grade inflammation, and the presence of sequestra or an involucrum (new bone formation adjacent to a sequestrum). Acute osteomyelitis is potentially curable with antibiotic therapy alone, but chronic osteomyelitis requires surgical debridement in addition to antibiotic therapy for cure.

> Chronic osteomyelitis requires surgical debridement plus antibiotic therapy for cure.

Long-bone osteomyelitis

The usual causative agent is *Staphylococcus aureus*, or occasionally streptococcus species. Perform blood cultures, and obtain suitable specimens of bone or pus for cultures and histology if necessary; ideally before administering antibiotics.

For empirical therapy, use:

cloxacillin 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly

then switch to flucloxacillin 1 g (child: 25 mg/kg up to 1 g) orally, 6-hourly

If high dose oral flucloxacillin causes nausea and vomiting, the dose in adults may be reduced to:

flucloxacillin 500 mg orally, 6-hourly

PLUS

probenecid 1 g orally, daily

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefazolin 2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly[59] Non-EML

then switch to cefalexin 1 g (child: 25 mg/kg up to 1 g) orally, 6-hourly Non-EML

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, or proven methicillin-resistant Staphylococcus aureus (MRSA), use:

vancomycin IV infusion: adults 15 to 20 mg/kg actual body weight up to 2 g (consider loading dose 25 to 30 mg/kg for critically ill adults); see appendix for dose intervals and dosing in children

Followed by ONE of the following oral antibiotic options depending on susceptibility testing:

clindamycin 450 mg (child: 10 mg/kg up to 450 mg) orally, 8-hourly Non-EML

OR

trimethoprim+sulfamethoxazole 160+800 mg (child 1 month or older: 4+20 mg/kg up to 160+800 mg) orally, 12-hourly

OR, for multi-drug-resistant MRSA, use the combination of:

rifampicin 300 mg (child: 7.5 mg/kg up to 300 mg) orally, 12-hourly

PLUS

fusidic acid 500 mg (child: 12 mg/kg up to 500 mg) orally, 8-hourly (reduce to 12-hourly if not tolerated) Non-EML

Rifampicin should **not** be given as a single agent due to the rapid development of resistance.

Duration of therapy depends on whether the infection is acute or chronic, and the age of the patient, see Table 13.1, page 236.

In adult patients with risk factors including a history of injecting drugs, postoperative infection, current or recent confirmed urinary tract or gastrointestinal infection or healthcare-acquired infection, the spectrum of potential pathogens is broader—treat as for vertebral osteomyelitis.

For adult patients with a contiguous foot or leg ulcer in the setting of diabetes or vascular insufficiency, see diabetic foot infection, page 223.

[59] If cefazolin is unavailable, use cefalotin 2 g (child: 50 mg/kg up to 2 g) IV 6-hourly

Modify therapy according to the results of cultures and susceptibility testing.

For long-bone osteomyelitis, an improvement in symptoms is expected over days to weeks, with minimal symptoms by the end of treatment.

Vertebral osteomyelitis

In children, vertebral osteomyelitis is usually associated with *Staphylococcus aureus*; for empirical therapy, see long-bone osteomyelitis for regimens.

For empirical therapy of vertebral osteomyelitis in adults, in addition to the most common pathogen *S. aureus*, there is a need to cover the possibility of a wide variety of other pathogens including Gram negative organisms, coagulase-negative staphylococci and enterococci. Tuberculosis infection should also be considered. Due to the wide variety of possible pathogens, collection of bone or pus specimens to perform cultures and histopathology is recommended where possible.

In adults, use initially:

ceftriaxone 2 g IV, daily[60]

PLUS

cloxacillin 2g IV, 6-hourly

Modify therapy according to the results of cultures and susceptibility testing.

For vertebral osteomyelitis, ongoing pain may be expected for months after the completion of treatment and does not, in itself, indicate that the infection is unresolved.

[60] If ceftriaxone is not available, substitute cefotaxime 1 g IV 8-hourly

Suggested duration of therapy for long-bone or vertebral osteomyelitis (Table 13.1)

	Age	Duration of antibiotic therapy (modify according to clinical response)	
		Intravenous	Total duration (can be completed with oral therapy)
Acute osteomyelitis	neonate	4 weeks	4 weeks (all IV)
	child	minimum 1 week*	minimum 4 weeks
	adult	4 weeks	minimum 6 weeks
Chronic osteomyelitis	child	may not be necessary	minimum 6 weeks
	adult	2 weeks	many months

Children usually require a shorter duration of therapy than adults because their bones have an excellent blood supply. Intravenous therapy should generally be continued until blood culture results are negative, the child is afebrile and has clinically improved and erythrocyte sedimentation rate (ESR) is decreasing. *Some children need a longer duration of intravenous therapy than recommended in Table 13.1

For **adults** who are clinically improving, emerging evidence supports an earlier switch to oral therapy than suggested in Table 13.1. Expert advice is recommended to select an appropriate oral antimicrobial regimen that is as effective as intravenous therapy.

Open fractures

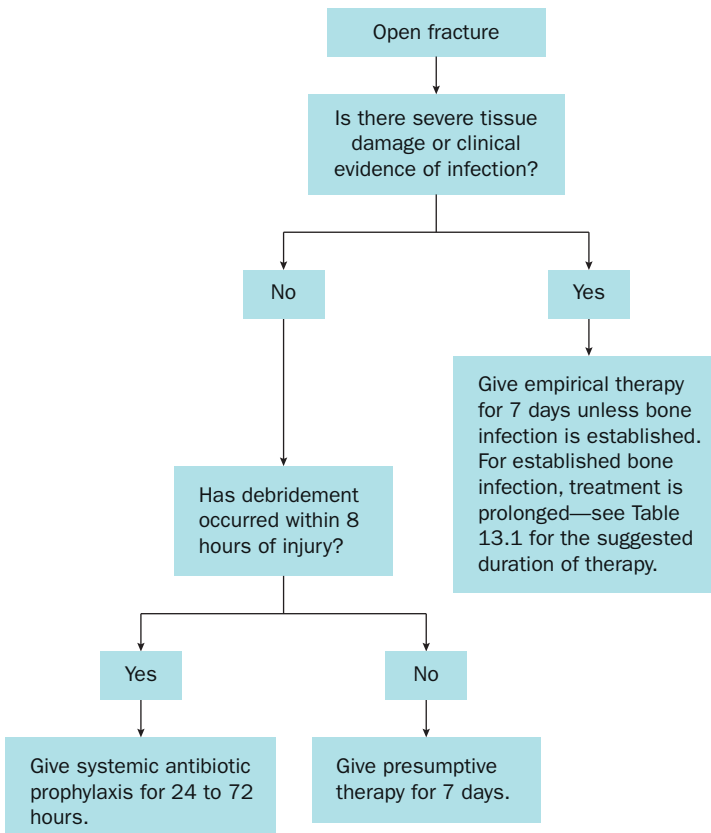
General principles

Open (compound) fractures are those where the bone has broken the skin and the fracture is exposed to the external environment. Urgent orthopaedic consultation is essential. Thorough debridement, irrigation, and fracture stabilisation (by internal or external means) are critical for preventing infection.

Ascertain the tetanus immunisation status of all patients with open fractures and give tetanus toxoid if indicated.

The choice and duration of antibiotic therapy for open fracture (prophylaxis, presumptive therapy or empirical therapy) depends on the nature and extent of tissue damage, and the timeliness of debridement, see Figure 13.1 below.

Antibiotic management of open fractures (Figure 13.1)



Prophylaxis for open fractures

cloxacillin 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly

PLUS

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

Alternatively, as a single agent, use:

cefazolin 2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly[61] Non-EML

The total duration of prophylaxis should be no more than 72 hours.

Presumptive therapy

Use one of the regimens for prophylaxis above, but continue for 7 days (IV + oral), switching to one of the oral regimens below. If intravenous therapy is required for more than 3 days, or is contraindicated, **replace** gentamicin with:

ceftriaxone 2 g IV daily

Empirical therapy for established infection

cloxacillin 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly

PLUS

ceftriaxone 2 g IV daily

For patients with **delayed nonsevere** hypersensitivity to penicillins, give:

cefazolin 2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly Non-EML

Additional anaerobic activity is recommended for **severe injuries** that are heavily contaminated with material embedded in bone or deep soft tissues (eg agriculture injuries, injuries involving sewage). For such injuries, **add** metronidazole to the above regimens. Use:

metronidazole 500 mg (child: 12.5 mg/kg up to 500 mg) IV, 12-hourly OR
metronidazole 400 mg (child: 10 mg/kg up to 400 mg) orally 12-hourly

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins,

[61] If cefazolin is unavailable, use cefalotin 2 g (child: 50 mg/kg up to 2 g) IV 6-hourly

or if there has been significant fresh or salt water exposure, use:

ciprofloxacin 400 mg (child: 10 mg/kg up to 400 mg) IV, 8-hourly

PLUS

clindamycin 600 mg (child: 15 mg/kg up to 600 mg) IV, 8-hourly Non-EML

For oral continuation therapy in presumptive therapy or established bone infection, use:

amoxicillin+clavulanate 500+125 mg (child: 15 mg/kg amoxicillin component up to 500 mg) orally, 8-hourly

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefalexin 1 g (child: 25 mg/kg up to 1 g) orally, 6-hourly Non-EML

PLUS

metronidazole 400 mg (child: 10 mg/kg up to 400 mg) orally, 12-hourly

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, or if there has been significant fresh or salt water exposure, use:

ciprofloxacin 750 mg (child: 20 mg/kg up to 750 mg) orally, 12-hourly

PLUS

clindamycin 450 mg (child: 10 mg/kg up to 450 mg) orally, 8-hourly Non-EML

Maxilla or mandible fractures

Antibiotic prophylaxis is not required for closed or open facial fractures that do not require surgical management. Refer all patients with maxillofacial trauma to a specialist as soon as possible for further review and management.

Presumptive antibiotic therapy may be required for wounds at high risk of infection or significantly contaminated wounds. Facial fractures requiring surgical management may require surgical antibiotic prophylaxis, given within 120 minutes of the procedure (see Table 3.1, page 45). Antibiotic prophylaxis between injury and the perioperative period is usually not necessary.

If antibiotic therapy is required, use

amoxicillin+clavulanate 500+125 mg (child: 15 mg/kg amoxicillin component up to 500 mg) orally, 8-hourly

Do not continue prophylaxis for severe injuries for more than 24 hours after definitive wound closure. Regardless of injury severity, the total duration of prophylaxis should be no more than 72 hours, even if soft tissue coverage is not achievable. For empiric therapy of established infection treat for 5 days.

For more severe infection with systemic features, use:

cefazolin 2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly[62] Non-EML

PLUS

metronidazole 500 mg (child: 12.5 mg/kg up to 500 mg) IV, 12-hourly
OR metronidazole 400mg oral 12-hourly

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

clindamycin 600 mg (child: 15 mg/kg up to 600 mg) orally, 8-hourly Non-EML

Once systemic signs have improved, switch to oral therapy as for mild infection. Total duration of treatment (IV + oral) is 14 days.

For presumptive therapy for other facial fractures, see page 322.

Septic arthritis

Empirical therapy for septic arthritis is as for long-bone osteomyelitis, see page 233. Consider *N. gonorrhoeae* in sexually active adults; treat as for gonococcal sepsis, see page 99.

Diagnostic specimens should include blood culture and a joint aspirate, so that alternative or coexisting diagnoses, such as an acute crystal arthropathy, can be excluded and antibiotic therapy directed. Where possible take specimens before starting antibiotic therapy. Early orthopaedic consult is desirable.

Duration of treatment is given in Table 13.2:

[62] If cefazolin is unavailable, use cefalotin 2 g (child: 50 mg/kg up to 2 g) IV 6-hourly

Suggested duration of therapy for septic arthritis (Table 13.2)

Age	Duration of antibiotic therapy (modify according to clinical response) [NB1]	
	Intravenous (minimum)	Total duration (completed with oral therapy)
neonate	3 weeks	3 weeks (all IV)
child	3 days	3 weeks
adult	2 weeks	4 weeks
NB1: These treatment durations do not apply to gonococcal arthritis.		

Urgent surgical drainage and microbiological examination of pus maybe required. Modify antibiotics according to culture and sensitivity as appropriate.

Infection of bone and joint prostheses

Bone and joint infections where prosthetic material, eg prosthetic joints or fracture fixation devices, are present are extremely complex to manage. Expert advice should be sought early. Combined specialist surgical and medical input is generally important; prolonged duration of antibiotic therapy +/- removal of prosthetic material where feasible is often required.

14. Urinary tract infections

Urinary tract infections (UTIs) include cystitis (infection/inflammation of the bladder or urethra), pyelonephritis (infection of the renal parenchyma), prostatitis and renal abscess. A UTI may variably be described as "complicated" when there is extension of infection beyond the bladder (eg in pyelonephritis) or where the infection occurs in the context of an underlying structural abnormality of the renal tract (eg renal calculi) or in a vulnerable host (eg poorly controlled diabetic). Complicated UTIs are more commonly associated with serious complications or treatment failure and may require longer treatment courses. Diagnosis of a bacterial urinary tract infection is based on the presence of symptoms, with a significant concentration of uropathogenic bacteria, generally with pyuria, in a properly collected urine sample.

Urinary tract infections in adults

Acute cystitis in adults

Cystitis typically presents with dysuria, frequency and/or urgency; fever is rare. Urine cultures are not mandatory in non-pregnant women with suspected uncomplicated cystitis, but should be performed (if possible before the administration of antibiotics), in pregnant women, men, and in all patients with recent antibiotic use, treatment failure or recurrent infection.

Amoxicillin is not recommended for empirical treatment of cystitis due to high rates of resistance. Amoxicillin+clavulanate has an unnecessarily broad spectrum of activity for empirical therapy for cystitis and should be avoided. Do not use quinolones (eg norfloxacin, ciprofloxacin) for first line treatment because their use is associated with the development of resistance, and they are the only oral drugs now available for infections caused by *Pseudomonas aeruginosa* and some multidrug-resistant bacteria.

Non-pregnant women

For otherwise well young women, without comorbidities, symptomatic treatment (analgesia, without antibiotics) may be appropriate for the

management of acute cystitis; most become symptom free within 1 week. The risk of acute pyelonephritis or sepsis is low, although it may be reduced by antibiotic therapy.

Where antibiotics are prescribed, for empirical therapy, use:

trimethoprim 300 mg orally, daily at night for 3 days

OR

cefalexin 500 mg orally, 12-hourly for 5 days Non-EML

OR

nitrofurantoin 100 mg orally, 6-hourly for 5 days

If urine culture and susceptibility testing were performed and the pathogen is resistant to empirical therapy, do not modify therapy if symptoms of cystitis are improving.

If the pathogen is resistant to empirical therapy and symptoms of cystitis are not improving, use the narrowest spectrum antibiotic to which the pathogen is susceptible.

Men

The majority of UTIs in adult males occur in the elderly, in association with abnormalities of the urinary tract (eg bladder outlet obstruction from prostatic hypertrophy) or with instrumentation. UTI in younger males is uncommon; all younger males with recurrent UTI should be investigated to exclude an underlying abnormality.

In men, longer antibiotic courses are required. Obtain urine samples for culture and susceptibility testing prior to treatment. For empirical therapy while awaiting the results of investigations, use:

trimethoprim 300 mg orally, daily at night for 7 days

OR

cefalexin 500 mg orally, 12-hourly for 7 days Non-EML

OR

nitrofurantoin 100 mg orally, 6-hourly for 7 days

The presence of marked systemic symptoms (eg high fever, rigors), pelvic or perineal pain or a history of recurrent cystitis, may suggest accompanying prostatitis; a gentle digital rectal examination for prostatic oedema and tenderness should be performed. Do not use nitrofurantoin unless the patient is afebrile and prostatitis is considered unlikely, because therapeutic concentrations of nitrofurantoin are not reached in the prostate.

If urine culture and susceptibility testing were performed and the pathogen is resistant to empirical therapy, do not modify therapy if symptoms of cystitis are improving.

If the pathogen is resistant to empirical therapy and symptoms of cystitis are not improving, use the narrowest spectrum antibiotic to which the pathogen is susceptible.

If relapse occurs, pyelonephritis or prostatitis should be considered and treatment given as below.

Treatment failures are usually due to a resistant organism, an unsuspected underlying abnormality of the urinary tract or re-infection with a similar organism.

Urethritis should be considered as an alternate diagnosis to cystitis in sexually active men.

Pregnant women

In asymptomatic infection, treatment should be delayed until culture and sensitivity results are known. If empirical treatment is indicated, use:

nitrofurantoin 100mg orally, 6-hourly for 5 to 7 days

(avoid nitrofurantoin during the last four weeks of pregnancy, ie from week 36, due to an increased risk of neonatal jaundice and haemolytic anaemia)

OR

cefalexin 500mg orally, 12-hourly for 5 to 7 days Non-EML

Although trimethoprim was traditionally avoided in pregnancy, evidence shows that it can be safely used in the second and third trimesters. Use:

trimethoprim 300 mg orally, daily at night for 3 days

Adjust antibiotic therapy as required once culture and sensitivity results are available.

Acute pyelonephritis in adults

Pyelonephritis is suggested by the presence of fever, flank/costovertebral angle tenderness, and/or other signs of systemic illness. Attempt to define or exclude underlying anatomical or functional abnormality. Urine should be sent for culture, ideally prior to antibiotic therapy. Imaging should be strongly considered to rule out complications eg obstruction or an abscess which may require surgical drainage, especially if symptoms fail to resolve.

Nitrofurantoin is unsuitable for pyelonephritis (or prostatitis) as its tissue concentration is inadequate.

Treatment should be directed by culture and susceptibilities.

Acute pyelonephritis in non-pregnant women and men

Mild pyelonephritis

For empirical therapy of mild pyelonephritis (low-grade fever, no nausea or vomiting), use:

amoxicillin+clavunate 500+125 mg orally, 8-hourly for 10 to 14 days

For adults with hypersensitivity to penicillins, use:

ciprofloxacin 500 mg orally, 12-hourly for 7 days

Modify empirical therapy based on the results of cultures and susceptibility testing. If the pathogen is susceptible to any of the following narrower-spectrum antibiotics, stop the empirical regimen and switch to:

amoxicillin 500 mg orally 8-hourly for 10 to 14 days

OR

trimethoprim 300 mg orally, daily for 10 to 14 days

OR

cefalexin 500 mg orally, 6-hourly for 10 to 14 days Non-EML

OR

trimethoprim+sulfamethoxazole 160+800 mg orally, 12-hourly for 10 to 14 days

If resistance to all of the above drugs is confirmed, or if *Pseudomonas* species is isolated (and is susceptible), use:

ciprofloxacin 500 mg orally, 12-hourly for 7 days

Do not perform post-treatment urine culture to confirm resolution of infection for asymptomatic patients, except for men where prostatitis is suspected.

Severe pyelonephritis

Infection is usually caused by Gram negative organisms (usually *E. coli*, but also *Klebsiella* or *Proteus* species). Infection can also be caused by *Staphylococcus saprophyticus* and, less commonly, enterococci and *Streptococcus agalactiae* (group B streptococcus).

For empirical therapy, use:

ampicillin 2 g IV, 6-hourly

PLUS

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients, and dosing in children

For patients hypersensitive to penicillins, gentamicin can be used alone.

If the prolonged use of an aminoglycoside is undesirable eg in the elderly, in the presence of significant renal impairment, or following a previous adverse reaction, use as a single drug (unless immediate or delayed severe hypersensitivity to penicillins):

ceftriaxone 2 g IV, daily[63]

Ceftriaxone and cefotaxime are not effective against *Pseudomonas*, enterococci or organisms that produce extended-spectrum beta-lactamase (ESBL) enzymes.

In hospitalised patients, or those who have had recent international travel (within 6 months) to highly endemic regions (eg Asia, including India), multi-resistant Gram negative bacteria including extended-spectrum beta-

[63] If ceftriaxone is unavailable, use cefotaxime 1 g IV 8-hourly

lactamases (ESBLs) should be considered and covered empirically in critically unwell patients; seek expert advice.

Modify empirical therapy based on the results of culture and susceptibility testing and clinical response, with early conversion to oral therapy once fever has settled and oral intake is tolerated. If susceptibility results are not available by 72 hours and empirical IV therapy is still required, cease the gentamicin-containing regimen and use ceftriaxone as above.

The total duration of therapy (IV + oral) is usually 10 to 14 days. Do not perform post-treatment urine culture to confirm resolution of infection for asymptomatic patients, except for men where prostatitis is suspected.

Acute pyelonephritis in pregnancy

Acute pyelonephritis in pregnancy has been associated with adverse maternal and foetal outcomes.

For the empirical therapy of pregnant women with pyelonephritis, while awaiting the results of investigations, use:

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients

PLUS

ampicillin 2 g IV, 6-hourly

> Pregnancy is not a contraindication for the use of gentamicin in the treatment of acute pyelonephritis.

If gentamicin is contraindicated for another reason, as monotherapy use:

ceftriaxone 2 g IV, daily[64]

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use gentamicin as a single drug (as above) for empirical therapy.

Modify empirical therapy based on the results of culture and susceptibility testing. If susceptibility results are not available by 72 hours and empirical intravenous therapy is still required, stop the gentamicin-containing

[64] If ceftriaxone is unavailable, use cefotaxime 1 g IV 8-hourly

regimen and use ceftriaxone as above (unless immediate or delayed severe hypersensitivity to penicillins).

Switch to oral therapy once the patient is clinically stable. Oral therapy should be based on the results of culture and susceptibility testing. If susceptibility is confirmed, suitable regimens include:

amoxicillin 500 mg orally, 8-hourly

OR

cefalexin 500 mg orally, 6-hourly Non-EML

OR

amoxicillin+clavulanate 500+125 mg orally, 8-hourly

Although trimethoprim has traditionally been avoided in pregnancy, evidence shows that it can be safely used in the second and third trimesters. Use:

trimethoprim 300 mg orally, daily

The total duration of therapy (IV + oral) is 10 to 14 days, depending on clinical response.

Confirm the infection has resolved by repeating urine culture 1 to 2 weeks after treatment is completed. If persistent bacteriuria is identified, see recurrent UTI and bacteriuria in pregnancy below.

If *Streptococcus agalactiae* (group B streptococcus [GBS]) is detected in urine at any stage of pregnancy, intrapartum prophylaxis for GBS is usually indicated, see page 76.

Recurrent UTI in non-pregnant women and men

Recurrent infections occur either as relapse of a previously treated infection or, more commonly, because of re-infection. Where relapse is suspected (eg an infection by the same organism within 2 weeks of completing antibiotic therapy), urine samples should be taken for culture and susceptibility testing and the urinary tract should be investigated for possible functional or anatomical abnormalities. In men, chronic prostatitis should be considered. A UTI relapse should be treated as above for mild pyelonephritis for a duration of 10 to 14 days.

Consider prophylaxis for women who have frequent symptomatic infections (eg two or more infections during a 6-month period or three or more infections over a 12-month period), with:

trimethoprim 150 mg orally, daily at night

OR

cefalexin 250 mg orally, daily at night Non-EML

OR

nitrofurantoin 50 to 100 mg orally, daily at night

Review the need for prophylactic therapy after 3 to 6 months.

Long-term use of nitrofurantoin has been associated with an increased risk of rare adverse effects, including pulmonary toxicity, hepatotoxicity and peripheral polyneuropathy. Monitor for these adverse effects clinically, and with liver function and kidney function tests. Polyneuropathy is more likely to occur in patients with impaired kidney function.

Post-menopausal women may benefit from a trial of topical (intra-vaginal) oestrogen therapy.

Recurrent UTI and bacteriuria in pregnancy

Following the resolution of a urinary tract infection (UTI), recurrent bacteriuria occurs in up to one-third of pregnant women. Perform repeat urine culture at antenatal visits to monitor for recurrent bacteriuria. Choose treatment for recurrent bacteriuria based on the results of culture and susceptibility testing (see above for suitable regimens).

Treat an acute episode of recurrent UTI as for cystitis or pyelonephritis, as appropriate.

Consider giving antibiotic prophylaxis to pregnant women with recurrent bacteriuria, or bacteriuria and risk factors for pyelonephritis (eg immune compromise, diabetes, neurogenic bladder). Use:

cefalexin 250 mg orally, daily at night for the remainder of the pregnancy Non-EML

OR

nitrofurantoin 50 mg orally, daily at night (avoid nitrofurantoin during the last four weeks of pregnancy, ie from week 36, due to an increased risk of neonatal jaundice and haemolytic anaemia)

Urinary tract infections in children

Perform urine cultures in all children with suspected UTI.

Treat UTI as cystitis if the child has bacteriuria and localising symptoms (eg dysuria, frequency, urgency, lower abdominal discomfort). Treat UTI as pyelonephritis if the child has bacteriuria and either fever or loin pain or tenderness.

Acute cystitis in children

For infants younger than one month, treat as for neonatal sepsis (see page 83). Children 1 month or older can be treated with oral antibiotics.

For empirical therapy, use:

trimethoprim+sulfamethoxazole (child 1 month or older: 4+20 mg/kg up to 160+800 mg) orally, 12-hourly for 3 days

OR

cefalexin 12.5 mg/kg up to 500 mg orally, 6-hourly for 3 days Non-EML

Or, if suspension available

trimethoprim 4 mg/kg up to 150 mg orally, 12-hourly for 3 days

If culture and susceptibility testing indicate the pathogen is resistant to empirical therapy, do not modify therapy if symptoms of cystitis are improving.

If the pathogen is resistant to empirical therapy and symptoms of cystitis are not improving, use the narrowest spectrum antibiotic to which the pathogen is susceptible. If the pathogen is susceptible, suitable alternatives are:

amoxicillin 15 mg/kg up to 500 mg orally, 8-hourly for 3 days

OR

amoxicillin+clavulanate 15 mg/kg amoxicillin component up to 500 mg orally, 8-hourly for 3 days

If resistance to all of the above drugs is confirmed, provided the pathogen is susceptible, suitable alternatives are:

ciprofloxacin 12.5 mg/kg up to 500 mg orally, 12-hourly for 3 days

OR

norfloxacin 10 mg/kg up to 400 mg orally, 12-hourly for 3 days Non-EML

Children with cystitis caused by *Pseudomonas aeruginosa* often have coexisting urological abnormalities. Treat children who have cystitis caused by *P. aeruginosa* with ciprofloxacin or norfloxacin as above; however, a longer treatment duration is often required—seek expert advice.

Do not perform post-treatment urine culture to confirm resolution of infection for asymptomatic children.

Acute pyelonephritis in children

For infants younger than one month, treat as for neonatal sepsis (see page 83).

Use IV antibiotics initially for children 1 month or older who have risk factors for serious illness, or who are septic, dehydrated or unable to maintain oral intake. For children who do not meet these criteria, use oral antibiotics.

When oral therapy is indicated, treat as for cystitis above, but continue therapy for 7 to 10 days.

When IV therapy is indicated, use:

ampicillin 50 mg/kg up to 2 g IV, 6-hourly

PLUS

gentamicin IV daily - infant and child: 1 month to < 10 years 7.5 mg/kg up to 320 mg, children ≥ 10 years: 6 mg/kg up to 560 mg (use higher doses in critically ill patients); see appendix for more information

For children hypersensitive to penicillins, use gentamicin as a single drug for initial therapy.

If gentamicin is contraindicated, use as a single drug (unless immediate or delayed hypersensitivity to penicillins):

ceftriaxone (child 1 month or older) 50 mg/kg up to 2 g IV, daily

OR

cefotaxime 50 mg/kg up to 1 g IV, 8-hourly

Switch to oral therapy once the patient is clinically stable. Oral therapy should be based on the results of culture and susceptibility testing. The total duration of therapy (IV + oral) is 7-10 days, depending on clinical response.

Antibiotic prophylaxis for UTI in children

Do not routinely give antibiotic prophylaxis to infants or children following the first episode of UTI. Antibiotic prophylaxis is no longer routinely used for cases of vesicoureteric reflux (VUR). Antibiotic prophylaxis for UTI in children increases the risk of infection with multidrug-resistant bacteria. However, prophylaxis should be considered for infants and children with recurrent UTI or VUR grades III to V—seek expert advice.

If prophylaxis is indicated, use

For infants and children over 2 months:

trimethoprim+sulfamethoxazole 2+10 mg/kg up to 80+400 mg orally, at night

OR

nitrofurantoin 1 mg/kg up to 50 mg orally, at night

For children less than 2 months, use:

amoxicillin 10 mg/kg orally, at night

OR

cefalexin 10 mg/kg up to 250 mg orally, at night Non-EML

Review the need for prophylaxis after 6 months.

Do not broaden the spectrum of antibiotic prophylaxis to target multidrug-resistant bacteria.

Long-term use of nitrofurantoin has been associated with an increased risk of rare adverse effects, including pulmonary toxicity, hepatotoxicity and peripheral polyneuropathy.

Catheter–associated bacteriuria & urinary tract infections in adults and children

Bacteriuria, and/or pyuria, are common in patients with an indwelling urinary catheter (IDC), but should **only be treated if symptomatic** eg suprapubic or flank pain, or fever, rigors, altered mentation or other systemic symptoms in the absence of another identifiable cause. Cloudy or malodourous urine has **not** been shown to reliably predict bacteriuria or UTI.

Where treatment is required, urine should be sent for culture and susceptibility testing, ideally prior to commencement of antibiotic therapy. Bacteria colonising the catheter may not necessarily be present in the bladder and causing the infection. If possible, the catheter should be removed, and a midstream urine sample then obtained. If ongoing catheterisation is required, the catheter should be replaced and the urine sample collected through the new catheter. If not possible, take the urine sample from the port in the drainage system, not the drainage bag. There is no role for culturing the IDC tip post-removal, as organisms grown commonly represent colonisation rather than infection.

Where possible, the catheter should be permanently removed to facilitate effective treatment. If ongoing catherisation is necessary, the catheter should be replaced with a new catheter. Empirical antimicrobial therapy should be selected on the basis of the most recent urine culture results, pending repeat cultures. Where no prior culture results are available, treat as for non-catheter–associated UTI. Duration of therapy is generally 7 days, although up to 14 days may be required depending upon the severity and extent of the initial infection, organism cultured and clinical response.

Prevention of catheter–associated UTI involves the avoidance of unnecessary catheterisation, and early removal of short-term catheters where required. Aseptic technique should be used for placement of catheters and a closed drainage system maintained. Unless symptomatic infection is present, prophylactic antibiotics should not be routinely administered at the time of catheter placement, change or removal.

Asymptomatic bacteriuria

Asymptomatic bacteriuria is generally defined as the presence of $\geq 10^5$cfu/mL bacteria in a well collected urine sample, with or without pyuria, in the absence of urinary tract symptoms (eg fever, dysuria, frequency). It is common, particularly in women, and increases in frequency with age, and is generally self-limiting. Multiple studies have shown that antibiotic therapy is **not** of benefit, except in specific circumstances (see below). Therapy leads to no reduction in the frequency of symptomatic infection, no benefit in long term kidney function, is associated with a high frequency of recurrence in bacteriuria once ceased, and is associated with an increased risk of adverse events and of antibiotic resistance.

Hence, screening for and treating bacteriuria that is asymptomatic is **not recommended**, except for:

- Pregnant women: bacteriuria may progress to pyelonephritis
- Patients undergoing elective urological procedures.

If asymptomatic bacteriuria recurs in a pregnant woman, or the organism is *Streptococcus agalactiae* (Group B streptococcus), seek expert obstetric advice.

Acute bacterial prostatitis

Acute prostatitis usually presents with fever, marked acute lower urinary tract symptoms (eg frequency, dysuria), perineal pain and extreme prostatic tenderness on rectal examination. It can be complicated by the development of an abscess or bacteraemia. Infection is usually caused by the same pathogens associated with other UTIs.

Perform urine and/or prostatic fluid microscopy and culture. Consider imaging if prostatic abscess is suspected clinically.

For empirical therapy of mild to moderate infection, treat with oral antibiotic therapy as per mild acute pyelonephritis in adults above with amoxicillin+clavulanate, or ciprofloxacin for penicillin hypersensitivity. For severe infection, treat as for severe pyelonephritis, as above. A longer duration of therapy of usually 2-4 weeks (IV and oral) is required for acute prostatitis, with duration dependent upon disease severity and response.

Chronic bacterial prostatitis

Chronic bacterial prostatitis is rare; most (90% to 95%) patients with symptoms of chronic prostatitis (eg chronic pelvic pain) have a non-infective aetiology; repeated courses of antibiotic treatment should be avoided. Where infection is present, it is usually caused by the same pathogens associated with other UTIs. Diagnosis requires microscopy and culture of urine and expressed prostatic secretions; patients with symptoms of prostatitis but negative cultures and no white blood cells in prostatic secretions are unlikely to have chronic bacterial prostatitis.

If infection is proven, therapy should be guided by culture and sensitivity tests. Suitable regimens include:

trimethoprim 300 mg orally daily for 4 weeks

OR

ciprofloxacin 500 mg orally, 12-hourly for 4 weeks

OR

norfloxacin 400 mg orally, 12-hourly for 4 weeks [Non-EML]

If culture is negative, consider chlamydia infection; see page 278.

Recurrence of chronic bacterial prostatitis is common. Do not repeat courses of antibiotic therapy unless a recognised uropathogen is found on culture from a symptomatic patient.

Acute epididymo-orchitis

Epididymo-orchitis most commonly occurs as a complication of a urethral infection caused by sexually transmitted pathogens (usually *Chlamydia trachomatis* or *Neisseria gonorrhoeae*) in sexually active men, or a urinary tract infection caused by enteric Gram negative bacteria in non-sexually active men. For epidiymo-orchitis suspected to be caused by a sexually transmitted pathogen, see page 257.

For epididymo-orchitis suspected to be caused by an organism from the urinary tract in **adults**, treat as for acute bacterial prostatitis for 14 days; in

prepubertal boys, take a midstream urine sample for culture and treat as for a urinary tract infection in children but for a duration of 14 days.

Candiduria

The presence of Candida in urine is common, particularly in association with indwelling catheters, and does not necessarily indicate renal tract infection. Antifungal therapy is not usually indicated and should not be initiated without expert advice.

15. Genital and sexually transmitted infections

General principles

For patients with a suspected sexually transmitted infection, it is important to investigate for other sexually transmitted pathogens (eg HIV and hepatitis viruses). Many sexually transmitted infections are asymptomatic; therefore, routine screening is essential to detect infection.

Contact tracing is an integral part of patient management. The aim of contact tracing is to limit ongoing disease transmission, identify patients (including asymptomatic patients) who should be treated to minimise the incidence of complications, and prevent re-infection from an untreated sexual contact. Contact tracing is a priority for some sexually transmitted infections, such as HIV infection, syphilis or chlamydial or gonococcal infection, but is not required for genital herpes or warts. It is recommended and encouraged that oral treatment for gonococcal and chlamydial infections be directly observed by the health care provider. Also, if the sexual partner(s) is not able to visit the health facility, provide the index patient with an additional treatment course to be taken at home by the partner(s).

Epididymo-orchitis

Introduction

Epididymo-orchitis most commonly occurs as a complication of a urethral infection caused by sexually transmitted pathogens in sexually active men, or a urinary tract infection caused by enteric Gram negative bacteria in non-sexually active men or prepubertal boys. Men who engage in insertive anal sex are at risk of infection with sexually acquired enteric pathogens in addition to other sexually transmitted pathogens.

The most common sexually transmitted pathogens in epididymo-orchitis are *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. Although *Ureaplasma urealyticum* and *Mycoplasma genitalium* have been implicated, a causal role has not been proven. Epididymo-orchitis can also develop after urinary tract

instrumentation. In a significant number of cases, no pathogen is identified.

Some alternative diagnoses in patients with acute scrotal pain or inflammation represent urological emergencies (eg Fournier gangrene, testicular torsion) and must be excluded.

Differentiating **sexually acquired** from **non-sexually acquired** epididymo-orchitis depends on clinical judgement and patient history. Collect a midstream urine sample for microscopy and culture, and susceptibility testing as required. If urethral discharge is present in a sexually active man collect a urethral swab for Gram stain, culture and susceptibility testing of *N. gonorrhoeae*; where available testing for *C. trachomatis* should also be performed.

If the diagnosis is uncertain, use the empirical regimen for sexually acquired epididymo-orchitis until the results of investigations are available.

Sexually acquired infection

Treat sexually active men with epididymo-orchitis empirically for chlamydial or gonococcal infection. Use:

ceftriaxone 250 mg IM, or 500 mg IV, as a single dose[65]

PLUS either

azithromycin 1 g orally, as a single dose

OR

doxycycline 100 mg orally, 12-hourly for 14 days

Treat men who engage in insertive anal sex empirically with the antibiotic regimen above; however, if response to treatment is poor, alternative antibiotic treatment may be required to treat enteric organisms—seek expert advice.

Modify therapy based on the results of investigations and clinical response. In severe cases, oral treatment may need to be continued for up to 3 weeks. For recurrent cases, increase the doses in the regimen above and use 500 mg ceftriaxone and azithromycin 2 g. There is a local increase in resistant gonococcal infections, and local protocols may change – refer to the most up

[65] IM injection of ceftriaxone is painful; reconstitute with lignocaine 1%.

to date Fiji guidelines.

For **immediate** or **delayed severe** penicillin hypersensitivity, seek expert advice.

Non-sexually acquired infection

For management see urinary tract infections, page 254.

Genital ulcer disease

Introduction

Herpes simplex virus (HSV) is the most common cause of genital ulcer disease; syphilis, chancroid and donovanosis should also be considered.

Herpes simplex virus

General considerations

Genital herpes is a sexually acquired infection that is caused by either herpes simplex virus (HSV) 1 or 2. Nonclassical presentations of genital herpes are common, so clinical diagnosis is unreliable. The majority of patients with HSV infection are undiagnosed.

Classically, recurrent genital herpes presents as clusters of painful blisters in the genital area. These erode rapidly to form ulcers that spontaneously heal over 1 to 2 weeks. Lesions may also occur at other sites along sacral dermatomes (such as the surrounding skin or buttocks, behind the knee or even on the dorsum of the foot). Although initial infection is often asymptomatic, if symptoms occur they can be severe, with numerous widespread genital ulcers that can take weeks to heal without treatment. Over time, recurrences generally occur less frequently, and the infection is usually less painful and has a shorter duration.

Antiviral therapy for HSV is not curative, but it shortens the episode if started within 72 hours of the onset of symptoms. Immunocompromised patients, including those with HIV infection, can have prolonged, widespread and more painful episodes of genital, perianal or oral herpes. Sometimes these patients require prolonged treatment or higher doses of antiviral drugs, and may require prophylaxis; seek expert advice.

For children with suspected anogenital herpes, seek expert advice.

Management

Initial infection (first clinical episode genital herpes)

For initial infection, use:

aciclovir 400 mg orally, 8-hourly for 5- 10 days

Start treatment as soon as the clinical diagnosis is made. If clinical response is rapid, stop treatment after 5 days.

Episodic treatment

Recurrences of HSV can be treated with episodic therapy, which should be started concurrently with the onset of prodromal symptoms or with the onset of lesions. Because viral replication in recurrent infection is short-lived, short courses of therapy are effective. Use:

aciclovir 800 mg orally, 8-hourly for 2 days

OR

aciclovir 400 mg orally, 8-hourly for 5 days

Suppressive treatment

Suppressive treatment is indicated for frequent, severe recurrences; it reduces recurrences by 70% to 80%, but transmission can still occur. Use:

aciclovir 400 mg orally, 12-hourly; reassess at 3 months

Treatment may be ongoing, or it may be interrupted every 3 months to determine the natural history of the disease and restarted in the event of recurrence. Long-term suppressive antiviral therapy is considered safe. For immunocompromised patients, or patients with recurrences despite suppressive treatment, higher doses of antiviral therapy may be required—seek expert advice.

Evaluate sexual partners for genital lesions and treat if required. Advise abstinence from sexual activity while lesions are present and counsel the patient and their partner(s) about the natural history of the disease with emphasis on the potential for recurrences. Encourage screening for other sexually transmitted infections including HIV after confidential counselling.

Suppressive therapy for women with recurrent genital herpes during **late pregnancy** reduces the chance of recurrence at delivery. After 36 weeks' gestation, it is reasonable to increase the dosing frequency to:

aciclovir 400 mg orally, 8-hourly, until delivery

Chancroid

Chancroid (soft chancre) is caused by *Haemophilus ducreyi* and should be considered in the differential diagnosis of any patient with a painful genital ulcer. Nearly 50% of cases have painful inguinal adenopathy. Diagnosis is usually made clinically. Use:

azithromycin 1 g orally, as a single dose

Where not available, alternative agents include

erythromycin 500 mg orally, 6-hourly for 14 days

OR

ciprofloxacin 500 mg orally, 12-hourly for 3 days.

OR

ceftriaxone 500 mg IM or IV, as a single dose[66]

Symptomatic improvement is usually seen within 3 days, and resolution of lesions within 7 days. Observe patients until ulcer is completely healed.

Sexual partners within the 3 weeks prior to the onset of symptoms in the infected patient should be examined and treated with the above recommended regimen, whether symptomatic or not.

Genital warts

Genital warts are caused by certain strains of Human Papilloma Virus (HPV). Genital warts can be extensive and painful, but for the majority of patients these are largely a cosmetic concern. The goal of treatment is the removal of exophytic warts and relieving signs and symptoms, rather than eradication of HPV.

HPV transmission is by genital-skin to genital-skin contact. However, the

[66] IM injection of ceftriaxone is painful; reconstitute with lignocaine 1%.

period of infectivity and latency of HPV is not known, so it may not be possible to determine which sexual partner the virus was acquired from. Contact tracing is not required.

External genital or perianal warts

Topical preparations and cryotherapy are effective treatments. They can be used as monotherapy or in combination. Topical preparations are more convenient and less painful, and can be used for bulky lesions. For a small number of accessible lesions, periodic cryotherapy can be effective treatment. Cryotherapy may be used as an adjunct to topical preparations for recalcitrant lesions. For extensive or refractory warts, surgical referral may be required. For topical preparations use:

> podophyllotoxin 0.5% solution or gel applied to each wart twice daily for 3 consecutive days, followed by 4 days of no treatment; repeat the cycle up to 4 times until warts resolve.

Pelvic inflammatory disease

Introduction

Pelvic inflammatory disease (PID) is an important cause of infertility. PID includes endometritis, chorioamnionitis, salpingitis, tubo-ovarian abscess, and pelvic cellulitis and/or pelvic peritonitis.

PID is usually polymicrobial, sexually acquired infection is usually caused by *C. trachomatis* or *N. gonorrhoeae*; *M. genitalium* infection can be involved. Vaginal flora is commonly involved in mixed infection with one or more sexually acquired pathogens. Postprocedural pelvic infection (or non-sexually acquired pelvic infection) is caused by vaginal flora, including anaerobic bacteria, facultative Gram negative bacteria and *Mycoplasma hominis*. In a significant number of cases of PID, no pathogen is identified.

If PID is suspected, where possible collect an endocervical swab for Gram stain and culture of *N. gonorrhoeae* for susceptibility testing.

Differentiating sexually acquired from non-sexually acquired infection depends on clinical judgement and patient history. A sexually acquired infection is more likely in patients who have had unprotected sex, particularly

with a new partner. Non-sexually acquired infection is likely if there has been mechanical disruption of the cervical barrier (eg due to pregnancy termination or after delivery; surgery; following insertion of an intrauterine contraceptive device [IUCD]). If the diagnosis is uncertain, use the empirical regimen for sexually acquired infection until the results of investigations are available.

Sexually acquired infection

Prompt empirical treatment of sexually acquired PID reduces the risk of tubal damage and, consequently, infertility or ectopic pregnancy. For severe infection surgical drainage may be required.

Mild to moderate infection

ceftriaxone 250 mg IM or IV, as a single dose[67]

PLUS

metronidazole 400 mg orally, 12-hourly for 10-14 days

PLUS

doxycycline 100 mg orally, 12-hourly for 14 days

OR (for women who are pregnant or patients suspected to be nonadherent to doxycycline)

azithromycin 1 g orally, as a single dose

If the above regimen is not available, use:

amoxicillin 2.5 g as a single dose

PLUS

amoxicillin+clavulanate 500+125 mg as a single dose[68]

PLUS

probenecid 1 g as a single dose

PLUS

azithromycin 1 g as a single dose

Followed by (commencing the next day)

[67] IM injection of ceftriaxone is painful; reconstitute with lignocaine 1%.

[68] Where amoxicillin+clavulanate is not available, increase amoxicillin dose to 3 g

amoxicillin 500 mg 8-hourly for 7 days

PLUS

metronidazole 400 mg orally, 12-hourly for 14 days

Severe infection

ceftriaxone 2 g IV, daily

PLUS

azithromycin 500 mg IV or I g orally, daily

PLUS

metronidazole 500 mg IV, 12-hourly OR metronidazole 400 mg orally, 12-hourly

If the above regimen is not available, use:

ampicillin 2 g IV, 6-hourly

PLUS

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients

PLUS

metronidazole 500 mg IV, 12-hourly OR metronidazole 400 mg orally, 12-hourly

PLUS

doxycycline 100 mg orally, 12-hourly

For patients with **delayed nonsevere** hypersensitivity to penicillins use the ceftriaxone containing regimen. For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients

PLUS

azithromycin 500 mg IV or 1 g orally, daily

PLUS

metronidazole 500 mg IV, 12-hourly OR metronidazole 400 mg orally, 12-hourly

Modify therapy based on the results of investigations and response to treatment. If the results of susceptibility testing are not available by 72 hours and empirical IV therapy is still required, cease the gentamicin-containing regimen and seek expert advice.

Continue IV therapy until there is substantial clinical improvement, then use oral metronidazole plus doxycycline (as for mild to moderate infection above), to complete at least 2 weeks (IV + oral) of treatment.

Perform contact tracing and investigate sexual contacts for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. While awaiting test results, presumptively treat current sexual partner(s) with:

azithromycin 1 g orally, as a single dose

If *N.gonorrhoeae* is identified in the **index** case, presumptively treat sexual contacts.

Postprocedural pelvic infection

Postprocedural pelvic infection (non-sexually acquired pelvic infection) is considered severe if the patient has severe pain, fever (38°C or higher), systemic features (eg tachycardia, vomiting), sepsis or septic shock or suspected tubo-ovarian abscess.

Nonsevere postprocedural pelvic infection

For empirical therapy, use:

amoxicillin+clavulanate 500+125 mg orally, 8-hourly for 14 days

For patients hypersensitive to penicillins, use:

trimethoprim+sulfamethoxazole 160+800 mg orally, 12-hourly for 14 days

PLUS

metronidazole 400 mg orally, 12-hourly for 14 days

Assess the response to therapy within 72 hours and if the patient has not improved, re-evaluate the diagnosis and consider switching to intravenous therapy as for severe postprocedural pelvic infection.

Severe postprocedural pelvic infection

For empirical therapy, as a three-drug regimen, use:

ampicillin 2 g IV, 6-hourly

PLUS

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients

PLUS

metronidazole 500 mg IV, 12-hourly

For patients with **delayed nonsevere** hypersensitivity to penicillins, as a two-drug regimen, use:

ceftriaxone 2 g IV, daily[69]

PLUS

metronidazole 500 mg IV, 12-hourly

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

gentamicin IV: adult 4 to 5 mg/kg (7 mg/kg for critically ill adults); see appendix for dose intervals, calculating dose in overweight or obese patients

PLUS

clindamycin 600 mg IV, 8-hourly Non-EML

Modify therapy based on the results of investigations. If the results of susceptibility testing are not available by 72 hours and empirical IV therapy is still required, cease the gentamicin-containing regimen and use the ceftriaxone-based regimen recommended as above (unless immediate or severe sensitivity to penicillins).

Continue IV therapy until there is substantial clinical improvement, then use oral therapy as for nonsevere postprocedural infection to complete a total treatment duration (IV + oral) of at least 2 weeks.

Bartholin's abscess

Surgical drainage is required; consider antibiotic therapy. Where necessary; use:

trimethoprim+sulfamethoxazole 160+800 mg orally, 12-hourly for 7 days

An alternative regimen is:

amoxicillin+clavulanate 500+125 mg orally, 8-hourly for 7 days

PLUS

clindamycin 300 mg orally, 6-hourly, for 7 days Non-EML

Infective proctitis

Anorectal symptoms are common among men who have sex with men (MSM). Mucopurulent rectal discharge, bleeding, tenesmus and pain indicate moderate to severe proctitis. The symptoms can be mistaken for inflammatory bowel disease (discharge may be difficult to distinguish from diarrhoea), but are likely to be caused by a sexually transmitted infection in individuals who engage in receptive anal sex. Empirical treatment of symptomatic sexually acquired proctitis should treat HSV, *N. gonorrhoeae* and *C. trachomatis*. Seek expert advice.

For empirical therapy of infective proctitis, use:

ceftriaxone 500 mg IM or IV as a single dose[70]

PLUS

doxycycline 100 mg orally, 12-hourly for 7 days. Men who have sex with men may require a longer duration for lymphogranuloma venereum

PLUS

oral antiviral therapy for genital herpes

[70] IM injection of ceftriaxone is painful; reconstitute with lignocaine 1%.

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, seek expert advice.

Modify therapy based on the results of investigations. If *C. trachomatis* or *N. gonorrhoeae* is identified, perform a test of cure 1 month after the start of treatment.

Perform contact tracing and investigate sexual contacts for *C. trachomatis* and *N. gonorrhoeae*. If a pathogen is identified in the index case, presumptively treat contacts for that pathogen. If a pathogen is identified in a sexual contact, treat the infection and undertake contact tracing for that individual.

Lymphogranuloma venereum

Classical genital lymphogranuloma venereum (LGV) presents as a transient painless genital ulcer followed by inguinal lymphadenopathy; it is caused by *Chlamydia trachomatis* L1–L3 serovars.

For LGV infection, use:

azithromycin 1 g orally, once weekly for 3 weeks

OR

doxycycline 100 mg orally, 12-hourly for 21 days

OR, as a less preferred agent, use:

erythromycin 500 mg orally, 6-hourly for 21 days

Dual treatment for gonorrhoea should also be given.

For patients with LGV, investigate and treat all sexual contacts in the month preceding the onset of symptoms. Full treatment courses as above are usually administered to contacts even if asymptomatic due to the risk of serious complications.

Syphilis

Introduction

Syphilis is caused by *Treponema pallidum*. The diagnosis of syphilis is

usually made by serological testing. Irrespective of clinical presentation, anyone suspected of having a STI should have a serological test for syphilis (and HIV).

Diagnosis of active syphilis is made with both:

- a reactive nontreponemal test (either venereal disease research laboratory [VDRL] test or rapid plasma reagin [RPR])
- a positive *Treponema pallidum*-specific antibody test.

Neither test alone is adequate for diagnosis.

False-positive nontreponemal tests (RPR) are common; furthermore, nontreponemal tests may remain reactive at a low titre despite successful treatment. *T. pallidum*-specific tests also usually remain positive despite successful treatment. Either type of test may be negative in very early infection; therefore, treatment should be given to persons presenting with clinical features of primary syphilis (eg genital ulcers) and tests should be repeated if clinically indicated. For asymptomatic patients, repeat tests are generally recommended 6 weeks after the suspected time of disease transmission. Nontreponemal tests are often nonreactive in late latent or tertiary syphilis.

Seek expert advice about long-term follow-up, including repeat serological testing and assessment for complications. This is essential for patients who are pregnant, hypersensitive to penicillins or who have HIV infection.

Penicillin remains the drug of choice. Although treatment failure with penicillin has occurred, there is no clear genetic basis for penicillin resistance in *T. pallidum*. Evidence of genetic resistance has been reported for azithromycin (usually after previous macrolide therapy), but not for other drugs (eg doxycycline or ceftriaxone). If drugs other than penicillin are used, close follow-up is essential.

Screen for other sexually transmitted infections including HIV after confidential counselling.

Contact tracing is important.

Early syphilis

For treatment of syphilis in pregnant women, see separate section.

Early syphilis includes primary, secondary and early latent syphilis of < 2 years duration.

The initial clinical manifestation of syphilis is termed primary syphilis, typified by chancre (an anogenital or, less commonly, extragenital painless ulcer with indurated edges). Progression to secondary syphilis may occur over the following months and presents as an acute systemic illness with rash, condylomata lata (clusters of soft, moist lumps in skin folds of the anogenital area), mucosal lesions, hepatitis or meningitis.

Early latent syphilis is infection of less than 2 years' duration where the patient is asymptomatic.

For treatment of early syphilis, use:

benzathine penicillin 2.4 million units (1.8 g) IM, as a single dose

OR

procaine penicillin 1.5 million units (1.5 g) IM, daily for 10 days

Penicillin is the preferred agent to treat syphilis – where true penicillin allergy, use:

doxycycline 100 mg orally, 12-hourly for 14 days

OR (unless immediate or delayed severe hypersensitivity to penicillins)

ceftriaxone 1 g IM/IV, daily for 10-14 days[71]

For HIV-infected patients with early syphilis, see also neurosyphilis.

Advise the patient to avoid sexual activity until the lesions have resolved. Clinical and serological follow-up should occur at 3 and 6 months.

Patients should have a CSF examination (to exclude neurosyphilis) as well as repeat treatment if:

- signs or symptoms persist, and re-infection has been ruled out
- nontreponemal RPR titres rise, or fail to decline four-fold within 3 months in primary or secondary syphilis or by 6 months in early latent syphilis.

For patients with primary syphilis, all sexual contacts in the 3 months preceding the onset of symptoms require serological testing and presumptive treatment.

[71] IM injection of ceftriaxone is painful; reconstitute with lignocaine 1%.

For patients with secondary syphilis, all sexual contacts in the 6 months preceding the onset of symptoms require serological testing and presumptive treatment.

For patients with early latent syphilis, all sexual contacts in the 12 months preceding the onset of symptoms require serological testing and presumptive treatment.

The recommended presumptive treatment for sexual contacts is:

benzathine penicillin 2.4 million units (1.8 g) IM, as a single dose

Modify treatment based on the results of investigations and patient presentation. Seek expert advice if true penicillin allergy.

Late syphilis

For treatment of late syphilis in pregnant women, see separate section.

Late latent syphilis

Late latent syphilis is defined as latent (asymptomatic) syphilis of longer than 2 years' duration, or of unknown duration. Seek expert advice about the need for and interpretation of lumbar puncture. This is particularly important in patients who have previously been treated for syphilis or in patients with HIV infection (see neurosyphilis).

For treatment of late latent syphilis, use:

benzathine penicillin 2.4 million units (1.8 g) IM, once weekly for 3 consecutive weeks (the interval between doses should not be more than 14 days)

OR

procaine penicillin 1.5 million units (1.5 g) IM, daily for 20 days

Penicillin is the preferred agent to treat syphilis – where true penicillin allergy, use:

doxycycline 100 mg orally, 12-hourly for 30 days

Repeat RPR at 6 and 12 months.

Patients should be evaluated for neurosyphilis if there is either:

- neurological signs or symptoms, or
- treatment failure (clinically or serologically).

Tertiary syphilis

Tertiary syphilis refers to syphilis of longer than 2 years' duration, or of unknown duration, with cardiovascular, central nervous system (neurosyphilis) or skin and bone (gummatous syphilis) involvement. Expert advice is essential.

For the treatment of tertiary syphilis, use:

benzylpenicillin 3 million units (1.8 g) IV, 4-hourly for 15 days

Penicillin is the preferred agent to treat syphilis – where true **delayed nonsevere** penicillin allergy, use:

ceftriaxone 2 g IV, daily, for 10-14 days[72]

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, seek expert advice.

For **cardiovascular syphilis** or **neurosyphilis**, concomitant treatment with prednis(ol)one, (20 mg orally, 12-hourly for 3 doses), may be administered initially with penicillin to reduce the likelihood of a Jarisch–Herxheimer reaction.

Neurosyphilis

Neurological involvement can occur during any stage of infection and does not always produce neurological symptoms. If neurosyphilis is suspected, consider performing neurological imaging initially; however, diagnosis requires analysis of the CSF via lumbar puncture—seek expert advice about the need for and interpretation of lumbar puncture.

HIV-infected patients with **early syphilis** are at an increased risk of neurological complications. Initial treatment is as per standard regimens. However, they should be evaluated clinically and serologically 3, 6, and 12 months after therapy. If symptoms persist or recur, or if nontreponemal RPR titres rise or fail to decline four-fold within 6 to 12 months, examine CSF to distinguish treatment failure (due to neurosyphilis) from re-infection,

[72] If ceftriaxone is not available, substitute cefotaxime 1 g IV 8-hourly

and treat accordingly.

HIV-infected patients with **late syphilis** who also have neurological symptoms should have their CSF examined before starting treatment.

Patients who have CSF consistent with neurosyphilis should be managed as for tertiary syphilis. If CSF pleocytosis is present initially, repeat CSF examination (RPR and cell count) every 6 months until the cell count is normal. Re-treat if there is no decrease in the cell count at 6 months, or if it is not normal by 2 years.

Pregnancy and congenital syphilis

Pregnant women should be screened for syphilis using serological testing early in pregnancy, at first booking to antenatal clinic. Screening should be repeated in the third trimester and preferably again at delivery.

Treat pregnant women with:

> benzathine penicillin 2.4 million units (1.8 g) IM, once weekly for 3 consecutive weeks (the interval between doses should not be more than 14 days)

Where benzathine penicillin cannot be used, treat as per the stage of syphilis

> procaine penicillin 1.5 million units (1.5 g) IM, daily for 10 days for early syphilis and 20 days for late syphilis (especially after 20 weeks gestation)

Penicillin is the preferred agent to treat syphilis – where true penicillin allergy, use:

For **delayed nonsevere** hypersensitivity:

> ceftriaxone 1 g IM/IV, daily for 10-14 days[73] [74]

For **immediate** or **delayed severe** hypersensitivity

> erythromycin 500 mg orally, 6-hourly for 14 days for early syphilis and 30 days for late syphilis

Do not use tetracyclines in pregnant women or newborns. Macrolides do not

[73] If ceftriaxone is not available, substitute cefotaxime 1 g IV 8-hourly
[74] IM injection of ceftriaxone is painful; reconstitute with lignocaine 1%.

reliably cross the placenta, and azithromycin therapy has failed to prevent congenital syphilis.

Treatment for early syphilis during the second half of pregnancy may precipitates a Jarisch–Herxheimer reaction which carries a risk of premature labour and/or foetal distress. Therefore, after treatment, advise women that if they notice fever, contractions or a reduction in foetal movement, they need urgent obstetric review.

Sexual partners should be screened and given presumptive treatment, regardless of results.

Following treatment, monthly RPR testing should be performed for the duration of the pregnancy. A repeat treatment course is indicated if:

- the sexual partner was not treated simultaneously
- the RPR titre is not falling within 6 weeks.

Congenital syphilis

The risk of congenital syphilis is low if a mother with positive serology or active syphilis received adequate penicillin treatment 4 weeks or longer before delivery, her partner was adequately treated simultaneously, and she was not re-infected.

Infants of RPR-positive mothers should be treated if any of the following is present:

In mothers

- syphilis was untreated or inadequately treated during pregnancy
- syphilis during pregnancy was treated with a non-penicillin regimen
- syphilis during pregnancy was treated with an appropriate regimen but the expected decrease in RPR titres did not occur after therapy
- syphilis was treated less than one month before delivery
- syphilis treatment is not documented
- syphilis was treated before or during pregnancy but with insufficient serological follow-up during pregnancy to assess the response to treatment and current infection status.

In infants

- any evidence of active syphilis (clinically or on X-ray)

- RPR titres at birth are higher than in the mother
- the baby is positive for a FTA-Abs IgM test.

If the infant has NO evidence on physical examination or X-ray of congenital syphilis, but the mother or infant has **any** of the other above-mentioned features, give the infant:

procaine penicillin 50 000 units/kg IM, daily for 10 days

OR

benzylpenicillin 50 000 units/kg/dose (30 mg/kg/dose) IV for 10 days

First week of life: 12-hourly

Week 2-4 of life: 8-hourly

From 4 weeks: 6-hourly

Repeat the RPR every 3 months until negative. The infant's titre should decline four-fold by 3 months and be negative at 6 months. Repeat treatment if titre has not declined by four-fold at 3 months, or remains positive at 6 months.

If the infant has NO evidence of congenital syphilis, AND the mother has been adequately treated with no signs of re-infection (ie NONE of the above-mentioned features are present), give the infant:

benzathine penicillin 50 000 units/kg IM, as a single dose

An infant with any of the following features is considered to have congenital syphilis:

- Clinical signs of syphilis
- Neurological manifestations of syphilis
- X-Ray changes.

CSF examination should be performed for RPR, cell count and protein estimation. The following abnormalities may indicate neurosyphilis:

- reactive CSF RPR
- leucocyte count is greater than 5/mm3
- protein is greater than 400mg/L.

Treat as for congenital syphilis.

Repeat the RPR every 3 months until negative. Consider neurosyphilis and repeat treatment if remains positive. Retreatment of the neonate should occur in consultation with a specialist paediatrician.

In cases of neurosyphilis, ongoing serum and CSF analysis should be undertaken every 6 months until the CSF white cell count is normal and the CSF RPR is nonreactive. The CSF white cell count should decline by 6 months after successful treatment, and all CSF abnormalities should resolve by 2 years after treatment. Retreatment is needed if titres do not fall or clinical signs of disease persist or develop.

Syphilis in children (from 1 year)

If this is a late diagnosis of congenital syphilis, or neurological involvement is present, use:

> benzylpenicillin 50 000 units/kg (30 mg/kg) up to 3 million units IV, 4-6 hourly for 10-14 days

For acquired syphilis, with no neurological involvement, use:

> benzathine penicillin 50 000 units/kg up to 2.4 million units IM, weekly for 3 consecutive weeks
>
> OR
>
> benzylpenicillin 50 000 units/kg (30 mg/kg) up to 3 million units IV, 4-6 hourly for 10 days, then switch to benzathine penicillin 50 000 units/kg up to 2.4 million units IM, as a single dose

Any diagnosis of syphilis in children mandates referral to a paediatrician for management and evaluation for possible sexual abuse.

Urethritis and cervicitis

Introduction

Urethritis is characterised by urethral irritation, dysuria and discharge and cervicitis is characterised mainly by discharge, but both are often asymptomatic. *Chlamydia trachomatis* and *Neisseria gonorrhoeae* are the most common causes, and may lead to serious complications, such as

pelvic inflammatory disease and/or infertility. *Mycoplasma genitalium* causes a significant minority of cases of urethritis and probably cervicitis, and has similar complications; other organisms are occasionally implicated. In 50% or more of cases no pathogen is identified.

Collect urethral swab (if urethral discharge is present) or endocervical swab for Gram stain and culture of *N. gonorrhoeae* for susceptibility testing. Self-collected urine and high vaginal samples are acceptable for patients who prefer noninvasive testing; however, clinical examination is preferable.

Empirical treatment for both gonococcal and chlamydial infection is recommended until the results of investigations are available—use the regimen recommended for gonococcal infection because this also treats chlamydial infection.

Post-treatment follow-up is recommended. A test of cure is advised at 1 month if patient adherence to treatment is questionable or if second-line treatment has been used. A test of re-infection is recommended at 3 to 6 months in all patients.

It is recommended and encouraged that oral treatment for gonococcal and chlamydial infections be directly observed by the health care provider.

If a sexually transmitted infection is likely, consider contact tracing and presumptive treatment of contacts with azithromycin (1 g orally, as a single dose). If a pathogen is isolated in a sexual contact, treat the infection and undertake contact tracing for this individual.

Gonococcal infection

Diagnosis of gonococcal infection should be confirmed by culture where possible, and antibiotic sensitivity tests performed. All patients should also have serological tests for syphilis and HIV after confidential counselling.

> Patients treated for gonococcal infection also need to be treated for potential concurrent chlamydial infection.

Follow-up cultures should be obtained 5 days following completion of treatment for all gonococcal infections.

Sexual partners of the index case within the preceding 30 days of onset

of symptoms should be examined and appropriate samples cultured if symptomatic. Give presumptive therapy for both gonorrhoea and chlamydial infections.

Uncomplicated urethral, endocervical, rectal or pharyngeal infection

Use:

ciprofloxacin 250 mg orally, as a single dose

OR

ceftriaxone 250 mg IM, as a single dose[75]

OR

cefixime 400 mg orally, as a single dose Non-EML

If the isolate is sensitive to penicillin, use:

amoxicillin 2.5 g orally, as a single dose

PLUS

amoxicillin+clavulanate 500+125 mg orally, as a single dose[76]

PLUS

probenecid 1 g orally, as a single dose

PLUS presumptive treatment for chlamydia

Chlamydial or other nongonococcal infection

Currently chlamydial testing is not available in Fiji, thus all patients with urethral or vaginal discharge syndrome are treated presumptively. For the treatment of chlamydial or other nongonococcal infection, use:

azithromycin 1 g orally, as a single dose

OR

doxycycline 100 mg orally, 12-hourly for 7 days

Where doxycycline is contraindicated (eg children younger than 8 years of

[75] IM injection of ceftriaxone is painful; reconstitute with lignocaine 1%.
[76] If amoxicillin+clavulanate is unavailable, increase the amoxicillin dose to 3 g

age or pregnancy), use:

erythromycin 500 mg orally, 6-hourly for 7 days

PLUS presumptive treatment for gonorrhoea. Give presumptive treatment to sexual partner(s).

A prolonged duration of treatment is required for patients with complications, including patients with concomitant reactive arthritis.

If symptoms persist or recur, give a second course of antibiotic therapy, investigate the aetiology further (especially for *M. genitalium*), and assess the risk of re-infection. See expert advice.

Post-sexual assault prophylaxis

For cases of sexual assault, discussion with the relevant sexual assault referral service is advised. For cases involving children, seek expert advice for prophylaxis and management.

Investigations for sexually transmitted infections and pregnancy and for forensic purposes should be performed on a case-by-case basis. The collection of specimens for forensic evidence should be undertaken by an experienced professional, and should follow established regional or local protocols.

Perform baseline screening for the following sexually transmitted pathogens: *Chlamydia trachomatis* (where available), *Neisseria gonorrhoeae*, *Treponema pallidum* (syphilis), hepatitis B virus (HBV), hepatitis C virus (HCV) and HIV. Perform screening during the first presentation after the assault (before treatment), and on follow-up. If a pathogen is isolated, treat the infection.

Empirical therapy should cover gonorrhoea and chlamydia. If presentation within 72 hours, HIV PEP may be required as per HIV guidelines. Syphilis may be covered by this regimen, but other sexually transmitted infections may not be prevented. It is important that the patient is followed up with both clinical examination and serological tests.

All survivors of sexual assault should be treated.

For post-sexual assault prophylaxis in adults, use:

ceftriaxone 500 mg IM or IV, as single dose[77]

PLUS

azithromycin 1 g orally, as a single dose

Alternatively, where the above regimen is not available, use:

amoxicillin 2.5 g orally, as a single dose

PLUS

amoxicillin+clavulanate 500+125 mg orally, as a single dose[78]

PLUS

probenecid 1 g orally, as a single dose

PLUS

azithromycin 1 g orally, as a single dose

Postexposure prophylaxis against HIV and HBV (for individuals who do not have immunity for HBV on baseline screening) should also be given; see prevention of infection: medical pages 72 (HBV) and 74 (HIV).

For post-sexual assault prophylaxis in children, use (as a four drug regimen):

ceftriaxone 25 mg/kg up to 250 mg IM as a single dose

OR

ciprofloxacin 15 mg/kg up to 500 mg orally as a single dose.

PLUS

azithromycin 15 mg/kg up to 1 g orally, as single dose

PLUS

metronidazole 30 mg/kg up to 2 grams orally, as a single dose OR 15 mg/kg up to 1 g orally 12-hourly for 2 doses

PLUS

benzathine penicillin 50 000 units/kg up to 2.4 million units IM as a single dose

[77] IM injection of ceftriaxone is painful; reconstitute with lignocaine 1%.
[78] If amoxicillin+clavulanate is unavailable, increase the amoxicillin dose to 3 g

Vulvovaginitis

Bacterial vaginosis

(non-specific vaginitis; Gardnerella vaginosis)

Bacterial vaginosis is a polymicrobial clinical syndrome caused by a reduction of the normal *Lactobacillus* species in the vagina, and overgrowth of anaerobic and other fastidious bacteria (including *Gardnerella vaginalis*). It is a common cause of malodorous vaginal discharge. It is not a proven sexually transmitted infection; treatment of sexual partners is not required.

For symptomatic patients, use:

metronidazole 2 g orally, as a single dose

OR

metronidazole 400 mg orally, 12-hourly for 7 days

OR

clindamycin 300 mg orally, 12-hourly for 7 days

OR

tinidazole 2 g orally, as a single dose Non-EML

Single-dose metronidazole has better adherence than extended treatments; however, the cure rate is lower and retreatment may be necessary. Use treatment regimens with a longer duration for recurrent infection.

Clindamycin is preferred in women who are pregnant; oral clindamycin can be used at any stage of pregnancy.

Candidiasis

Use:

clotrimazole 200 mg intravaginally, daily at night for 3 days Non-EML

OR

clotrimazole 500 mg intravaginally, as a single dose Non-EML

OR

Other topical azole vaginal cream or pessary as per product information

OR

fluconazole 150 mg orally, as a single dose

Treatment of sexual partners is not necessary unless candidal balanitis is present; if so treat with topical antifungals.

Trichomoniasis

Women with trichomoniasis (caused by *Trichomonas vaginalis*) classically present with vulval itch, inflamed vagina and cervix and a vaginal discharge that may be yellow-green and frothy and associated with an offensive fishy odour. However, 10% to 50% of cases are asymptomatic. The diagnosis is confirmed by microscopy of a fresh wet preparation (which shows the presence of motile trichomonads). Screen patients for other sexually transmitted pathogens.

Empirical treatment and investigation of sexual partners is indicated, even if they are asymptomatic.

For initial or isolated infections, use:

metronidazole 2 g orally, as a single dose

OR

tinidazole 2 g orally, as a single dose Non-EML

For recurrent infections, use:

metronidazole 400 mg orally, 12-hourly for 7 days

Consider single-dose treatment with metronidazole (as above) for all symptomatic pregnant patients, because trichomoniasis in pregnancy is associated with adverse pregnancy outcomes (eg premature rupture of membranes, preterm delivery and low birth weight). Despite this, treatment does not necessarily result in a reduction in perinatal morbidity.

16. Mycobacterial infections

Tuberculosis

Overview

Tuberculosis (TB) is a multisystem disease with signs and symptoms that often mimic other diseases. TB should be considered in anyone who presents with unexplained fever or night sweats, weight loss (or failure to thrive in children), generalised malaise or feeling unwell, or with a persistent cough (>2 weeks) with or without haemoptysis. TB may also commonly present with:

- Persistent SOB or pleuritic chest pain
- Unexplained lymph node swelling (cervical, submandibular or submental)
- Persistent headache (> 2 weeks) or neurological signs
- Chronic back pain or stiffness with or without lower limb weakness.

All people with symptoms suggestive of TB should be identified as presumptive TB cases and appropriately investigated.

Appropriate initial investigations for suspected pulmonary TB include an early morning sputum (EMS) for microscopy and/or GeneXpert testing. A good quality spot sputum may be collected if an EMS is not possible. This test may need to be repeated if the diagnosis is suspected but not confirmed. A chest X-ray should also be performed where available. Mycobacterial culture is done where indicated by the National Tuberculosis Programme (NTP).

All cases of suspected extra-pulmonary TB (eg meningitis, vertebral osteomyelitis, peritonitis or pleural effusion) must be referred to divisional facilities for investigation. Diagnostic tests may include microscopy and GeneXpert on other body fluids (eg CSF or pleural fluid) and radiological studies (X-ray and/or CT scan).

A diagnosis of active TB infection may be definitive (either “bacteriologically confirmed”, or with positive histopathology), or presumptive (“clinically

diagnosed" by a clinician in consultation with a TB Control Officer).

Management of patients with TB requires:

- close consultation with specialists who have appropriate training and experience
- reference to local policies and guidelines
- prompt notification of all cases to the relevant jurisdictional public health authorities
- contact tracing.

Strict adherence to TB therapy is essential. Adherence is improved by comprehensive patient and family education using verbal and written information, close follow-up, and provision of directly observed therapy (DOT).

Pre-therapy considerations

Screening

Before starting therapy for TB, ascertain the HIV status of all patients (ensuring appropriate consent processes are followed). In addition:

- document the patient's weight
- assess liver function (perform liver function tests, discuss alcohol consumption, check viral hepatitis B status and review hepatotoxic medications)
- assess kidney function (U+E, Cr)
- assess visual acuity and check colour vision
- perform full blood count (FBC)
- check a blood glucose level

Provide advice on contraception for women of childbearing age, due to the potential for drug interactions between antituberculosis therapy and oral contraceptives resulting in a reduced efficacy of hormonal methods.

Consider the potential for drug interactions between the antituberculosis therapy (particularly rifampicin) and the patient's existing drug regimen. In particular, rifampicin can increase the metabolism of warfarin (making it less effective); monitor the INR closely, particularly when commencing and ceasing rifampicin therapy.

All cases of newly diagnosed TB must be registered on the TB Register via a "Case notification" form.

Therapy

Introduction

Once a diagnosis of TB is made, treatment must be commenced immediately. Modern regimens for fully drug-susceptible TB have an initial cure rate of over 98% and a five-year relapse rate of under 5%.

Patients who have been previously treated for TB (**retreatment cases**) are more likely to have drug-resistant infection; sputum (or other body fluid where appropriate for extra-pulmonary TB) MUST be sent for GeneXpert (Xpert MTB-RIF) testing and mycobacterial culture and Drug Susceptibility Testing (DST). The treatment regimen should be adjusted as necessary when DST results become available.

Standard short-course therapy for all **new cases** is 2 months of **intensive phase** treatment with isoniazid, rifampicin, pyrazinamide and ethambutol followed by 4 months of **continuation phase** treatment with isoniazid and rifampicin. This total duration of 6 months of treatment may be extended by the treating physician based on the **advice of the NTP or designated TB officer** for the continuation phase only due to extent of disease and/or clinical response.

For all **retreatment cases**, the **intensive phase** is lengthened to 3 months, while the **continuation phase** is 5 months. This minimum treatment duration of 8 months may also be extended based on clinical response and/or extent of disease.

Standard short-course therapy is **only** suitable if:

- the organisms are susceptible to isoniazid, rifampicin and pyrazinamide
- the patient tolerates and adheres to the regimen
- there is no evidence of miliary (disseminated) or central nervous system TB
- extensive cavitation is not present on the initial chest X-ray.

Monitor the response to treatment and extend the duration of therapy if the response is not satisfactory.

Monitor the patient's weight at regular intervals (particularly in children) and adjust drug doses if necessary.

Adjunctive corticosteroid use is indicated for some patients, see corticosteroid use in tuberculosis.

Regimen

NOTE: The Fiji TB Guidelines/Manual 2017 recommends alternative treatment regimens for retreatment cases; updated WHO recommendations released following its publication are reflected in this guideline.

Fixed Dose Combination (FDC) treatment was introduced in Fiji in 2011; currently 90% of patients receive this therapy.

> FDC should be used for both the intensive and continuation phases of any TB therapy.

Initiation of TB treatment with loose dose formulations

When initiating treatment (eg in divisional or sub-divisional hospitals) loose dose formulations are often used. Seek advice from the TB Program regarding appropriate FDC formulations for continuing therapy.

For the treatment of TB using loose dose formulations where indicated, use:

isoniazid 5 mg/kg (child < 15 years: 10 mg/kg) to a maximum dose of 300 mg orally daily

PLUS

rifampicin 10 mg/kg (child < 15 years: 15 mg/kg) to a maximum dose of 600 mg orally daily

PLUS

ethambutol 15 mg/kg (child < 15 years: 20 mg/kg) up to a maximum dose of 1200 mg orally daily

PLUS

pyrazinamide 25 mg/kg(child < 15 years: 35 mg/kg) up to a maximum dose of 2500 mg orally daily

Children, pregnant and breastfeeding women, and adults with malnutrition, alcohol abuse or HIV/AIDS should also receive pyridoxine (vitamin B6) therapy for the prevention of isoniazid-induced peripheral neuropathy; use:

> pyridoxine 25 mg orally, daily for 6 months; increase up to 100-200 mg orally, daily if symptoms/signs of peripheral neuropathy develop

Patients with extensive pulmonary TB, or with some types of extra-pulmonary TB, require a longer duration of the "continuation phase" (the intensive phase remains unchanged); in general:

- central nervous system eg TB meningitis: 9-12 months
- osteoarticular eg vertebral osteomyelitis / Pott's disease: 12 – 15 months dependent on clinical response
- extensive pulmonary TB: up to 12 months

Consider also extending the duration of treatment for patients with TB that is slow to respond, regardless of the site of infection. Discussion with the NTP or designated TB officer is recommended.

The family, including the primary caregiver, should be advised through a case conference on precautionary measures in terms of TB prevention and care. On discharge from hospital a community directly observed therapy (DOT) provider should be nominated. Contact tracing should be performed.

Pulmonary tuberculosis

Infection control is particularly important for pulmonary TB because it is the predominant infectious form. All patients with presumed or known pulmonary TB should be separated from other patients, placed in adequately ventilated areas, educated on cough etiquette and respiratory hygiene and assessed for risk of TB transmission.

Patients with TB caused by fully drug-susceptible organisms are considered non-infectious after at least 2 weeks of the daily regimen of the standard short-course DOTS therapy is completed. Even if the sputum is still smear-positive, these patients are considered non-infectious provided that the patient is adherent and responding to treatment (in particular, reduced cough and fever).

Precautions against airborne transmission may be required for longer than 2 weeks in patients:

- with HIV infection
- with extensive cavitation
- who are smear-positive and at high risk of drug resistance
- with laryngeal TB.

Extrapulmonary tuberculosis

Extrapulmonary TB is not an infection risk if there is no lung disease. Many forms of extrapulmonary TB (eg lymph node, pleural, genitourinary, musculoskeletal) can be treated with standard short-course therapy, but this requires expert advice. Patients with miliary (disseminated) and central nervous system TB should be treated for 9-12 months.

Adjunctive surgical management (eg for relief of ureteric obstruction or spinal cord compression) is sometimes required.

Lymph nodes infected with TB (tuberculosis lymphadenitis) can increase in size or form sinuses during and after treatment. This response is an immunological reaction to dead bacilli and does not necessarily indicate treatment failure.

Corticosteroid use in tuberculosis

Corticosteroids are not routinely used in the treatment of TB; however, they are of benefit in patients with:

- neurological TB (eg TB meningitis)
- TB pericarditis
- extensive pulmonary TB.

Where used they should be commenced at the same time as the antituberculous therapy. They may occasionally also be necessary for other forms of TB; expert advice should be sought.

Dosing of corticosteroids is complex. A typical regimen is:

> prednis(ol)one 50 mg (child: 1 mg/kg up to 50 mg) orally, daily for 2 to 3 weeks, then taper the dose gradually according to clinical response, for up to 10-12 weeks.

Corticosteroids may also be used for the management of immune reconstitution inflammatory syndrome (IRIS) in patients with TB-HIV

coinfection. 30 days of therapy at a tapered dose is usually adequate for this indication.

Drug-resistant tuberculosis

Drug-resistant tuberculosis remains uncommon in Fiji. Isolated isoniazid or rifampicin resistance may occasionally be seen. Multidrug-resistant TB (MDR-TB; defined as TB resistant to at least isoniazid and rifampicin) is increasingly prevalent globally. Suspect resistance if:

- Previous TB treatment, or history of loss to follow-up
- TB treatment failure
- TB and HIV coinfection
- Migrant from a MDR-TB endemic country
- Contact of a drug-resistant TB case

If MDR-TB is suspected, the patient must be referred immediately to the nearest Divisional DOTS centre in Lautoka Hospital (Western Division), Tamavua Twomey Hospital (Central/Eastern Divisions) or Labasa Hospital (Northern Division). The Divisional DOTS centres will coordinate referral to the National TB Centre for MDR in Tamavua Twomey Hospital. Expert consultation through WHO is mandatory to guide treatment. Extended duration multidrug regimens are necessary and guided by clinical response.

Tuberculosis management in special patient groups

Tuberculosis in children

Children with TB have often acquired the infection from recent contact with an adult; children are not usually infectious. Children are particularly susceptible to invasive disease (miliary [disseminated] and meningeal TB), especially if they have not received Bacille Calmette-Guérin (BCG) vaccination.

Standard short-course therapy is appropriate for children with TB. Compared to adults, children require higher mg/kg doses of antituberculous drugs to achieve effective serum concentrations. Adverse effects are rare in children.

Tuberculosis in women who are pregnant or breastfeeding

Untreated TB is a greater hazard to a pregnant woman and her foetus than

its treatment. Treat TB in pregnant women with standard DOT short-course therapy.

All infants of mothers with smear-positive pulmonary disease require preventive treatment with isoniazid (see latent tuberculosis for dose) and close monitoring.

Breastfeeding should not be discouraged in women receiving TB treatment. The concentrations of antituberculous drugs in breast milk are very low, and consequently do not provide effective treatment for TB or latent tuberculosis in a breastfed infant.

Tuberculosis and HIV infection

The management of TB in patients infected with HIV is complex—seek expert advice. Unless the doctor has the expertise to manage both HIV infection and TB, close liaison between treating physicians is essential.

Rifampicin induces hepatic cytochrome (CYP) P450 enzymes, so it has clinically significant drug interactions with antiretroviral drugs. Specialist advice is required to avoid toxicity and/or suboptimal treatment. For further details, consult a comprehensive drug interactions resource (eg the University of Liverpool [UK] website <www.hiv-druginteractions.org>).

Tuberculosis and Advanced Hepatic or Renal disease

Patients with significant renal or hepatic impairment may require a "tailor-made" regimen with alternate drug dosing; consult a specialist prior to commencing therapy.

Monitoring antituberculous therapy

Each review, check adherence with the patient. Collect sputum, if possible, at the end of 2 months of treatment; repeat at 3, 5 and 6 months for new cases, and again at 8 months for retreatment cases. If the sputum is smear-positive at the 5th month of treatment, sputum must be sent for Drug Susceptibility Testing, and the patient re-registered and recommenced on a retreatment regimen. The Divisional DOTS centres coordinate this.

A CXR should be performed following the 2nd or 3rd month of treatment, and again at 6 months.

Ask patients who are taking ethambutol about visual adverse effects at each visit. Check visual acuity and colour vision before starting treatment and then at monthly intervals, especially if therapy is continued for longer than 2 months. Checking for visual adverse effects is particularly important in people with kidney impairment because ethambutol accumulates (due to decreased clearance). Discontinue ethambutol immediately, advise NTP colleagues and refer to an ophthalmologist if signs of ocular toxicity develop. Switching to loose dose formulations with the exclusion of ethambutol is ideal.

Educate patients about the risk and symptoms of hepatitis and monitor liver function. Liver function monitoring is particularly important for older patients, and patients with abnormal baseline liver biochemistry, pre-existing liver disease, chronic viral hepatitis or hazardous alcohol consumption. Minor elevation of serum transaminases is common and usually does not require discontinuation of therapy. Withdraw all drugs immediately if clinical jaundice develops or if the patient develops significantly elevated serum transaminases (four-fold rise from baseline); refer immediately to a specialist.

Latent TB Infections

People with *Mycobacterium tuberculosis* infection without active disease have latent tuberculosis (TB). Latent TB can be identified by a positive tuberculin skin test. Individuals with positive tests should be closely examined for evidence of active TB. Consider HIV testing in all patients with latent TB.

> Exclude active tuberculosis in all patients infected with *Mycobacterium tuberculosis*.

Treatment of latent TB (chemoprophylaxis) reduces the incidence of progression to active disease. Once active disease has been excluded, consider treatment of latent TB in:

- patients with HIV infection
- recent tuberculin converters
- close contacts of a patient with smear-positive pulmonary TB
- patients who are immunocompromised or are receiving immunosuppressive drugs

- patients younger than 35 years with no known TB contact.

A less intensive regimen can be used for treatment of latent TB because the number of organisms involved is small. In Fiji, latent TB is treated with combination therapy with isoniazid and rifampicin for 3-4 months.

Therapy may be commenced using loose dose formulations or FDC based on the regimen below, but should be switched to FDC where possible for continuing treatment – seek advice from the TB Program for the most appropriate FDC available. Where loose dose formulation is commenced, use:

> isoniazid 5 mg/kg (child: 10 mg/kg) to a maximum dose of 300 mg orally, daily for 3 to 4 months
>
> PLUS
>
> rifampicin 10 mg/kg (child: 15mg/kg) to a maximum dose of 600 mg (child < 14 years and < 50 kg maximum dose of 450 mg) orally, daily for 3-4 months

An alternative regimen is monotherapy with isoniazid for 6-9 months, use:

> isoniazid 5 mg/kg (child: 10mg/kg) to a maximum dose of 300 mg orally, daily for 6-9 months

Monitor liver function as for treatment of active TB (see monitoring antituberculosis therapy), and educate patients about the symptoms of hepatitis.

Alternatives to isoniazid may be required for contacts of patients with isoniazid-resistant TB, or if there is potential for isoniazid resistance, or if isoniazid is not tolerated—seek expert advice.

Nontuberculous mycobacteria

Nontuberculous mycobacteria (NTM) are environmental organisms that occasionally cause respiratory, cutaneous or disseminated infection. Person-to-person transmission rarely occurs. Patients with these infections should be referred to a specialist physician of internal medicine.

17. Malaria

Introduction

Malaria is caused by Plasmodium parasites, which are transmitted to humans through the bites of infected mosquitoes. Five Plasmodium species infect humans: *P. falciparum, P. vivax, P. knowlesi, P. malariae* and *P. ovale*.

Malaria must be considered in any patient who has visited a malarious area and presents with a febrile illness. For patients with suspected malaria, send a blood sample in an EDTA tube to an appropriate laboratory for examination, including thick and thin blood films.

While malaria usually occurs within a few weeks of infection, disease can occasionally be delayed for many months.

A single negative blood film does not exclude the diagnosis of malaria, particularly if the patient has recently taken antimalarials. Some antibiotics commonly used by travellers (eg. trimethoprim+sulfamethoxazole, tetracyclines, quinolones) have antimalarial activity, which can modify or suppress malaria symptoms and make diagnosis by blood film more difficult.

In many countries, travellers can purchase antimalarial drugs without a prescription, but they should be warned that counterfeit products are common.

Treatment

Uncomplicated malaria

Uncomplicated malaria can generally be treated with oral therapy. If the patient is unable to tolerate oral therapy, treat as for severe malaria and seek expert advice. Treatment for uncomplicated malaria caused by *P. falciparum* and *P. knowlesi* should be initiated in hospital because a small proportion of patients deteriorate after starting therapy.

Artemether+lumefantrine (an artemisinin-based combination) is the treatment of choice for uncomplicated malaria. Chloroquine is no longer

recommended for the treatment of malaria because high-grade chloroquine-resistant *P. falciparum* malaria has spread to most malaria-endemic areas of the world, and high-grade chloroquine-resistant *P. vivax* malaria occurs in several areas of the Asia–Pacific region. Do not use atovaquone+proguanil to treat malaria if it was used for prophylaxis.

> Do not use atovaquone+proguanil to treat malaria if it was used for prophylaxis.

For uncomplicated malaria, use:

- artemether+lumefantrine tablets 20+120 mg to be taken with fatty food or full-fat milk for a total of six doses Non-EML
  - adult and child more than 34 kg: 4 tablets orally at 0, 8, 24, 36, 48 and 60 hours
  - child 5 to 14 kg: 1 tablet orally at 0, 8, 24, 36, 48 and 60 hours
  - child 15 to 24 kg: 2 tablets orally at 0, 8, 24, 36, 48 and 60 hours
  - child 25 to 34 kg: 3 tablets orally at 0, 8, 24, 36, 48 and 60 hours

Alternative, less preferred, alternatives are:

- atovaquone+proguanil tablets 250+100 mg ***(adult formulation)*** to be taken with fatty food or full-fat milk Non-EML
  - adult and child more than 40 kg: 4 tablets orally daily for 3 days
  - child 11 to 20 kg: 1tablet orally daily for 3 days
  - child 21 to 30 kg: 2 tablets orally daily for 3 days
  - child 31 to 40 kg: 3 tablets orally daily for 3 days

Alternatively, use the combination of:

- quinine sulfate 600 mg (adult less than 50 kg: 450 mg) (child: 10 mg/kg up to 600 mg) orally, 8-hourly for 7 days[79]
- PLUS EITHER

[79] Both quinine sulfate and quinine bisulfate are available as 300 mg tablets. Quinine sulfate 600 mg is approximately equivalent to quinine bisulfate 900 mg. **Quinine sulfate** is listed on the Fiji EML.

doxycycline 100 mg (child 8 years or older: 2 mg/kg up to 100 mg) orally, 12-hourly for 7 days (which can start after day 1 of quinine therapy)

OR (for pregnant women or children younger than 8 years)

clindamycin 450 mg (child: 10 mg/kg up to 450 mg) orally, 8-hourly for 7 days Non-EML

Artemisinin resistance has been reported in some areas of the Greater Mekong Sub-region (Thailand, Vietnam, Cambodia, Laos and Myanmar [Burma]), resulting in reduced efficacy of artemisinin-based combination therapy against *P. falciparum* (but not other malaria species). For patients with malaria caused by *P. falciparum* (either alone or with other species) acquired from this region and who respond slowly to artemether+lumefantrine (ie persisting parasitaemia after 72 hours of therapy), **switch** to oral quinine sulfate plus either doxycycline or clindamycin as above, for 7 days.

P. vivax and *P. ovale* can exist as **dormant parasites (hypnozoites)** in the liver, which can reactivate to cause relapsed malaria. The regimens for the blood-stage of uncomplicated malaria (see above) do not eliminate hypnozoites, so concurrent treatment with primaquine is required for malaria caused by these species to eliminate dormant liver parasites. Primaquine can cause severe haemolysis in patients who are glucose-6-phosphate dehydrogenase (G6PD) deficient. If the patient is G6PD deficient, seek expert advice.

For *P. vivax* infection, once G6PD deficiency has been excluded, **use concurrently**:

primaquine 30 mg (child: 0.5 mg/kg up to 30 mg) orally, daily, or if nausea occurs 15 mg (child: 0.25 mg/kg up to 15 mg) orally, 12-hourly. Treat for a minimum of 14 days or, in adults more than 70 kg, until a total cumulative dose of 6 mg/kg is reached[80]

For *P. ovale* infection, once G6PD deficiency has been excluded, **use**

[80] Treatment failure with primaquine can occur in malaria caused by *P. vivax*, especially when the infection has been acquired in Indonesia, Timor-Leste or Pacific Island Nations. Evidence suggests that relapses of malaria caused by *P. vivax* are more common if primaquine is not administered concurrently with treatment for the blood-stage of malaria, or if the total cumulative dose was less than 6 mg/kg (eg only 14 days treatment in adults more than 70 kg).

concurrently:

primaquine 15 mg (child: 0.25 mg/kg up to 15 mg) orally, daily for 14 days

If a relapse of malaria occurs despite treatment with primaquine, seek expert advice.

Primaquine is also effective at eliminating the transmissible stages of *P. falciparum*, preventing the transfer of parasites from human hosts to mosquitoes. Once G6PD deficiency has been excluded, **add**:

primaquine 15 mg (child: 0.25 mg/kg up to 15 mg) orally, as a single dose

Severe malaria

Severe malaria is usually caused by *Plasmodium falciparum*, but may also be caused by other *Plasmodium* species (particularly *P. knowlesi*). Urgent treatment of malaria is essential if the patient has any of the following features:

- any degree of altered consciousness, jaundice, oliguria, respiratory distress, severe anaemia or hypoglycaemia
- a parasite count more than 100 000/mm^3 (more than 2% of red blood cells parasitised)
- vomiting
- clinical acidosis or metabolic acidosis on blood biochemistry
- acute kidney injury.

Start IV therapy and seek expert advice on further management. For severe malaria, use:

artesunate (adult and child) 2.4 mg/kg IV, on admission and repeat at 12 hours and 24 hours, then once daily until oral therapy is tolerated[Non-EML]

OR (if parenteral artesunate is not immediately available)

quinine dihydrochloride (adult and child) 20 mg/kg IV over 4 hours as a loading dose, then 10 mg/kg IV over 4 hours (starting 4 hours after the loading dose is completed), 8-hourly until oral therapy is tolerated[81]

[81] For obese patients, use ideal body weight (see appendix 8) to calculate the dose of quinine.

The IV **loading dose of quinine** is not required if the patient has received:

- 3 or more doses of quinine or quinidine in the last 48 hours
- mefloquine prophylaxis in the last 24 hours
- a treatment dose of mefloquine in the last 3 days.

For patients receiving IV quinine, measure blood pressure and blood glucose concentration frequently (because quinine stimulates insulin secretion and can cause hypoglycaemia). Cardiac monitoring is also necessary. If treatment with IV quinine continues for longer than 48 hours, dose adjustment may be necessary, especially in patients with renal impairment (see appendix 5)—seek expert advice.

Mortality from severe *P. falciparum* malaria is lower with IV artesunate (an artemisinin derivative) than with IV quinine. Although the impact of artemisinin resistance on the efficacy of IV artesunate in severe malaria is not yet known, combination therapy with IV artesunate plus IV quinine may be required—seek expert advice.

Switch to oral treatment when the patient has clinically improved. Give a full course (6 doses) of artemether+lumefantrine, as for uncomplicated malaria. Second-line oral regimens include a full course (3 days) of atovaquone+proguanil, OR oral quinine combined with either doxycycline or clindamycin to complete a total of 7 days of treatment with quinine— see uncomplicated malaria.

Depending on the species of malaria, concurrent treatment with primaquine may also be indicated.

Prophylaxis

Introduction

Malaria prophylaxis is complicated by the development of multidrug-resistant strains of *Plasmodium falciparum* throughout the world, particularly in Southeast Asia.

Recommendations for malaria prophylaxis from different health authorities and experts vary considerably. For specific geographical locations, useful information about the risk of malaria and antimalarial susceptibility patterns

is available from:

- World Health Organization (WHO). International travel and health 2017. <www.who.int/ith/en>
- Centers for Disease Control and Prevention (CDC). CDC Health information for international travel (Yellow book) 2018. < https://wwwnc.cdc.gov/travel/page/yellowbook-home>.

Vector avoidance

Significant protection is conferred by simple measures that minimise the potential for mosquito bites, such as:

- applying effective insect repellent and using other insecticide products (eg mosquito coils or vaporising mats)
- wearing light-coloured long trousers and long-sleeved shirts in the evening
- sleeping in screened accommodation or using mosquito nets, which can be pyrethroid impregnated
- avoiding outside activities between dusk and dawn
- avoiding perfume and aftershave.

Chemoprophylaxis

No chemoprophylaxis regimen is guaranteed to prevent malaria. Consequently, when prescribing chemoprophylaxis, the risk of disease and the efficacy of the drug(s) must be balanced against the potential for drug toxicity. Consider the following factors when assessing the risk of acquiring malaria:

- the country and area visited
- the time of year
- the duration of the visit
- the type of activities undertaken.

In some places, including many major cities and tourist resorts in malaria-endemic countries, the risk of malaria is low and prophylaxis is not required.

Consider malaria prophylaxis for Fijian immigrants from malarious areas who return to visit family and friends, because the risk of malaria is often under appreciated by these individuals.

Advise travellers to malarious areas that chemoprophylaxis is not always effective and they must seek urgent medical attention if they develop a fever while travelling or after returning.

> Fever in travellers to malarious areas requires urgent medical attention.

Malaria acquisition in pregnant women or asplenic patients is potentially very serious, so it is strongly recommended that these individuals do not travel to malarious areas, especially areas with drug-resistant *P. falciparum*.

Prophylaxis for children is difficult. Doxycycline is not recommended for children younger than 8 years, and mefloquine is not approved for paediatric use (though it has been widely used).

Chloroquine-resistant *P. falciparum* has spread worldwide, so chloroquine is not recommended for prophylaxis. Although the combination of chloroquine and proguanil was widely used for malaria prophylaxis in pregnant women and children, this regimen is no longer considered effective.

Do not use mefloquine for prophylaxis in the Greater Mekong Subregion (Thailand, Vietnam, Cambodia, Laos and Myanmar [Burma]), due to mefloquine resistance.

For prophylaxis of malaria, use:

atovaquone+proguanil tablets 250+100 mg ***(adult formulation)*** adult and child more than 40 kg: 1 tablet orally with fatty food or full-fat milk (to ensure adequate absorption of atovaquone), daily (starting 1 to 2 days before entering, and continuing for 7 days after leaving the malarious area) Non-EML

atovaquone+proguanil tablets 62.5+25 mg ***(paediatric formulation)*** child 11 to 20 kg: 1 tablet; 21 to 30 kg: 2 tablets; 31 to 40 kg: 3 tablets orally with fatty food or full-fat milk (to ensure adequate absorption of atovaquone), daily (starting 1 to 2 days before entering, and continuing for 7 days after leaving the malarious area) Non-EML

OR

doxycycline 100 mg (child 8 years or older: 2 mg/kg up to 100 mg) orally, daily (starting 1 to 2 days before entering, and continuing for 4 weeks after leaving the malarious area)

OR (in areas without mefloquine resistance)

mefloquine 250 mg (child 5 to 15 kg: 62.5 mg [= 1/4 tablet]; 16 to 30 kg: 125 mg [= 1/2 tablet]; 31 to 45 kg: 187.5 mg [= 3/4 tablet]; over 45 kg: 250 mg [=1 tablet]) orally, once weekly (starting 2 to 3 weeks before entering, and continuing for 4 weeks after leaving the malarious area) Non-EML

Unlike atovaquone+proguanil, doxycycline and mefloquine are not sufficiently effective against the primary liver stages of malaria, so prophylaxis with these drugs must continue for 4 weeks after leaving the malarious area.

Stand-by emergency treatment

Travellers who choose not to use chemoprophylaxis can be given a stand-by course of artemether+lumefantrine or atovaquone+proguanil to use if a febrile illness occurs and medical care is unlikely to be available within 24 hours (see uncomplicated malaria for doses). Travellers should be warned that medical attention is required for diagnosis, even if emergency treatment is taken, because there are many possible causes of febrile illness.

18. Miscellaneous infections

Filariasis

Filariasis is transmitted by the bite of some species of mosquitoes, flies and midges. There are eight recognised nematode causes of human filariasis. The most important are: *Wuchereria bancrofti*, *Brugia malayi* and *Brugia timori*, which cause lymphatic filariasis; *Onchocerca volvulus*, which causes river blindness; and *Loa loa*, which causes loaiasis. *Mansonella perstans*, *Mansonella ozzardi* and *Mansonella streptocerca* also infect humans.

Each infection has a unique presentation and management approach—seek expert advice. Treatment is usually with albendazole, ivermectin, diethylcarbamazine or doxycycline. Filariasis is often treated through mass treatment programs.

Leptospirosis

Leptospirosis is a zoonotic systemic infection caused by *Leptospira interrogans* serovars. It usually presents as an acute febrile illness with headache and myalgias, often accompanied by conjunctival suffusion. Gastrointestinal upset and cough may be present. In more severe cases, jaundice, acute kidney injury, haemoptysis or bleeding from other sites occurs. Epidemiological risk factors (eg farmer, livestock contact, local flooding) are commonly present. A suspected diagnosis may be supported by serology testing, for more information see *Fiji Leptospirosis Guidelines 2016*.

If leptospirosis is suspected clinically, in all cases start treatment before the diagnosis is confirmed.

For mild cases, where oral therapy is tolerated, use:

> doxycycline 100 mg (child 8 years or older: 2 mg/kg up to 100 mg) orally, 12-hourly for 7 days
>
> OR
>
> amoxicillin 500 mg (child: 15 mg/kg to a maximum of 500 mg) orally, 8-hourly for 7 days

If the above agents cannot be used, less preferred alternatives include:

erythromycin 500 mg (child: 12.5 mg/kg to a maximum of 500 mg) orally, 6-hourly (child: 8-hourly) for 7 days

OR (in adults only)

azithromycin 1 g orally, single dose, then 500 mg orally, twice daily for 2 days

OR

clarithromycin 500 mg orally, 12-hourly for 7 days [Non-EML]

Doxycycline is the preferred drug for empirical therapy because it also treats rickettsial infections, which have a similar presentation to leptospirosis; but avoid in pregnant or breastfeeding women or children < 8 years of age.

In more severe cases, use:

benzylpenicillin 2 million units (1.2 g) (child: 50,000 units/kg up to 2 million units) IV, 6-hourly for 7 days

OR

ceftriaxone 1-2 g (child 1 month or older: 100 mg/kg up to 2 g) IV, daily for 7 days

Alternative agents are:

cefotaxime 1 g (child: 25mg/kg to a maximum of 1g) IV, 6-hourly for 7 days

OR

ampicillin 1-2 g (child: 50 mg/kg to a maximum of 2 g) IV, 6-hourly for 7 days

OR

erythromycin 500 mg (child: 25 mg/kg to a maximum of 500 mg) IV by slow infusion, 6-hourly for 7 days

In cases requiring ICU admission, ceftriaxone is the preferred agent. Treat all severe cases for at least 7 days (IV + oral).

All more severe cases require early referral to the divisional hospital for inpatient care.

All suspected cases of leptospirosis require formal notification to the Divisional Medical Officer (DMO) or Sub-divisional Medical Officer (SDMO).

Rickettsial infections

Rickettsial infections usually present as a nonspecific febrile illness, often with a characteristic generalised rash. Fever may be preceded by localised tender lymphadenopathy, with an eschar at the site of the tick or mite bite. A small proportion of cases develop severe complications such as pneumonitis, encephalitis or septic shock.

To treat, use:

> doxycycline 100 mg (child: 2 mg/kg up to 100 mg) orally, 12-hourly for 7 days
>
> OR
>
> azithromycin 500 mg (child: 10 mg/kg up to 500 mg) orally on the first day, then 250 mg (child: 5 mg/kg up to 250 mg) orally, daily for a further 4 days

Doxycycline is recommended to treat rickettsial infections in children of all ages because it is the most effective treatment. The risk of dental adverse effects in young children is minimal, particularly when a single short course of doxycycline is used.

Rifampicin has also been used to treat rickettsial infections, and may be an alternative to azithromycin in pregnancy—seek expert advice.

For severe disease, seek expert advice.

Viral infections

Neonatal herpes simplex infection

In neonates, infection with herpes simplex virus (HSV) can present with isolated skin or mucous membrane lesions, encephalitis or disseminated infection. Management is complex and specialist advice is required. If specialist advice is not available immediately, see Figure 17.1 for initial management of neonates at risk of acquiring HSV.

If treatment is required, use:

aciclovir 20 mg/kg IV, 8-hourly

The duration of treatment depends on the clinical presentation. Disease affecting the skin, eyes and mouth requires a minimum of 14 days of IV therapy. At least 21 days of IV therapy is required for neonates with disseminated disease or encephalitis. Treatment for encephalitis should continue until HSV is no longer detected in the cerebrospinal fluid—seek expert advice. Seek expert advice on the duration of therapy in high-risk asymptomatic neonates.

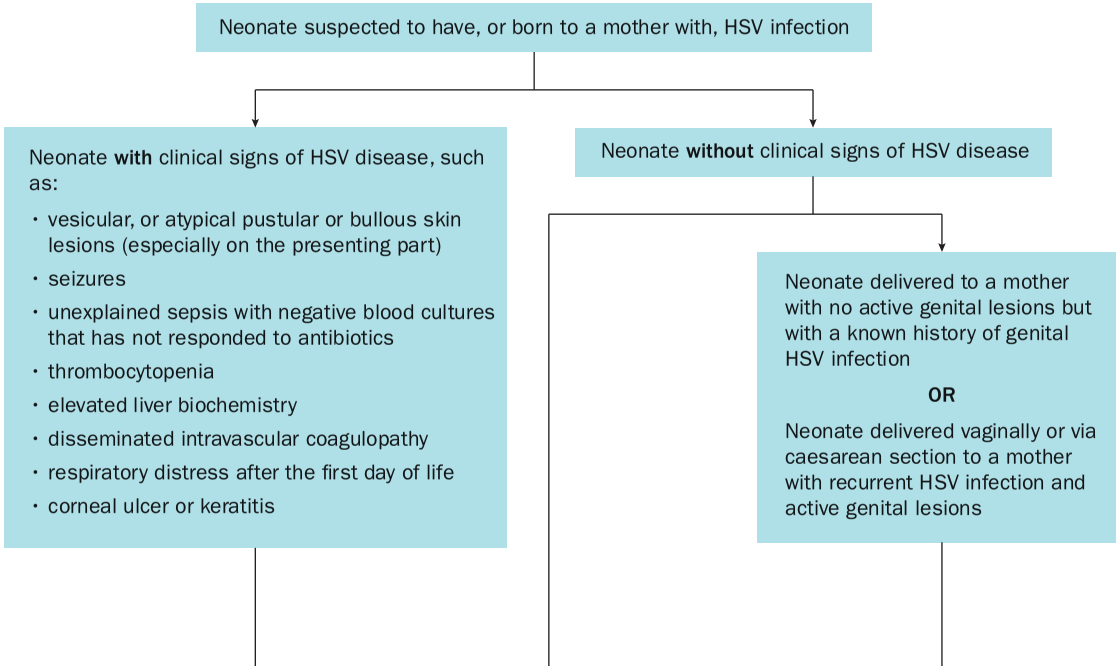
Oral aciclovir should not be used for initial treatment of HSV in neonates. However, there is evidence for oral suppressive therapy (after completion of the IV treatment course) to prevent neurological recurrence following encephalitis. Suppressive therapy with oral aciclovir can also be considered in preterm infants (to prevent early reactivation of disease) and in full-term neonates who have skin, eye or mouth lesions (to prevent cutaneous recurrence). Seek expert advice.

After successful treatment, monitor all infants closely for HSV recurrence. If recurrence occurs, seek expert advice.

For initial management of neonates suspected to have, or born to mothers with, HSV infection see Figure 18.1 on the following page.

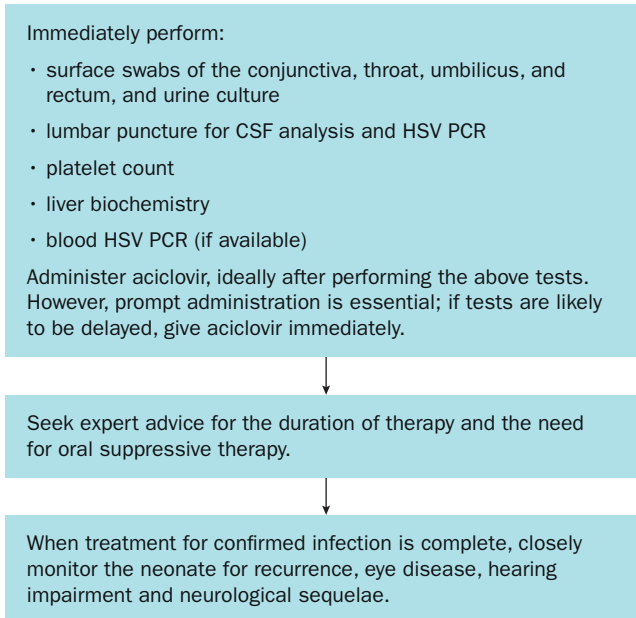
Initial management of neonates suspected to have, or born to mothers with, HSV infection (Figure 18.1)

Figure 18.1, part A



Neonate at low risk of HSV infection
Monitor neonate for signs of infection.
Consider investigations (as for neonate at high risk) if HSV infection is suspected
Neonate delivered vaginally to a mother with active genital lesions and no past history of genital HSV infection
OR
Neonate delivered to a mother with recent primary genital HSV infection (ie not seroconverted)
Neonate at high risk of HSV infection
See part B

Figure 18.1, part B



CSF = cerebrospinal fluid; HSV = herpes simplex virus; PCR = polymerase chain reaction

Adapted from Palasanthiran P, Starr M, Jones C, Giles M, editors. Management of perinatal infection. Sydney: Australasian Society for Infectious Diseases; 2014. <www.asid.net.au/resources/clinical-guidelines>

Varicella (chickenpox)

Immunocompetent patients without complications of varicella

Neonates are at an increased risk of severe disease and complications of varicella (chickenpox). For the management of perinatal varicella infections, seek expert advice.

Children without significant pre-existing skin disease do not require antiviral therapy for varicella because the benefits of treatment are only marginal. Children with significant pre-existing skin disease (eg eczema) require antiviral therapy because they are at greater risk of severe varicella (including extensive cutaneous varicella) and complications of varicella (eg pneumonitis, encephalitis, hepatitis).

For immunocompetent children with significant pre-existing skin disease, irrespective of the duration of rash, use:

> aciclovir 20 mg/kg up to 800 mg orally, 5 times daily for 7 days

Adults are at greater risk of severe disease and complications of varicella. Consider treatment for immunocompetent adults if it can be started within 36 hours of the onset of rash. Treatment is recommended for pregnant women if it can be started within 72 hours of the onset of rash. Use:

> aciclovir 800 mg orally, 5 times daily for 7 days

Immunocompromised patients or patients with complications of varicella

In **immunocompromised patients with severe disease** or in **immunocompetent patients with complications of varicella** (eg pneumonitis, encephalitis, hepatitis), irrespective of the duration of rash, use initially:

> aciclovir 10 to 12.5 mg/kg (child: 500 mg/m^2 [approximately 20 mg/kg for child 5 years or younger, 15 mg/kg for child older than 5 years]) IV, 8-hourly

Switch to oral therapy after clinical improvement and continue treatment for a minimum of 7 days (IV + oral). For treatment recommendations, see immunocompetent patients without complications of varicella.

For **immunocompromised patients with less severe disease**, irrespective

of the duration of rash, use oral therapy for 7 days. For treatment recommendations, see immunocompetent patients without complications of varicella.

For the management of varicella in adults with HIV infection, seek expert advice.

Superinfection of varicella skin lesions with *Streptococcus pyogenes* or *Staphylococcus aureus* can occur and should be treated as for impetigo or cellulitis.

Herpes zoster (shingles)

Herpes zoster (shingles) is caused by reactivation of the varicella-zoster virus. It is uncommon in childhood; incidence increases with age. Herpes zoster is characterised by a rash that presents with blisters in a dermatomal distribution on an erythematous base. The blisters erupt over a week and then heal over 2 weeks. The majority of patients with herpes zoster are not immunocompromised; however, in immunocompromised patients, systemic symptoms and a multidermatomal rash can complicate infection.

If there is ocular involvement, referral to an ophthalmologist may be required (see page 148).

If the rash has been present for less than 72 hours, antiviral treatment reduces acute pain, duration of the rash, viral shedding and ophthalmic complications. Whether antiviral therapy reduces the incidence of postherpetic neuralgia is contentious.

Antiviral treatment is indicated for immunocompetent patients who present within 72 hours of the onset of the rash, and for all immunocompromised patients regardless of the duration of the rash. Use:

> aciclovir 800 mg (child: 20 mg/kg up to 800 mg) orally, 5 times daily for 7 days

For **immunocompromised patients with disseminated disease**, admit to hospital for IV aciclovir therapy. Use:

> aciclovir 10 to 12.5 mg/kg (child: 500 mg/m^2 [approximately 20 mg/kg for child 5 years or younger; 15 mg/kg for child 5 years or older]) IV, 8-hourly

After significant clinical improvement, switch to oral antiviral therapy (as above) to complete 7 days of treatment (IV + oral).

19. Oral and dental infections

Periodontal disease

Periodontal disease is inflammation of the gingivae and the supporting structures of the teeth. The most common forms are gingivitis and periodontitis.

Gingivitis

Gingivitis is inflammation of the gingival tissues, which become red and swollen and bleed easily; it occurs as a result of undisturbed plaque. Management involves:

mechanical removal of plaque

chlorhexidine 0.2% mouthwash 10 mL rinsed in the mouth for 1 minute then spat out, 8- to 12-hourly for 5 to 10 days [Non-EML]

Periodontitis

Periodontitis is inflammation affecting the supporting structures of the teeth, resulting in loss of tooth support with progressive bone loss and, ultimately, loose teeth. It is often associated with oral malodour and bad taste. Major risk factors include smoking and poorly controlled diabetes.

Management requires:

- thorough toothbrushing and interdental cleaning
- patient education re: oral hygiene and smoking cessation
- dental scaling (to remove calculus and plaque)
- root planing for deeper pockets under local anaesthetic

Advanced periodontitis may require periodontal surgery with bone re-contouring.

> Antibiotic therapy is rarely required and is not effective without concomitant debridement.

Ulcerative / acute necrotising ulcerative gingivitis (ANUG)

Acute ulcerative gingivitis is an extremely painful infection of the periodontal tissues. It is characterised by punched-out interdental papillae, ulcers (often covered with a greyish membrane) and, usually, a fetid odour. It can be associated with systemic signs and symptoms. Acute ulcerative gingivitis is most commonly seen in young adult smokers. It is rarely, if ever, seen in children. Immediate management involves:

- gentle removal of as much plaque and necrotic debris as possible, using local anaesthesia if necessary
- local irrigation with chlorhexidine 0.2% mouthwash or hydrogen peroxide 6% solution (5 mL mixed with 10 mL of warm water)
- chlorhexidine mouthwash or hydrogen peroxide solution (as below) may also be used if pain limits the patient's ability to mechanically clean their teeth
- counselling and lifestyle adjustment (including smoking cessation)
- analgesics

In addition, if the patient is immunocompromised, or the infection is very severe or does not respond to the above therapy, refer to a dentist for review and **add**:

metronidazole 400 mg orally, 12-hourly for 3 to 5 days

If pain and inflammation restrict oral hygiene practices, recommend short-term use of a mouthwash to reduce plaque formation; use:

hydrogen peroxide 6% solution 5 mL, mixed with 10 mL of warm water, rinsed in the mouth for 1 minute then spat out, 12-hourly until pain has reduced Non-EML

OR

chlorhexidine 0.2% mouthwash 10 mL rinsed in the mouth for 1 minute then spat out, 8- to 12-hourly until pain has reduced Non-EML

Note: With prolonged use (more than a few days), chlorhexidine may cause a superficial discolouration of the teeth and fillings.

Alternative antiseptics available from private pharmacies may also be appropriate to use.

Periodontal abscess

A periodontal abscess usually occurs in patients with existing periodontal disease and/or uncontrolled diabetes.

Treatment requires drainage of pus with scaling, root planing and/or extraction. If systemic signs and symptoms are present, the patient is not responding to local treatment, or the patient is immunocompromised, treat as per spreading odontogentic infections below.

Patients who do not respond to treatment and wish to retain their teeth require specialist management.

Acute dentoalveolar (odontogenic) infections

Acute odontogenic (or tooth-related) infections are common. The infection usually consists of mixed anaerobic and aerobic oral bacteria. The process of odontogenic infection always commences in the vicinity of the tooth. If ignored or inappropriately treated, it progresses to a localised abscess, then spreads beyond the confines of the jaws to the facial or neck soft tissues. The medical status of the patient is very important, particularly if the patient is immunocompromised.

All odontogenic infections require clinical dental management to remove the source of infection and establish drainage. Referral to a dentist is mandatory. Antibiotics should only be considered when the infection has spread to associated tissues or tissue spaces and has produced facial swelling, or when there are systemic symptoms and fever present. Treatment with antibiotics alone, without active dental treatment, can lead to more severe episodes.

Localised odontogenic infections

Odontogenic infections require active dental treatment to drain any pus and removal of the source of the infection via extraction, endodontic (root canal) treatment or periodontal treatment.

Antibiotics should not be used for dental pain, pulpitis or infection localised to the teeth, or to delay providing dental treatment. Treatment with antibiotics alone, without active dental treatment, can lead to more severe

episodes of acute odontogenic infection with risk of airway compromise.

A localised dental abscess is a collection of pus that can be periapical, pericoronal or periodontal in origin; management differs.

Dental treatment options for acute localised odontogenic infections (Box 19.1)

Periapical abscess

- endodontic (root canal) treatment
- tooth extraction

Periodontal abscess

- periodontal treatment (debridement)
- tooth extraction

Pericoronal infection, including abscess

- tooth extraction (treatment of choice)
- remove or recontour the opposing tooth
- topical treatment (if dental treatment delayed)
  - irrigate with sterile saline solution
  - use warm saline or chlorhexidine mouthwashes

Spreading odontogenic infections

General considerations

Spreading odontogenic infections may be superficial (involving the canine or buccal spaces) or deep (involving the upper neck). Systemic features associated with spreading odontogenic infection include pallor, sweating, tachycardia, and an axillary temperature above 38°C (oral temperatures are unreliable for infections originating in the mouth). Sepsis or airway compromise can occur.

Treatment of spreading odontogenic infection, regardless of whether the infection is an abscess (a collection of pus) or cellulitis (an infected inflammatory swelling), is by:

- drainage of pus

- removing the cause (via endodontic or periodontal treatment, or extraction)
- patient support with analgesia and rehydration
- consideration of antibiotics.

Superficial spreading infections

Most superficial infections can be treated with local surgical or dental treatment alone. If there is swelling as well as systemic signs and symptoms, use antibiotic therapy in addition to local surgical or dental treatment, use:

metronidazole 400 mg (child: 10 mg/kg up to 400 mg) orally, 12-hourly for 5 days

PLUS either

phenoxymethylpenicillin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly for 5 days

OR

amoxicillin 500 mg (child: 15 mg/kg up to 500 mg) orally, 8-hourly for 5 days

OR (as a single preparation)

amoxicillin+clavulanate 500+125 mg (child 2 months or older: 15 mg/kg amoxicillin component up to 500 mg) orally, 8-hourly for 5 days

For patients hypersensitive to penicillins use, as a single drug:

clindamycin 300 mg (child: 7.5 mg/kg up to 300 mg) orally, 8-hourly for 5 days Non-EML

Review all patients within 48 to 72 hours of commencing treatment.

Spreading odontogenic infections with severe or systemic features (including Ludwig angina)

Odontogenic infections that spread to the submandibular and pharyngeal spaces in the upper neck are potentially life-threatening, as there is a risk of airway obstruction. Any patient who has trismus and cannot open their mouth more than 2 cm (interincisal) must be assessed for signs of airway

compromise. Signs and symptoms of airway compromise include stridor (noisy breathing), dyspnoea (difficult breathing), dysphagia (difficulty in swallowing), and elevation and firmness of the tongue.

These patients must be assessed urgently by a dentist and/or oral or maxillofacial surgeon, and by an anaesthetist or another specialist in airway management. They require urgent hospital admission to facilitate inpatient care with consideration for special investigations.

Management involves drainage, removal of the tooth, culture and susceptibilities of causative organisms, and treatment with intravenous fluid therapy and antibiotics.

For empirical antibiotic, in conjunction with surgical intervention, use:

benzylpenicillin 3 million units (1.8 g) (child 75 000 units/kg up to 3 million units) IV 4-hourly

PLUS

metronidazole 500 mg (child: 12.5 mg/kg up to 500 mg) IV OR 400 mg (child: 10 mg/kg up to 400 mg) orally 12-hourly

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefazolin 2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly[82] Non-EML

PLUS

metronidazole 500 mg (child: 12.5 mg/kg up to 500 mg) IV OR 400 mg (child: 10 mg/kg up to 400 mg) orally 12-hourly

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, as a single drug regimen, use:

clindamycin 600 mg (child: 15 mg/kg up to 600 mg) IV, 8-hourly Non-EML

Modify therapy based on the results of cultures and susceptibility testing. Switch to oral therapy once swelling and trismus subside (and the patient can swallow) as per superficial spreading odontogenic infection for a further 5 days.

[82] If cefazolin is unavailable, use cefalotin 2 g (child: 50 mg/kg up to 2 g) IV 6-hourly

Infection following dentoalveolar surgery

Signs of infection following dentoalveolar surgery include:

- cellulitis (hot, tense swelling)
- fluctuation
- purulent discharge from the surgical site for more than 72 hours after surgery
- pain and swelling that either worsens or fails to improve 48 hours after surgery
- persistent fever - greater than 39°C at 48 hours or more after surgery.

Perform a full blood count (FBC), erythrocyte sedimentation rate (ESR) and X-ray to confirm and characterise infection.

Management must include drainage of any pus and wound irrigation.

Most postoperative dental infections can be managed by dental treatment alone. However, if the patient is immunocompromised or has systemic features of infection, consider using antibiotic therapy in addition to dental treatment. If indicated, use:

metronidazole 400 mg (child: 10 mg/kg up to 400 mg) orally, 12-hourly

PLUS EITHER

phenoxymethylpenicillin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly

OR

amoxicillin 500 mg (child: 15 mg/kg up to 500 mg) orally, 8-hourly

OR as a single preparation:

amoxicillin+clavulanate 500+125 mg (child 2 months or older: 15 mg/kg amoxicillin component up to 500 mg) orally, 8-hourly

For patients hypersensitive to penicillin, as a single drug, use:

clindamycin 300 mg (child: 7.5 mg/kg up to 300 mg) orally, 8-hourly Non-EML

Duration of treatment is 5 days. Review the patient 48 to 72 hours after starting treatment to check response. Advise the patient to seek prompt

dental review if their condition deteriorates or if the infection has not resolved within 5 days.

Antibiotics are not indicated for alveolitis (dry socket).

Severe postsurgical infections that have spread beyond the confines of the jaw are clinically similar to spreading infections and should be managed similarly (see spreading odontogenic infections).

Salivary gland infections

Swellings of the large major salivary glands (parotid, submandibular and sublingual glands) are common presentations and, in many cases, do not represent infection. Acute suppurative sialadenitis (including parotitis) is usually due to infection with *Staphylococcus aureus*, although it may occasionally be polymicrobial in adults. The glands are enlarged, often hot and tense and pus may be expressed from the gland duct. The patient is usually ill and may be dehydrated.

Acute suppurative sialadenitis may require surgical review. Consider intraductal or surgical drainage if fluctuant. Rehydration may be required. For antibiotic therapy, use:

> cloxacillin 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly, until improved
> ***then switch to*** flucloxacillin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

> cefazolin 2 g (child: 50mg/kg up to 2 g) IV, 8-hourly until improved[83]
> ***then switch to*** cefalexin 500mg (child: 12.5mg/kg up to 500mg) orally, 6-hourly Non-EML

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

> clindamycin 600 mg (child: 15 mg/kg up to 600 mg) IV, 8-hourly until improved
> ***then switch to*** clindamycin 450 mg (child: 10mg/kg up to 450 mg) orally, 8-hourly Non-EML

[83] If cefazolin is unavailable, use cefalotin 2 g (child: 50 mg/kg up to 2 g) IV 6-hourly

OR

erythromycin 500 mg (child: 12.5 mg/kg up to 500 mg) orally or IV, 6-hourly

Treat for a total of 10 days (IV + oral).

Oral mucosal disease

Oral candidiasis

Effective management relies on a correct diagnosis and identification of underlying predisposing factors, such as ill-fitting dentures, incorrect use of corticosteroid inhalers and poor oral hygiene, which should be addressed.

Common risk factors for oral candidiasis (Table 19.1)

Local factors	Systemic factors
• dentures • salivary gland hypofunction • corticosteroid inhalers • poor oral hygiene • smoking	• immune compromise (eg poorly controlled diabetes) • drugs (eg inhaled and systemic corticosteroids, antibiotics)

For antifungal therapy in adults and children from 2 years, use:

miconazole 2% gel 2.5 mL (child 6 months to 2 years: 1.25 mL) placed directly in the mouth and on the tongue then swallowed, 6-hourly after food, for 7 to 14 days [Non-EML]

OR

nystatin (adult and child) 100 000 units/mL suspension 1 mL place directly in the mouth and on the tongue then swallowed, 6-hourly after food, for 7 to 14 days

Advise denture wearers to apply the antifungal to the cleaned fitting surfaces of the dentures before inserting them.

For neonates and children younger than 2 years, use:

nystatin 100 000 units/mL suspension 1 mL topically (then swallowed),

4 times daily, after feeding, for 7 to 14 days; continue treatment for 2 to 3 days after symptoms resolve

OR

miconazole 2% gel 1.25 mL topically (inside the mouth and on the tongue) then swallowed, 4 times daily, after feeding, for 7 to 14 days; continue treatment for at least 7 days after symptoms resolve Non-EML

If the patient does not respond to topical therapy, or is immunocompromised or diabetic, consider systemic therapy with:

fluconazole 300 mg (child: 3 mg/kg up to 300 mg) orally, on day 1, then 150 mg (child: 1.5 mg/kg up to 150 mg) orally, daily for a total of 7-14 days[84]

Angular cheilitis

Angular cheilitis presents as an erythematous skin plaque usually with formation of fissuring at one or both corners of the mouth. The condition is usually a mixed infection with *Candida* coexisting synergistically with staphylococci and streptococci.

It may be associated with iron, vitamin B_{12} or folate deficiency; any suspected deficiencies must be confirmed by laboratory testing before commencing on any supplements.

For antifungal therapy, use:

miconazole 2% cream or gel Non-EML applied topically to the angles of the mouth, 6-hourly for 14 days

Alternative azole creams available in private pharmacies may also be used.

A mild topical corticosteroid can be used in addition to the topical antifungal, to treat the associated inflammatory dermatitis; use:

hydrocortisone 1% cream topically to the angles of the mouth, twice daily until inflammation subsides

After inflammation subsides, continue treatment with a topical antifungal alone for 14 days after symptoms resolve.

[84] Only 150 mg are capsules available in Fiji, therefore doses must be in multiples of 150 mg

Facial fractures

Facial fractures involving mucous membranes may benefit from prophylactic antibiotic therapy; where indicated use:

amoxicillin+clavulanate 500+125 mg (child: 15 mg/kg amoxicillin component up to 500 mg) orally, 8-hourly for 5 days

For patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefalexin 500 mg orally, 6-hourly for 5 days Non-EML

For patients with **immediate** or **delayed severe** hypersensitivity to penicillins, use:

gentamicin 4 to 5 mg/kg (child 1 month – 10 years: 7.5 mg/kg, child > 10 years: 6 mg/kg) IV, as a ***single dose***

PLUS either

erythromycin 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly for 5 days

OR

clindamycin 300 mg (child: 7.5 mg/kg up to 300 mg) orally, 8-hourly for 5 days Non-EML

Antibiotics and dental procedures: general information

Antibiotic prophylaxis is the administration of an antibiotic before a dental procedure to minimise the risk of bacterial infection. It is only given when the risk of infection is high. Infection can occur at:

- a distant site, usually the heart (endocarditis), through the haematogenous route, OR
- an oral surgical site (eg following dentoalveolar surgery)

If required, antibiotic prophylaxis should be given just before the procedure. The aim is to achieve high plasma and tissue concentrations at the time contamination is most likely. Prescribing antibiotics after the procedure is of no prophylactic value.

For a discussion of antibiotic prophylaxis of endocarditis in patients undergoing a dental procedure, see page 54.

Prophylaxis is not recommended before dental procedures in patients with prosthetic joints, as the risk of infection is very small.

For most dentoalveolar procedures in fit immunocompetent patients, antibiotic prophylaxis is **not** required or recommended.

Antibiotic prophylaxis should be considered for:

- Surgical removal of a bone-impacted tooth or periapical surgery in a patient with a history of recurrent infections (patients with evidence of active infection in the area of planned surgery do not have a prophylactic indication but may have a therapeutic indication for antibiotics)
- Dentoalveolar surgery in immunocompromised patients (including those with poorly controlled diabetes).

If antibiotic prophylaxis is required, give:

phenoxymethylpenicillin 2 g (child: 40 mg/kg up to 2 g) orally, 1 hour before the procedure

OR

amoxicillin 2 g (child: 50 mg/kg up to 2 g) orally, 1 hour before the procedure

OR

ampicillin 2 g (child: 50 mg/kg up to 2 g) IV, just before the procedure

OR

ampicillin 2 g (child: 50 mg/kg up to 2 g) IM, 30 minutes before the procedure

OR

benzylpenicillin 2 million units (1.2 g) (child: 50,000 units/kg up to 2 million units) IV, just before the procedure

For patients hypersensitive to penicillin, use:

clindamycin 600 mg (child: 15 mg/kg up to 600 mg) orally, 1 hour before the procedure Non-EML

OR

clindamycin 600 mg (child: 15 mg/kg up to 600 mg) IV over at least 20 minutes, just before the procedure Non-EML

Appendix 1: Principles of gentamicin use

For administration of gentamicin (including route and rate of administration), see appendix 6.

Introduction

Overview

Aminoglycosides are highly effective drugs for therapy of Gram negative infections. However, there is growing awareness of aminoglycoside-related toxicity; concerns about toxicity must be balanced against the known advantages.

There are few absolute contraindications to aminoglycoside use, though they should be used cautiously in several patient groups.

Contraindications

Gentamicin and other aminoglycosides should not be used in patients with:

- a history of vestibular or auditory toxicity caused by an aminoglycoside
- a history of serious hypersensitivity reaction to an aminoglycoside (rare)
- myasthenia gravis.

Precautions

Gentamicin and other aminoglycosides should be avoided, unless the infection is life-threatening or there is no other appropriate safer alternative, in patients with:

- age over 50 years, beyond a single dose
- pre-existing renal impairment (creatinine clearance less than 40 mL min) or rapidly deteriorating renal function, beyond a single dose
- pre-existing significant auditory impairment (hearing loss or tinnitus)
- pre-existing vestibular condition (dizziness, vertigo or balance problems)

Adverse effects

Nephrotoxicity

Aminoglycoside-induced nephrotoxicity is common, and typically manifests as non-oliguric, or even polyuric, kidney failure. It is generally reversible and is usually associated with prolonged treatment courses (longer than 5 to 7 days) and pre-existing renal impairment. Additional risk factors for nephrotoxicity are in the box below.

Risk factors for gentamicin-related nephrotoxicity (Box A1.1)

Patient factors	Treatment factors	Concurrent drugs	
Advanced age	Prolonged treatment	Vancomycin	Cyclosporin
Pre-existing renal impairment	Higher dosage	NSAIDs	Iodide contrast media
Dehydration	Multiple-daily dosing	Amphotericin	Colistin
Hepatic dysfunction		Diuretics	

Routine biochemistry and serum creatinine (U+E, Cr) should be checked, where possible, prior to commencing an aminoglycoside, then at least 2 to 3 times each week, or more frequently if renal function is unstable. Note a rise in serum creatinine can be delayed in acute kidney injury.

Vestibular and auditory toxicity

Aminoglycoside-induced vestibular and auditory toxicity occur rarely, but are usually irreversible and can be debilitating. They are not predicted by plasma concentrations. Symptoms may become apparent early in the course of treatment, or weeks after therapy has stopped.

For prolonged aminoglycoside therapy, all patients should be informed of the potential for vestibular and auditory toxicity, and instructed to report any balance or hearing problems. In particular, patients receiving gentamicin should be asked regularly about:

- gait ataxia and imbalance

- oscillopsia (the subjective sensation of bouncing vision) or blurred vision during head movement
- hearing loss, or tinnitus.

Contrary to popular belief, spontaneous vertigo is not a feature of vestibular toxicity.

For prolonged therapy, bedside vestibular function testing should be performed at least 2 times a week; formal vestibular function testing and high-frequency audiometric testing should be considered, if available.

If vestibular or auditory toxicity is noted, stop gentamicin and seek expert advice.

Empirical therapy

The gentamicin dosage for empirical therapy for non-critically ill patients is given in Tables A1.1 and A1.2 for adults and Table A1.6 for neonates and children. Doses in critically ill patients (requiring ICU admission) differ. See Tables A1.4 and A1.5.

The dosage depends on the patient's renal clearance, and the volume of distribution of gentamicin, which is related to lean (or ideal) body weight. Doses are therefore based on weight (mg/kg) and adjusted for the patient's renal function.

Use actual body weight to calculate the dose except if the patient is obese (body mass index [BMI] 30 kg/m^2 or more). For obese patients calculate the adjusted body weight (see Box A1.2) to calculate the dose. For obese patients with a BMI of 35 kg/m^2 or more, seek expert advice.

Dosing in empirical therapy should not continue beyond 48 hours (ie a maximum of three empirical doses at 0, 24 and 48 hours); given the 'post-antibiotic effect' of aminoglycosides, **this effectively provides 72 hours of therapy**. For patients with renal impairment (CrCl less than 40 mL/min), a single dose of aminoglycoside, with no subsequent doses, can be life-saving and is generally safe.

Gentamicin dosing in non-critically ill adults

Empirical gentamicin dosage in non-critically ill adults (renal function known) (Table A1.1)

Creatinine clearance (CrCl) [NB1]	Dose [NB2], [NB3]	Maximum dose	Dosing frequency	Maximum number of empirical doses [NB4]
more than 60 mL/min	4 to 5 mg/kg	560 mg	24-hourly	3 doses (at 0, 24 and 48 hours)
40 to 60 mL/min	4 to 5 mg/kg	480 mg	36-hourly	2 doses (at 0 and 36 hours)
less than 40 mL/min	4 mg/kg	400 mg	single dose, then seek expert advice for subsequent dosing or selection of alternative drug	

NB1: Use the Cockcroft-Gault formula or online calculator to estimate CrCl. If serum creatinine is less than 60 micromol/L, use a value of 60 micromol/L in the Cockcroft-Gault formula or online calculator. eGFR should not be used to calculate gentamicin doses.

NB2: Use actual body weight except if the patient is obese (body mass index [BMI] 30 kg/m^2 or more), use adjusted body weight (see Box A1.2) to calculate the dose. For obese patients with a BMI of 35 kg/m^2 or more, seek expert advice.

NB3: Round dose to the nearest multiple of 40 mg.

NB4: These dose regimens all effectively provide 72 hours of therapy.

Empirical gentamicin dosage in non-critically ill adults (renal function is not known) (Table A1.2)

Age	Initial dose	Maximum dose
12 – 29 years	5 mg/kg	560 mg
30 – 50 years	5 mg/kg	480 mg
> 50 years	4 mg/kg	400 mg

Adjusted body weight

To calculate the adjusted body weight in obese patients use the formula below, or an online calculator eg www.mdcalc.com/ideal-body-weight-

adjusted-body-weight

Adjusted body weight formula (Box A1.2)

adjusted body weight = IBW + 0.4 × (actual body weight – IBW)

To estimate IBW for adults, see Table A.3 below. A child's ideal body weight can be estimated using the corresponding weight for the height percentile on the growth chart (eg <www.cdc.gov/growthcharts>) or, if the child's height cannot be determined, the average weight-for-age (50th centile) on the growth chart [NB1]

IBW = ideal body weight

NB1: Alternative methods of estimating ideal body weight are described by Phillips S, Edlbeck A, Kirby M, Goday P. Ideal body weight in children. Nutr Clin Pract 2007;22(2):240-5. <www.ncbi.nlm.nih.gov/pubmed/17374798>

Ideal body weight (Table A1.3)

Height		Ideal body weight (kg) [NB1]	
cm	inches	women	men
155	61	48	53
160	63	53	57
165	65	57	62
170	67	62	66
175	69	66	71
180	71	71	75
185	73	75	80
190	75	80	84
195	77	84	89
200	79	89	93
205	81	93	98
210	83	98	102
215	85	102	107
220	87	107	111

NB1: Ideal weight for men = 50 kg + 0.9 kg per cm over 152 cm (2.3 kg per inch over 5 feet)

Ideal weight for women = 45.5 kg + 0.9 kg per cm over 152 cm (2.3 kg per inch over 5 feet)

Critically ill adults with severe sepsis

A higher initial gentamicin dose of 7 mg/kg daily may be appropriate for some critically ill patients with severe sepsis or septic shock (usually those requiring intensive care support), due to an increased volume of drug distribution and enhanced renal drug clearance. Higher doses also ensure that pathogens with a relatively high minimum inhibitory concentration (MIC) to gentamicin (eg *Pseudomonas aeruginosa*) are adequately treated.

In patients with known or likely pre-existing renal impairment (such as patients with older age > 50 years), a lower gentamicin dose should be used (eg CrCl 40 to 60 mL/min: 4-5 mg/kg; CrCl less than 40 mL/min: 4 mg/kg). However, prompt antibiotic initiation in critically ill patients confers a significant survival benefit, so **do not** delay gentamicin administration to ascertain renal function.

Empirical gentamicin dosage in critically ill adults (renal function known) (Table A1.4)

Creatinine clearance (CrCl) [NB1]	Critically ill patients [NB4]	Maximum dose	Dosing frequency	Maximum number of empirical doses [NB4]
more than 60 mL/min	7 mg/kg	640 mg	24-hourly	3 doses (at 0, 24 and 48 hours)
40 to 60 mL/min	5 mg/kg	480 mg	36-hourly	2 doses (at 0 and 36 hours)
less than 40 mL/min	4 mg/kg	400 mg	single dose, then seek expert advice for subsequent dosing or selection of alternative drug	

NB1: Use the Cockcroft-Gault formula or online calculator to estimate CrCl. If serum creatinine is less than 60 micromol/L, use a value of 60 micromol/L in the Cockcroft-Gault formula or online calculator.. eGFR should not be used to calculate gentamicin doses.

NB2: Use actual body weight except if the patient is obese (body mass index [BMI] 30 kg/m^2 or more), use adjusted body weight (see Box A1.2) to calculate the dose. For obese patients with a BMI of 35 kg/m^2 or more, seek expert advice.

NB3: Round dose to the nearest multiple of 40 mg.

NB4: These dose regimens all effectively provide 72 hours of therapy.

Empirical gentamicin dosage in critically ill adults (renal function is not known) (Table A1.5)

Indication	Age	Initial dose^	Maximum dose
Severe sepsis	adult ≤ 50 years	7 mg/kg	640 mg
+/- shock (critically ill)	>50 years	5 mg/kg	480 mg

Gentamicin dosing in neonates and children

Empirical gentamicin dosage for the treatment of infection in neonates and children [NB1] [NB2] (Table A1.6)

Age	Dose [NB1] gentamicin	Dosing frequency	Maximum number of empirical doses [NB2]
neonates younger than 30 weeks postmenstrual age [NB3]	5 mg/kg	48-hourly	2 doses (at 0 and 48 hours)
neonates 30 to 34 weeks postmenstrual age [NB3]	5 mg/kg	36-hourly	2 doses (at 0 and 36 hours)
neonates 35 weeks postmenstrual age or older [NB3]	5 mg/kg	24-hourly	3 doses (at 0, 24 and 48 hours)

children 1 month to younger than 10 years	7.5 mg/kg up to 320 mg [NB7] [NB5]	24-hourly	3 doses (at 0, 24 and 48 hours)
children 10 years and older	6 mg/kg up to 560 mg children with septic shock or requiring intensive care support: 7 mg/kg [NB4]	24-hourly	3 doses (at 0, 24 and 48 hours)

NB1: Do not use the dosages in this table for children with cystic fibrosis or receiving chemotherapy, or for synergistic therapy for streptococcal or enterococcal endocarditis

NB2: For children with impaired kidney function (estimated glomerular filtration rate less than 50 mL/minute/1.73 m^2), give a single dose, then seek expert advice for subsequent dosing or selection of an alternative antibiotic. Use the modified Schwartz formula to estimate glomerular filtration rate in children older than 1 year.

NB3: Postmenstrual age is the time elapsed between the first day of the last menstrual period and birth (gestational age) plus the time elapsed after birth (postnatal age).

NB4: For obese children, use adjusted body weight (see Box A1.2) to calculate the dose

NB5: The dose cap does not apply to children with septic shock or requiring intensive care support.

Multiple-daily (synergistic) dosing

When given in combination with some cell-wall–active drugs (eg penicillins, glycopeptides), aminoglycosides provide useful synergistic killing of some difficult-to-treat pathogens (eg enterococci, viridans streptococci), provided the pathogen does not have high-level resistance to the aminoglycoside.

Most studies suggest that a detectable aminoglycoside plasma concentration throughout the dosing period is necessary for effective synergistic activity. Multiple-daily dosing (gentamicin 1 mg/kg 8-hourly or 12-hourly, depending on renal function) is generally required to achieve this, unless there is substantial renal impairment.

Seek specialist advice for the management of these patients.

Surgical prophylaxis

A single dose of aminoglycoside (usually gentamicin) is indicated for surgical prophylaxis in a limited number of procedures. Dosing is either 2 mg/kg or 5 mg/kg, depending on the procedure (see Table 3.3, page 52).

Monitoring aminoglycoside plasma concentrations

If gentamicin therapy is required beyond 48 hours, plasma concentration monitoring should be commenced where available. The aim of monitoring is to ensure adequacy of dosing and to reduce the risk of toxicity.

For once-daily or less frequent dosing of aminoglycosides, clinical efficacy is correlated with the area under the concentration–time curve (AUC). The appropriate target AUC depends on the minimum inhibitory concentration (MIC) of the pathogen, because the ratio of the AUC to MIC appears to best predict aminoglycoside efficacy.

Dose optimisation software provides the most sophisticated method for AUC monitoring because it accounts for significant individual variation in aminoglycoside pharmacokinetics. Where plasma concentration monitoring is available, seek expert advice or follow local protocols on when and how many levels should be taken in relation to dosing, the use of dose optimisation software or nomograms, and adjusting the dose based on levels.

> Where plasma concentration monitoring is available, seek expert advice for interpreting levels and dose adjustment.

Where available, measure plasma levels at least twice weekly if renal function is normal and stable. If renal function is changing rapidly or substantially (eg critically ill patients with severe sepsis, suspected acute kidney failure), monitoring should be more frequent (in some cases daily).

If renal function is deteriorating substantially, consider stopping gentamicin—seek expert advice.

Appendix 2: Principles of vancomycin use

For administration of vancomycin (including route and rate of administration), see appendix 6.

Introduction

The primary indication for vancomycin is treatment (and, in some situations, prophylaxis) of infection with methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-resistant coagulase-negative staphylococcal species (eg *Staphylococcus epidermidis*) or *Enterococcus faecium*. Vancomycin also has a role in the treatment and prophylaxis of Gram positive infection in patients hypersensitive to penicillins.

Where available, plasma concentration monitoring is recommended for all patients treated with vancomycin for longer than 48 hours, both to avoid underdosing and to minimise the risk of toxicity, especially in patients with renal impairment.

Adverse reactions include:

- Nephrotoxicity: usually reversible with cessation of therapy. Increased risk with prolonged therapy and when administered with other nephrotoxic agents (eg aminoglycosides, frusemide, contrast media).
- "Red man syndrome': infusion-related reaction, manifesting as flushing (usually involving the face and upper body) and sometimes pruritus, dyspnoea and hypotension. It is not an allergic reaction, and usually resolves with reduction in the infusion rate eg by half. Where required, antihistamines can be used as premedication.
- Thrombocytopaenia: may be profound; reversible with cessation of the drug.

To reduce the risk of infusion-related reactions such as 'red man' syndrome, vancomycin should be infused at a rate **not exceeding 10 mg/minute**. If 'red man' syndrome occurs, extend the infusion time.

Vancomycin dosing in adults

Loading dose

A loading dose of vancomycin may be considered for critically ill patients requiring ICU admission. The recommended loading dose is **25 to 30 mg/kg** (actual body weight). The loading dose should be omitted in patients with a creatinine clearance of < 20mL/min.

Maintenance dosing

An appropriate starting maintenance dose with normal renal function is 15 to 20 mg/kg (actual body weight). The subsequent dosing and frequency of administration depends on the patient's weight and renal function; in patients with a creatinine clearance (CrCl) more than 60 mL/min, 12-hourly dosing is recommended for all indications.

If a loading dose is given, the first maintenance dose should be given 12 hours after the loading dose if CrCl ≥ 60 mL/min or 24 hours after if CrCl < 60 mL/min.

Vancomycin maintenance dosages for adults (Table A2.1)

Creatinine clearance	Initial maintenance dose
> 60 mL/min	15 to 20 mg/kg (actual body weight) up to 2 g 12-hourly
20 - 60 mL/min	15 to 20 mg/kg (actual body weight) up to 2 g 24-hourly
< 20 mL/min and not treated with dialysis	15 to 20 mg/kg (actual body weight) up to 2 g. The initial dosing interval is 48-72 hourly, however, seek expert advice. Ideally ongoing dosing intervals should be based on plasma concentration (ie dose again when levels less than 15 or 20 mg/L).
Haemodialysis and peritoneal dialysis	Seek expert advice.

Monitoring

Where available, subsequent dosage is determined by the results of trough

(predose) plasma concentration monitoring. The recommended target trough concentration for intermittent vancomycin dosing is **15 to 20 mg/L**. When treating central nervous system infection, a trough concentration up to 25 mg/L may be used to improve penetration of vancomycin into the cerebrospinal fluid.

Where plasma monitoring is not available, the table above provides a general guide to the appropriate dose and dosing interval.

Renal function should be assessed at the start of vancomycin therapy, and regularly thereafter.

Vancomycin dosing in children

For the intermittent vancomycin starting dosage in neonates and children, see Table A2.2. Subsequent doses are determined by the results of trough (predose) plasma concentration monitoring. The role of vancomycin loading doses and continuous infusions in children is currently unclear—seek expert advice.

In children receiving a **6-hourly** vancomycin regimen, the suggested target trough concentration is **10 to 20 mg/L**. Use the higher end of the target range (15 to 20 mg/L) for severe or complicated infections.

In children receiving a **12-hourly** vancomycin regimen, the suggested target trough concentration is **7 to 10 mg/L**.

Vancomycin maintenance dosages for neonates and children (Table A2.2)

Age		Starting dose (use actual body weight) [NB1]	Dosing frequency [NB2]
neonates younger than 30 weeks postmenstrual age [NB3]	postnatal age 0 to 14 days	10 mg/kg bacteraemia 15 mg/kg meningitis, pneumonia	18-hourly
	postnatal age 15 days or older	10 mg/kg bacteraemia 15 mg/kg meningitis, pneumonia	12-hourly
neonates 30 to 36 weeks postmenstrual age [NB3]	postnatal age 0 to 14 days	10 mg/kg bacteraemia 15 mg/kg meningitis, pneumonia	12-hourly
	postnatal age 15 days or older	10 mg/kg bacteraemia 15 mg/kg meningitis, pneumonia	8-hourly
neonates 37 to 44 weeks postmenstrual age [NB3]	postnatal age 0 to 7 days	10 mg/kg bacteraemia 15 mg/kg meningitis, pneumonia	12-hourly
	postnatal age 8 days or older	10 mg/kg bacteraemia 15 mg/kg meningitis, pneumonia	8-hourly
neonates 45 weeks postmenstrual age or older [NB3]		10 mg/kg bacteraemia 15 mg/kg meningitis, pneumonia	6-hourly
children [NB4]		15 mg/kg up to 750 mg	6-hourly
		OR	
		30 mg/kg up to 1.5 g	12-hourly

NB1: Use actual body weight to calculate the initial vancomycin dose, even in obese children (children with a body mass index above the 95th percentile but below the 99th percentile for their age and sex), because volume of distribution and clearance of vancomycin correlate with actual body weight. For morbidly obese children (children with a body mass index above the 99th percentile for their age and sex), seek expert advice.

NB2: For neonates with impaired kidney function unrelated to age, and for children with an estimated glomerular filtration rate less than 50 mL/minute/1.73 m^2, give a single 15 mg/kg dose and seek expert advice for subsequent dosing.

NB3: Postmenstrual age is the time between the first day of the last menstrual period and birth (gestational age) plus the time since birth (postnatal age).

NB4: Giving the total daily dose in four 6-hourly doses or two 12-hourly doses is therapeutically equivalent. Similarly, the total daily dose can be administered in three 8-hourly doses.

Appendix 3: Pneumonia severity scoring tools for community-acquired pneumonia in adults

Introduction

Tools for scoring pneumonia severity should not be used in isolation to decide management; but they are useful as an aid to clinical judgement.

SMART-COP and CORB are tools that are used to help determine the severity of community-acquired pneumonia (CAP) in adults. These tools assess the likelihood that a patient with CAP will require intensive respiratory or vasopressor support (IRVS), usually in an intensive care unit, and provide information about the patient's risk of mortality.

SMART-COP

To calculate a SMART-COP score [Note], use findings from the initial clinical assessment.

SMART-COP tool for assessing severity of community-acquired pneumonia (CAP) in adults (Figure A3.1)

CAP confirmed on chest X-ray

50 years old or less			more than 50 years old		
S	systolic BP less than 90 mm Hg	2 points	**S**	systolic BP less than 90 mm Hg	2 points
M	multilobar CXR involvement	1 point	**M**	multilobar CXR involvement	1 point
A	albumin less than 35 g/L	1 point	**A**	albumin less than 35 g/L	1 point
R	respiratory rate 25 br/min or more	1 point	**R**	respiratory rate 30 br/min or more	1 point
T	tachycardia 125 bpm or more	1 point	**T**	tachycardia 125 bpm or more	1 point
C	confusion (acute)	1 point	**C**	confusion (acute)	1 point
O	oxygen low PaO_2 less than 70 mm Hg, or O_2 saturation 93% or less, or PaO_2/FiO_2 less than 333	2 points	**O**	oxygen low PaO_2 less than 60 mm Hg, or O_2 saturation 90% or less, or PaO_2/FiO_2 less than 250	2 points
P	pH less than 7.35	2 points	**P**	pH less than 7.35	2 points

Total points score (maximum 11)

BP = blood pressure; bpm = beats per minute; br = breaths; CXR = chest X-ray; FiO_2 = fraction of oxygen in inspired air; PaO_2 = partial pressure of oxygen

Adapted from Charles PG, Wolfe R, Whitby M, Fine MJ, Fuller AJ, Stirling R, et al. SMART-COP: a tool for predicting the need for intensive respiratory or vasopressor support in community-acquired pneumonia. Clin Infect Dis 2008;47(3):375-84, by permission of Oxford University Press.

Interpretation of SMART-COP score

0 to 2 points	low risk of needing IRVS
3 to 4 points	moderate risk (1 in 8) of needing IRVS
5 to 6 points	high risk (1 in 3) of needing IRVS
7 or more points	very high risk (2 in 3) of needing IRVS

Severe CAP = a SMART-COP score of 5 or more points

In the Australian Community-Acquired Pneumonia Study (ACAPS) cohort, the accuracy for predicting patients who required IRVS (a SMART-COP score of 3 or more points) was:

- sensitivity = 92%
- specificity = 62%
- positive predictive value (PPV) = 22%
- negative predictive value (NPV) = 99%
- area under the receiver operating characteristic (ROC) curve = 0.87.

CORB

CORB tool for assessing severity of community-acquired pneumonia in adults (Figure A3.2)[85]

	Risk factor
C	acute onset confusion
O	oxygen saturation 90% or lower
R	respiratory rate 30 breaths/minute or more
B	systolic blood pressure lower than 90 mmHg, or diastolic blood pressure 60 mmHg or lower

↓

Severe CAP = the presence of at least two of these features

Use the most abnormal results within the first 24 hours of the patient's hospital stay.

In the ACAPS cohort, the accuracy of CORB for predicting the need for IRVS (two features of CORB present) was:

- sensitivity = 81%
- specificity = 68%
- PPV = 18%
- NPV = 98%
- area under the ROC curve = 0.74.

[85] Buising KL, Thursky KA, Black JF, MacGregor L, Street AC, Kennedy MP, et al. Identifying severe community-acquired pneumonia in the emergency department: a simple clinical prediction tool. Emerg Med Australas 2007;19(5):418-26. <www.ncbi.nlm.nih.gov/pubmed/17919214>

Appendix 4: Antimicrobials in pregnancy and breastfeeding

Drug use in pregnancy

A drug can have more than one harmful effect on the foetus. Individual effects depend on the time of foetal exposure to the drug.

The critical period for teratogenic effects is during organogenesis. This starts at about 17 days after conception and is complete by 60 to 70 days. Exposure to certain drugs during this period can cause major birth defects.

Some drugs can interfere with functional development of organ systems (eg central nervous system, integumentary system and cardiovascular system) in the second and third trimesters and produce serious consequences.

A woman may not be aware of her pregnancy until after the early stages of organogenesis. For this reason, drugs in the most severe category of risk (Category X) should not be prescribed to a woman of childbearing potential, unless a pregnancy test is negative and she is using an effective method of contraception.

However, there are several conditions in which long-term medication will be necessary in a woman of childbearing potential despite known harms of the drugs. At the time of initial prescribing in any such situation, the prescriber should discuss the desirability of reviewing medication requirements well before conception. For some disorders, it may be possible to change to a different category of drug. If a patient conceives while on medication and there has been no opportunity for earlier discussion with the prescriber, her medication should be reviewed as soon as possible.

The following check list may assist in deciding whether to prescribe a particular drug during pregnancy:

- Nonpharmacological treatment: Is such a treatment available and likely to be successful? Would such treatment be reasonable at least until the first trimester is complete? Most pregnant women strongly favour this type of treatment and concordance is likely to be high.

- **Harm–benefit analysis:** For the particular drug under consideration, what are the potential harms and benefits to the mother and harms to the foetus of prescribing? What are the harms and benefits (for each) of **not** prescribing?
- **Incidence of spontaneous congenital abnormality:** When drugs cannot be avoided, it may be appropriate to discuss the incidence of non–drug-related spontaneous abnormalities. This is often underestimated.
- **Education, documentation and communication:** Has the education of the woman and her partner regarding harms and benefits been properly documented in the patient's notes? Have those health professionals involved in obstetric management been informed? It may be appropriate to discuss the use of, and limitations of, available antenatal screening to detect abnormalities in the foetus. Couples will need to give some consideration to the consequences of an abnormal result.

Routine review later in the pregnancy includes consideration of whether dose alteration is indicated during delivery to avoid neonatal problems such as respiratory depression.

Australian categorisation of drugs in pregnancy

Table A4.1 lists the pregnancy category assigned by the Australian Therapeutic Goods Administration (TGA) for individual antimicrobial drugs. The TGA pregnancy categorisation is from the prescribing medicines in pregnancy database at the TGA website <www.tga.gov.au/hp/medicines-pregnancy.htm>.

The pregnancy categorisation system only applies to recommended therapeutic doses. It cannot be assumed that the classifications assigned to individual medicines are valid in situations such as:

- overdose
- occupational exposure
- other situations in which the recommended therapeutic dose has been exceeded.

> The Australian categorisation system is not hierarchical.

The Australian categorisation system differs from the US Food and Drug

Administration categorisation. The categorisation of medicines for use in pregnancy does not follow a hierarchical structure.

- Human data are lacking or inadequate for drugs in the B1, B2 and B3 categories.
- Subcategorisation of the B category is based on animal data.
- The allocation of a B category does not imply greater safety than a C category.
- Medicines in category D are not absolutely contraindicated during pregnancy.

For pharmaceutical products containing two or more active ingredients, the categorisation of the combination is based on the active ingredient with the most restrictive pregnancy categorisation.

Category A

Drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed.

Category B1

Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus having been observed.

Studies in animals have not shown evidence of an increased occurrence of foetal damage.

Category B2

Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus having been observed.

Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of foetal damage.

Category B3

Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus having been observed.

Studies in animals have shown evidence of an increased occurrence of foetal damage, the significance of which is considered uncertain in humans.

Category C

[Note [86]]

Drugs which, owing to their pharmacological effects, have caused or may be suspected of causing harmful effects on the human foetus or neonate without causing malformations. These effects may be reversible. Specialised texts should be consulted for further details.

Category D

Drugs which have caused, are suspected to have caused or may be expected to cause an increased incidence of human foetal malformations or irreversible damage. These drugs may also have adverse pharmacological effects. Specialised texts should be consulted for further details.

Category X

Drugs which have such a high risk of causing permanent damage to the foetus that they should not be used in pregnancy or when there is a possibility of pregnancy.

Drug use in breastfeeding

Table A4.1 provides advice on the safety of individual antimicrobial drugs in breastfeeding women.

[86] Category C in the Australian and Swedish categorisations of risk is a pharmacological effect category and differs from the US Food and Drug Administration (FDA) categorisation (where category C indicates greater likelihood of risk than B on the basis of adverse effects of any type in animal studies).

The benefits of breastfeeding are sufficiently important to recommend that it should not be discontinued or discouraged unless there is substantial evidence that the drug taken by the mother will be harmful to the infant, and no alternative treatment can be found.

> Unless there is significant risk to the infant from necessary maternal medication, breastfeeding should be continued.

Most drugs are excreted only to a minimal extent in breast milk, and in most cases the dosage to which the infant is ultimately exposed is very low and well below the therapeutic dose concentration for infants. For this reason, few drugs are totally contraindicated while breastfeeding.

When considering prescribing drugs (particularly longer-term) during breastfeeding, the following checklist may assist in guiding the decision:

- Woman's preference for breastfeeding: Most women have a strong preference for breastfeeding.
- Nonpharmacological treatment: If such a treatment is available and likely to be successful, it may allow the woman to breastfeed, at least until the period of maximum benefit to the infant has passed.
- Harm–benefit analysis: For the infant, there are demonstrable increases in immunocompetence (eg decreased rates of otitis media), and neurodevelopmental advantage (eg possible increased IQ in the older child). For the woman, physiological benefits of breastfeeding include better uterine involution, more delayed ovulation and decreased risk of breast cancer.
- Education, documentation and communication: The discussion regarding harm/benefit with the mother and her partner should be properly documented in the patient's notes. Other health professionals involved in postnatal management should be informed of medication changes.

The main consideration overall is that unless there is significant risk to the infant from necessary maternal medication, breastfeeding should be continued.

Antimicrobial drugs in pregnancy and breastfeeding (Table A4.1)

Antimicrobial	TGA pregnancy category [NB1]	Compatibility with breastfeeding [NB2]
aciclovir	B3	compatible
albendazole	D	compatible
amoxicillin	A	compatible; may cause diarrhoea in infant
amoxicillin+clavulanate	B1	compatible; may cause diarrhoea in infant
amphotericin (IV)	B3	compatible; absorption by infant unlikely
ampicillin	A	compatible; may cause diarrhoea in infant
artemether+lumefantrine	D (contraindicated in first trimester)	use with caution
artesunate	unlisted (do not withhold in severe malaria)	use with caution
atovaquone+proguanil	B2	use with caution
azithromycin	B1	compatible; may cause diarrhoea in infant
benzathine penicillin	A	compatible; may cause diarrhoea in infant
benzyl benzoate	B2	caution, insufficient data; prefer permethrin
benzylpenicillin	A	compatible; may cause diarrhoea in infant
cefalexin	A	compatible; may cause diarrhoea in infant
cefalotin	A	compatible; may cause diarrhoea in infant

cefotaxime	B1	compatible; may cause diarrhoea in infant
ceftazidime	B1	compatible; may cause diarrhoea in infant
ceftriaxone	B1	compatible; may cause diarrhoea in infant
cefuroxime	B1	compatible; may cause diarrhoea in infant
cefazolin	B1	compatible; may cause diarrhoea in infant
chloramphenicol	IV or oral (n/a) Not associated with an increased risk of birth defects. However, in the last trimester increases the theoretical risk of 'Grey baby syndrome.' A (topical)	oral or IV use: avoid topical use: compatible
ciprofloxacin	B3	compatible; may cause diarrhoea in infant
clarithromycin	B3	compatible; may cause diarrhoea in infant
clindamycin	A	compatible; may cause diarrhoea in infant
cloxacillin	see flucloxacillin	
colistimethate sodium (colistin)	B2	caution, insufficient data; may cause diarrhoea in infant
cotrimoxazole	see trimethoprim+sulfamethoxazole	

dapsone	B2	use with caution; monitor infant for haemolysis if preterm or younger than 1 month. Avoid if infant has glucose-6-phosphate dehydrogenase (G6PD) deficiency or hyperbilirubinaemia
dicloxacillin	B2	compatible; may cause diarrhoea in infant
doxycycline	D [NB4]	compatible for short courses (eg 10 days) if alternative drug not appropriate; may cause diarrhoea in infant
erythromycin (systemic)	A [NB5]	compatible; may cause diarrhoea in infant
ethambutol	A	compatible
flucloxacillin	B1	compatible; may cause diarrhoea in infant
fluconazole	D	compatible
gentamicin	D (but used for serious infections in pregnancy)	compatible; may cause diarrhoea in infant
imiquimod	B1	compatible
immunoglobulin, normal	unlisted	caution; insufficient data
isoniazid	A	compatible
ivermectin	B3	compatible
lamivudine	B3	use with caution [NB3]
maldison	B2	caution, insufficient data
mebendazole	B3	compatible
mefloquine	B3	compatible

meropenem	B2	compatible; may cause diarrhoea in infant
metronidazole	B2	systemic use: compatible; may cause some bitterness in breast milk and may cause diarrhoea in infant. Consider withholding breastfeeding for 12 to 24 hours after high single-dose (2 g) treatment
miconazole	A	compatible
mupirocin	B1	compatible
neomycin	D	compatible
nitrofurantoin	A (short-term therapy) Increased risk of neonatal jaundice and haemolytic anaemia during the last 4 weeks of pregnancy.	compatible if infant is healthy and older than 1 month; avoid if infant has glucose-6-phosphate dehydrogenase (G6PD) deficiency or is younger than 1 month
norfloxacin	B3	compatible; may cause diarrhoea in infant
nystatin	A	compatible
oseltamivir	B1	compatible
paromomycin	unlisted (see product information)	avoid, insufficient data
permethrin	B2	compatible
phenoxymethylpenicillin	A	compatible; may cause diarrhoea in infant
piperacillin+tazobactam	B1	compatible; may cause diarrhoea in infant

podophyllotoxin	D	avoid
primaquine	D	compatible if infant is healthy and older than 1 month; avoid if infant has glucose-6-phosphate dehydrogenase (G6PD) deficiency, is younger than 1 month or has hyperbilirubinaemia
procaine penicillin	A	compatible; may cause diarrhoea in infant
proguanil	B2	compatible
pyrantel	B2	compatible
pyrazinamide	B2	caution, insufficient data
pyrethrins	B2	compatible
pyrimethamine	B3	compatible
quinine	D (but has been routinely used in the treatment of malaria)	compatible; avoid if infant has glucose-6-phosphate dehydrogenase (G6PD) deficiency
rifampicin	C	compatible; may cause diarrhoea in infant. Monitor infant for jaundice
roxithromycin	B1	compatible; may cause diarrhoea in infant
sulfadiazine	C	use with caution; avoid if infant has glucose-6-phosphate dehydrogenase (G6PD) deficiency, is younger than 1 month or has hyperbilirubinaemia
tinidazole	B3	caution, insufficient data; may cause diarrhoea in infant

trimethoprim	B3	compatible
trimethoprim+ sulfamethoxazole	C	compatible in infants 1 month or older; may cause diarrhoea in infant. Other antibiotics preferred in younger or preterm neonates
vancomycin	B2	compatible; may cause diarrhoea in infant
voriconazole	B3	avoid, insufficient data

NB1: **Therapeutic Goods Administration (TGA) pregnancy categorisation** is from the Prescribing medicines in pregnancy database at the TGA website <www.tga.gov.au/hp/medicines-pregnancy.htm>.

NB2: **Definitions for compatibility with breastfeeding:**

- compatible—there are sufficient data available to demonstrate an acceptably low relative infant dose and/or no significant plasma concentrations and/or no adverse effects in breastfed infants
- use with caution—minor adverse effects in the breastfed infant have been reported, or there are insufficient data showing low relative infant dose and/or no significant plasma concentrations and/or no adverse effects in breastfed infants
- avoid, insufficient data—there are no data on transfer into milk, or on plasma concentrations or adverse effects in the breastfed infant
- avoid—significant plasma concentrations in exposed infants, or adverse effects in breastfed infants reported or predictable from the properties of the molecule.

NB4: Tetracyclines are safe for use during the first 18 weeks of pregnancy (16 weeks postconception) after which they may affect the formation of the baby's teeth and cause discolouration.

NB5: Observational studies in humans have reported cardiovascular malformations after exposure to medicinal products containing erythromycin in early pregnancy.

Appendix 5: Renal impairment and antimicrobial dosing

Introduction

In people with renal impairment, antimicrobials or their metabolites that are excreted entirely, or in part, by the kidneys can accumulate, and dosage adjustment may be required. For example, aminoglycosides and glycopeptides are excreted almost entirely by the kidneys, and rapidly reach toxic concentrations in patients with impaired renal function if standard dosing schedules are used. For many commonly used beta-lactam antibiotics, a significant proportion of the dose is excreted by the kidneys; dosage adjustment may be needed in patients with impaired renal function to avoid supratherapeutic concentrations.

It is crucial that dosage adjustments are informed by the patient's clinical status and comorbidities, the potential toxic effects of the relevant drug, and the likely consequences of underdosing. Furthermore, patients with renal impairment can be more susceptible to drug adverse effects; specific monitoring may be required. Appropriate drug information texts should be consulted.

Estimating glomerular filtration rate (GFR)

Dosage adjustment in patients with renal impairment is guided by an assessment of glomerular filtration rate (GFR), which is usually proportional to renal drug clearance; estimates of GFR are often used eg estimated creatinine clearance (CrCl) using the Cockcroft-Gault formula (see Box A5.1).

When used, estimated GFR (eGFR) should be adjusted for patients at extremes of weight because eGFR values are normalised to a body surface area of 1.73 m^2. This is achieved by multiplying the eGFR by the patient's body surface area (in m^2) and dividing by 1.73 m^2.

Due to the inherent limitations of GFR estimates as a basis for dosage adjustment, it is crucial that any dose adjustment is considered in the context of the patient's clinical status and comorbidities, the potential

toxic effects of the drug, and the likely consequences of underdosing. This is particularly pertinent for drugs with a narrow therapeutic index (eg aminoglycosides); for these drugs, therapeutic drug monitoring should be used to individualise dosing.

> It is crucial that dosage adjustments are informed by the patient's clinical status and comorbidities, the potential toxic effects of the relevant drug, and the likely consequences of underdosing.

Neither estimated CrCl (using the Cockcroft-Gault formula) nor eGFR (using the MDRD or CKD-EPI formula) accurately predict clearance in patients who have unstable renal function (eg patients in intensive care, patients with acute renal impairment, patients with febrile neutropenia); a measured (urinary) creatinine clearance is most accurate in this situation. Similarly, these formulas should not be used to estimate clearance in patients who have low muscle mass (eg cachectic patients).

> Neither estimated CrCl nor eGFR accurately predict clearance in patients who have unstable renal function or low muscle mass.

Cockcroft-Gault formula (Box A5.1)

The Cockcroft-Gault formula (below or with an online calculator) can be used to estimate creatinine clearance.

$$\text{Adult males: CrCl (mL/min)} = \frac{(140 - \text{age}) \times \text{weight (kg)}}{0.814 \times \text{serum creatinine (micromol/L)}}$$

Adult females: Multiply the above formula by 0.85

Lean body weight is the preferred weight descriptor for use in the Cockcroft-Gault formula, because creatinine is a muscle breakdown product; however, the calculation of lean body weight is relatively complicated. For patients who are overweight, for practicality, ideal body weight (see Table A5.1) can be used. For patients who are not overweight, actual body weight can be used.

Ideal body weight (Table A5.1)

Height		Ideal body weight (kg) [NB1]	
cm	inches	women	men
155	61	48	53
160	63	53	57
165	65	57	62
170	67	62	66
175	69	66	71
180	71	71	75
185	73	75	80
190	75	80	84
195	77	84	89
200	79	89	93
205	81	93	98
210	83	98	102
215	85	102	107
220	87	107	111

NB1: Ideal weight for men = 50 kg + 0.9 kg per cm over 152 cm (2.3 kg per inch over 5 feet)

Ideal weight for women = 45.5 kg + 0.9 kg per cm over 152 cm (2.3 kg per inch over 5 feet)

Dose modification in renal impairment

General considerations

In patients with impaired renal function, dosages can be altered by reducing the dose or by extending the interval between doses. For some antimicrobials, therapeutic drug monitoring is needed to minimise toxicity. Monitoring can also be used to ensure therapeutic concentrations are achieved (see appendix 2: principles of gentamicin use and appendix 3: principles of vancomycin use).

Read the following in conjunction with Table A5.2:

- The recommendations apply to adults. For antimicrobial dosing in children with renal impairment, seek expert advice.

Dialysis and continuous renal replacement therapy

Dosage guidelines are provided for adult patients undergoing intermittent haemodialysis and continuous ambulatory peritoneal dialysis (CAPD).

As a general rule, for drugs that are readily removed by intermittent haemodialysis, the dose should be withheld until after the dialysis session. To reduce the risk of missed doses, some renal units prefer to maintain the normal dosing schedule (ie dose at the same time as on nondialysis days) for drugs that are administered more than once daily.

Antimicrobial dosages for adults with impaired renal function

Use calculated creatinine clearance or eGFR normalised by patient body surface area (as described above) as an estimate of GFR when using this table.

Antimicrobial doses for adults with impaired renal function (Table A5.2)

aciclovir intravenous	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
10 to 50 mL/min	**25 to 50 mL/min:** 100% 12-hourly **10 to 25 mL/min:** 100% 24-hourly
less than 10 mL/min	50% 24-hourly
intermittent haemodialysis	as for GFR less than 10 mL/min; dose after dialysis
peritoneal dialysis	as for GFR less than 10 mL/min
aciclovir oral	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal

10 to 50 mL/min	dosage depends on the indication and patient's immune status; see product information
less than 10 mL/min	
intermittent haemodialysis	dosage depends on the indication and patient's immune status; see product information
peritoneal dialysis	
albendazole	
No dosage adjustment required	
amoxicillin	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
10 to 50 mL/min	**31 to 50 mL/min:** 100% 6-hourly **10 to 30 mL/min:** 100% 8-hourly
less than 10 mL/min	100% 12-hourly
intermittent haemodialysis	as for GFR less than 10 mL/min
peritoneal dialysis	as for GFR less than 10 mL/min
amoxicillin+clavulanate oral	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
10 to 50 mL/min	**30 to 50 mL/min:** normal
less than 10 mL/min	**less than 30 mL/min:** 500+125 mg 12-hourly
intermittent haemodialysis	as for GFR less than 30 mL/min
peritoneal dialysis	as for GFR less than 30 mL/min
amphotericin B desoxycholate	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
less than 50 mL/min	avoid; consider using a lipid formulation. If essential, normal
intermittent haemodialysis	if essential, normal (avoid during acute kidney injury)

peritoneal dialysis	if essential, normal (avoid during acute kidney injury)
ampicillin	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
10 to 50 mL/min	**31 to 50 mL/min:** 100% 6-hourly **10 to 30 mL/min:** 100% 8-hourly
less than 10 mL/min	100% 12-hourly
intermittent haemodialysis	as for GFR less than 10 mL/min
peritoneal dialysis	as for GFR less than 10 mL/min
artemether+lumefantrine	
no dose adjustment required, (monitor ECG and blood potassium concentration for GFR less than 10 mL, intermittent haemodialysis or peritoneal dialysis)	
artesunate	
no dose adjustment required	
atovaquone	
no dose adjustment required	
atovaquone+proguanil	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
10 to 50 mL/min	**30 to 50 mL/min:** normal
less than 10 mL/min	**less than 30 mL/min:** avoid fixed-dose combination; see individual drugs
intermittent haemodialysis	avoid fixed-dose combination; see individual drugs
peritoneal dialysis	avoid fixed-dose combination; see individual drugs
azithromycin	
No dosage adjustment required	
benzathine benzylpenicillin	

No dosage adjustment required	
benzylpenicillin	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
10 to 50 mL/min	75% at normal dosing interval
less than 10 mL/min	25 to 50% at normal dosing interval (maximum of 6 g per day)
intermittent haemodialysis	as for GFR less than 10 mL/min
peritoneal dialysis	as for GFR less than 10 mL/min
cefalexin	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
10 to 50 mL/min	normal
less than 10 mL/min	50 to 100% 8- to 12-hourly
intermittent haemodialysis	as for GFR less than 10 mL/min
peritoneal dialysis	as for GFR less than 10 mL/min
cefalotin (1 to 2 g loading dose may be required)	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
10 to 50 mL/min	**25 to 50 mL/min:** 1 to 1.5 g 6- to 8-hourly **10 to 25 mL/min:** 0.5 to 1 g 6- to 8-hourly
less than 10 mL/min	0.5 to 1 g 8- to 12-hourly
intermittent haemodialysis	as for GFR less than 10 mL/min
peritoneal dialysis	as for GFR less than 10 mL/min
cefazolin (2 g loading dose may be required)	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	**40 mL/min or more:** normal

10 to 50 mL/min	**20 to 40 mL/min:** 50% 8-hourly or 100% 12-hourly
less than 10 mL/min	**less than 20 mL/min:** 25% 12-hourly or 50% 24-hourly
intermittent haemodialysis	as for GFR less than 20 mL/min; dose after dialysis, or 100% on dialysis days only; dose after dialysis
peritoneal dialysis	as for GFR less than 20 mL/min
cefotaxime (2 g loading dose may be required)	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
10 to 50 mL/min	**20 to 50 mL/min:** 100% 8- to 12-hourly
less than 10 mL/min	**less than 20 mL/min:** 50% 8- to 12-hourly
intermittent haemodialysis	as for GFR less than 20 mL/min; dose after dialysis
peritoneal dialysis	as for GFR less than 20 mL/min
ceftazidime (1 to 2 g loading dose may be required)	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
10 to 50 mL/min	**31 to 50 mL/min:** 50% 8-hourly **16 to 30 mL/min:** 50% 12-hourly
less than 10 mL/min	**less than 16 mL/min:** 25 to 50% 24-hourly
intermittent haemodialysis	25 to 50% 24-hourly, or 50% 48-hourly; dose after dialysis
peritoneal dialysis	as for GFR less than 16 mL/min
ceftriaxone	
No dosage adjustment required	
cefuroxime	

Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
10 to 50 mL/min	normal
less than 10 mL/min	100% 24-hourly
intermittent haemodialysis	as for GFR less than 10 mL/min; dose after dialysis
peritoneal dialysis	as for GFR less than 10 mL/min
chloramphenicol	
No dosage adjustment required	
ciprofloxacin intravenous (for dosage adjustment in patients with infections caused by *Pseudomonas aeruginosa*, seek expert advice)	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
10 to 50 mL/min	**31 to 50 mL/min:** 100% 12-hourly **10 to 30 mL/min:** 50% 12-hourly or 100% 24-hourly
less than 10 mL/min	100% 24-hourly
intermittent haemodialysis	as for GFR less than 10 mL/min; dose after dialysis
peritoneal dialysis	as for GFR less than 10 mL/min
ciprofloxacin oral (for dosage adjustment in patients with infections caused by *Pseudomonas aeruginosa*, seek expert advice)	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
10 to 50 mL/min	**31 to 50 mL/min:** 500 mg 12-hourly **10 to 30 mL/min:** 250 mg 12-hourly or 500 mg 24-hourly
less than 10 mL/min	500 mg 24-hourly
intermittent haemodialysis	as for GFR less than 10 mL/min; dose after dialysis

peritoneal dialysis	as for GFR less than 10 mL/min
clarithromycin	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
10 to 50 mL/min	**30 to 50 mL/min:** normal
less than 10 mL/min	**less than 30 mL/min:** 50% 12-hourly
intermittent haemodialysis	as for GFR less than 30 mL/min
peritoneal dialysis	as for GFR less than 30 mL/min
clindamycin	
No dosage adjustment required	
cloxacillin	
No dosage adjustment required	
cotrimoxazole—see trimethoprim+sulfamethoxazole	
dapsone	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
10 to 50 mL/min	normal
less than 10 mL/min	50 to 100% 24-hourly
intermittent haemodialysis	as for GFR less than 10 mL/min; dose after dialysis
peritoneal dialysis	as for GFR less than 10 mL/min
doxycycline	
No dosage adjustment required	
erythromycin	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
10 to 50 mL/min	normal
less than 10 mL/min	50 to 75% at normal dosing interval
intermittent haemodialysis	as for GFR less than 10 mL/min
peritoneal dialysis	as for GFR less than 10 mL/min

ethambutol **(daily regimen)**	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	**30 to 60 mL/min:** 15 mg/kg 24-hourly
10 to 50 mL/min	**10 to 30 mL/min:** avoid; if essential, 7.5 to 10 mg/kg 24-hourly
less than 10 mL/min	avoid; if essential, 15 mg/kg 48-hourly
intermittent haemodialysis	avoid; if essential, 15 mg/kg on dialysis days only (after dialysis)
peritoneal dialysis	avoid; if essential, as for GFR less than 10 mL/min
flucloxacillin intravenous	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
10 to 50 mL/min	normal
less than 10 mL/min	50% 6- to 8-hourly
intermittent haemodialysis	as for GFR less than 10 mL/min
peritoneal dialysis	as for GFR less than 10 mL/min
flucloxacillin oral	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
10 to 50 mL/min	normal
less than 10 mL/min	100% 8-hourly
intermittent haemodialysis	as for GFR less than 10 mL/min
peritoneal dialysis	as for GFR less than 10 mL/min
fluconazole (give normal dosage for the first 48 hours as a loading dose)	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal

10 to 50 mL/min	**30 to 50 mL/min:** 50 to 100% 24-hourly **10 to 30 mL/min:** 25 to 50% 24-hourly
less than 10 mL/min	25 to 50% 24-hourly
intermittent haemodialysis	as for GFR less than 10 mL/min; dose after dialysis
peritoneal dialysis	as for GFR less than 10 mL/min
fusidic acid (fusidate sodium)	
No dosage adjustment required	
gentamicin	
See appendix 1	
griseofulvin	
No dosage adjustment required	
isoniazid	
No dosage adjustment required. In intermittent haemodialysis dose after dialysis	
ivermectin	
No dosage adjustment required	
lamivudine	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	**50 mL/min or more:** normal
10 to 50 mL/min	**less than 50 mL/min:** see product information
less than 10 mL/min	
intermittent haemodialysis	see product information
peritoneal dialysis	as for GFR 5 to 14 mL/min; see product information
mebendazole	
No dosage adjustment required	
mefloquine	
No dosage adjustment required	
meropenem	
Dosage adjustment based on GFR [NB2] [NB3]	

more than 50 mL/min	normal
10 to 50 mL/min	**26 to 50 mL/min:** 100% 8- to 12-hourly **10 to 25 mL/min:** 50% 8- to 12-hourly
less than 10 mL/min	50 to 100% 24-hourly
intermittent haemodialysis	as for GFR less than 10 mL/min; dose after dialysis
peritoneal dialysis	as for GFR less than 10 mL/min
metronidazole	
No dosage adjustment required	
nitrofurantoin	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	**more than 40 mL/min:** normal
10 to 50 mL/min	**10 to 40 mL/min:** avoid [NB5]
less than 10 mL/min	avoid
intermittent haemodialysis	avoid
peritoneal dialysis	avoid
norfloxacin	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
10 to 50 mL/min	100% 12- to 24-hourly
less than 10 mL/min	100% 24-hourly
intermittent haemodialysis	as for GFR less than 10 mL/min
peritoneal dialysis	as for GFR less than 10 mL/min
oseltamivir	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 30 mL/min	normal
10 to 30 mL/min	**treatment:** 75 mg 24-hourly **prophylaxis:** 75 mg 48-hourly OR 30 mg 24-hourly

less than 10 mL/min	no data; if essential: **treatment:** 75 mg 48-hourly OR 30 mg 24-hourly **prophylaxis:** 30 mg 48-hourly
intermittent haemodialysis	**treatment:** 75 mg at the onset of symptoms, then 30 mg after each dialysis session **prophylaxis:** 30 mg after dialysis, then 30 mg after alternate dialysis sessions
peritoneal dialysis	**treatment:** 75 mg at the onset of symptoms, then repeat dose after 5 days **prophylaxis:** 30 mg after dialysis, then 30 mg every 7 days
paromomycin	
no data	
phenoxymethylpenicillin	
No dosage adjustment required	
piperacillin+tazobactam	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	**more than 40 mL/min:** normal
10 to 50 mL/min	**20 to 40 mL/min:** 100% 8-hourly
less than 10 mL/min	**less than 20 mL/min:** 100% 12-hourly
intermittent haemodialysis	as for GFR less than 20 mL/min
peritoneal dialysis	as for GFR less than 20 mL/min
primaquine	
No dosage adjustment required	
procaine benzylpenicillin	
No dosage adjustment required	
proguanil	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	**60 mL/min or more:** normal

10 to 50 mL/min	**20 to 59 mL/min:** 50% 24-hourly **10 to 19 mL/min:** 25% 48-hourly
less than 10 mL/min	25% weekly
intermittent haemodialysis	as for GFR less than 10 mL/min
peritoneal dialysis	as for GFR less than 10 mL/min
pyrantel	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
less than 50 mL/min or dialysis	no data
pyrazinamide	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
10 to 50 mL/min	normal
less than 10 mL/min	50 to 100% at normal dosing interval
intermittent haemodialysis	25 to 30 mg/kg on dialysis days only; dose after dialysis
peritoneal dialysis	normal
quinine dihydrochloride (intravenous) (give a loading dose of 20 mg/kg over 4 hours; start the maintenance dose 4 hours after the loading dose is completed) (for severe malaria, do not reduce dose or interval in the first 48 hours)	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
10 to 50 mL/min	**20 to 50 mL/min:** 5 to 10 mg/kg 8-hourly **10 to 20 mL/min:** 5 to 10 mg/kg 12-hourly
less than 10 mL/min	5 to 10 mg/kg 24-hourly
intermittent haemodialysis	as for GFR less than 10 mL/min; dose after dialysis
peritoneal dialysis	as for GFR less than 10 mL/min
rifampicin	

Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
10 to 50 mL/min	normal
less than 10 mL/min	50 to 100% at normal dosing interval
intermittent haemodialysis	as for GFR less than 10 mL/min
peritoneal dialysis	as for GFR less than 10 mL/min
sulfadiazine (if GFR is less than 20 mL/min, monitor blood concentration if possible)	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
10 to 50 mL/min	**20 to 50 mL/min:** avoid; if essential, normal **10 to 20 mL/min:** avoid; if essential, 50% at normal dosing interval
less than 10 mL/min	avoid; if essential, 25% at normal dosing interval
intermittent haemodialysis	as for GFR less than 10 mL/min
peritoneal dialysis	as for GFR less than 10 mL/min
tenofovir disoproxil fumarate	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	**50 mL/min or more:** normal
10 to 50 mL/min	**30 to 49 mL/min:** 100% 48-hourly **10 to 29 mL/min:** 100% 72- to 96-hourly
less than 10 mL/min	100% weekly
intermittent haemodialysis	as for GFR less than 10 mL/min; dose after dialysis
peritoneal dialysis	as for GFR less than 10 mL/min
terbinafine	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
10 to 50 mL/min	100% 48-hourly
less than 10 mL/min	100% 48-hourly

intermittent haemodialysis	as for GFR less than 10 mL/min; dose after dialysis
peritoneal dialysis	as for GFR less than 10 mL/min
tinidazole	
No dosage adjustment required. In intermittent haemodialysis; dose after dialysis	
trimethoprim	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	**more than 30 mL/min:** normal
10 to 50 mL/min	**15 to 30 mL/min:** normal; monitor full blood count
less than 10 mL/min	**less than 15 mL/min:** avoid; if essential, up to 150 mg 24-hourly; monitor full blood count
intermittent haemodialysis	as for GFR less than 15 mL/min; dose after dialysis
peritoneal dialysis	as for GFR less than 15 mL/min
trimethoprim+sulfamethoxazole (standard treatment dosing)	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
10 to 50 mL/min	**26 to 50 mL/min:** normal for 14 days, then 50% at normal dosing interval **15 to 25 mL/min:** normal for 3 days, then 100% 24-hourly
less than 10 mL/min	**less than 15 mL/min:** avoid; if essential, normal for 3 days, then 100% 24-hourly
intermittent haemodialysis	as for GFR less than 15 mL/min; dose after dialysis if dosed 24-hourly
peritoneal dialysis	as for GFR less than 15 mL/min
trimethoprim+sulfamethoxazole (treatment of *Pneumocystis jiroveci* pneumonia)	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal

10 to 50 mL/min	**26 to 50 mL/min:** normal **15 to 25 mL/min:** 5+25 mg/kg at normal dosing interval for 2 days, then 5+25 mg/kg 12-hourly
less than 10 mL/min	**less than 15 mL/min:** 5+25 mg/kg 12- to 24-hourly
intermittent haemodialysis	as for GFR less than 15 mL/min; dose after dialysis if dosed 24-hourly
peritoneal dialysis	as for GFR less than 15 mL/min
vancomycin	
see appendix 2	
zidovudine	
Dosage adjustment based on GFR [NB2] [NB3]	
more than 50 mL/min	normal
10 to 50 mL/min	normal
less than 10 mL/min	100 mg 8-hourly
intermittent haemodialysis	as for GFR less than 10 mL/min
peritoneal dialysis	as for GFR less than 10 mL/min

ECG = electrocardiogram; GFR = glomerular filtration rate

NB1: Dosing in patients with renal impairment is complex, this table is intended as a guide only.

NB2: 'Normal' indicates that the standard dosage regimen for the specific indication in these guidelines should be used.

NB3: For multiple-daily doses, percentage dosage adjustments are calculated using the intermittent dose rather than the total daily dose (eg if standard dosing for drug X is 500 mg 6-hourly then: 50% at normal dosing interval = 250 mg 6-hourly; 100% 12-hourly = 500 mg 12-hourly).

Appendix 6: Administration of parenteral antimicrobials

Administration of injectable antimicrobial drugs in adults [NB1][NB2][NB3] (Table A6.1)

aciclovir	
250 mg / 10 mL	
compatible fluids	glucose 5%, Hartmann's, sodium chloride 0.9%, sodium chloride and glucose solutions
IV injection	contraindicated - may cause renal tubular damage
IV infusion	dilute to a maximum concentration of 5 mg/mL; shake to mix thoroughly and infuse over at least 1 hour.
IM injection	contraindicated - highly alkaline
notes	use reconstituted and diluted solutions immediately ampoules are stable for use up to 9 months after the foil sachet has been opened
ampicillin	
500 mg vial	
compatible fluids	sodium chloride 0.9%
IV injection	doses < 1 g only; give over 3-5 minutes
IV infusion	dilute with 50-100 ml and infuse over 30-40 minutes
IM injection	inject deep into a large muscle
notes	rapid IV administration may cause seizures use reconstituted and diluted solutions immediately
azithromycin	
500 mg vial	
compatible fluids	glucose 5%, Hartmann's, sodium chloride 0.9%, sodium chloride and glucose solutions
IV injection	not recommended

IV infusion	dilute in 250-500 mL and infuse over at least 1 hour; maximum concentration 2 mg/mL
IM injection	not recommended
notes	protect the vial from light. reconstituted solution is stable for 24 hours at room temperature.
benzylpenicillin	
600 mg (1 million units) vial	
compatible fluids	glucose 5%, sodium chloride 0.9%
IV injection	doses ≤ 2 million units only; use a concentration of 100 000 mg/mL because it is isotonic; inject slowly over 5 – 10 minutes
IV infusion	dilute in 100 mL and infuse over 30-60 minutes
IM injection	inject deep into a large muscle
notes	rapid IV administration of large doses may cause seizures. use reconstituted and diluted solutions immediately
cefalotin	
1 g vial	
compatible fluids	glucose 5%, Hartmann's, sodium chloride 0.9%
IV injection	doses < 2 g; inject slowly over 3-5 minutes
IV infusion	dilute with 50 to 100 mL and infuse over 30 minutes
IM injection	use a concentration of approximately 200 mg/mL; inject deep into the gluteal or lateral thigh muscle. IV route preferred as IM injection is painful.
notes	reconstituted solution stable for 24 hours when refrigerated at 2-8 °C. If precipitation occurs, shake vigorously while bringing to room temperature. IV administration of doses greater than 6 g daily for longer than 3 days may cause thrombophlebitis.
cefazolin	
500 mg vial, 1 g vial	

compatible fluids	glucose 5%, Hartmann's, sodium chloride 0.9%, sodium chloride and glucose solutions
IV injection	doses < 2 g; inject slowly over 3-5 minutes
IV infusion	dilute with 50 to 100 mL an infuse over 10-60 minutes
IM injection	reconstitute with 1% lignocaine; inject deep into a large muscle
notes	protect vial from light. reconstituted solution stable for 24 hours when refrigerated at 2-8 °C. Crystals may form; redissolve by shaking well and warming the vial in the hands.
cefotaxime	
500 mg vial	
compatible fluids	glucose 5%, glucose 10%, Hartmann's, sodium chloride 0.9%, sodium chloride and glucose solutions
IV injection	inject slowly over 3-5 minutes; more rapid injection may cause cardiac arrhythmias
IV infusion	dilute in 40-100 mL and infuse over 20-30 minutes
IM injection	reconstitute with lignocaine 1%; inject deep into the gluteal muscle; max 4 mL per site
notes	rapid IV injection may cause cardiac arrhythmias reconstituted solution stable for 24 hours when refrigerated at 2-8 °C when reconstituted with WFI; protect from light.
ceftriaxone	
250 mg vial, 1 g vial	
compatible fluids	glucose 5%, glucose 10%, sodium chloride 0.9%, sodium chloride and glucose solutions
IV injection	doses ≤ 1 g; inject over 2-4 minutes
IV infusion	dilute in about 40-50 mL and infuse over at least 30 minutes

IM injection	reconstitute with lignocaine 1%; inject deep into the gluteal muscle, max 1 g into each buttock; IM injection without lignocaine is very painful.
notes	incompatible with calcium containing solutions (eg Hartmann's) due to precipitation. Contraindicated in neonates receiving IV calcium-containing solutions; in other age groups ceftriaxone must not be administered at the same time as IV calcium-containing solutions; flush the line with a compatible fluid **before** and **after** ceftriaxone is given.
chloramphenicol	
1 g vial	
compatible fluids	glucose 5%, glucose 10%, sodium chloride 0.9%, sodium chloride and glucose solutions
IV injection	give over at least 1 minute
IV infusion	dilute with 50-100 mL; give over 30-40 minutes
IM injection	not recommended - absorption can be slow and unpredictable.; if required, inject slowly into a large muscle
notes	IV chloramphenicol can cause blood dyscrasias; monitor full blood count during treatment. use reconstituted and diluted solutions immediately
ciprofloxacin	
2 mg/mL / 50 mL bag	
compatible fluids	glucose 5%, glucose 10%, Hartmann's, sodium chloride 0.9%, sodium chloride and glucose solutions
IV injection	not recommended
IV infusion	infuse the dose into a large vein: 200 mg over at least 60 minutes, 400 mg over at least 120 minutes (for larger doses, increase infusion time proportionately).
IM injection	not recommended

notes	ensure the patient is well hydrated to prevent crystalluria; do not use urinary alkalinisers. may cause burning, pain, redness and swelling at the infusion site, especially if given over less than 1 hour. protect from light; do not refrigerate or freeze.
clindamycin	
various products available; note different storage conditions	
compatible fluids	glucose 5%,, Hartmann's, sodium chloride 0.9%, sodium chloride and glucose solutions
IV injection	not recommended
IV infusion	doses ≤ 600 mg dilute in 50 mL and infuse over at least 20 minutes doses up to 1200 mg dilute in 100 mL and infuse over at least 30-40 minutes; max rate 30 mg/minute
IM injection	do not inject more than 600 mg as a single dose at a single site; inject deep into a large muscle; may cause local irritation, pain and abscess
notes	Dalacin C® brand – store at 2-8 °C (refrigerated). Check storage conditions for other brands in product information. rapid administration may cause hypotension and cardiac arrest. do not give products which contain benzyl alcohol to neonates.
cloxacilin	
500 mg vial	
compatible fluids	glucose 5%, sodium chloride 0.9%
IV injection	doses < 1 g; inject slowly over 3-4 minutes
IV infusion	dilute in 100 mL and infuse over 30-60 minutes
IM injection	inject slowly into a large muscle (eg gluteus or lateral thigh); divide doses over 1 g and give in different sites.

notes	injection site reactions include pain after IM injection and phlebitis after IM injection use reconstituted and diluted solutions immediately.
fluconazole	
2 mg/mL / 100 mL bag	
compatible fluids	glucose 5%, Hartmann's, sodium chloride 0.9%
IV injection	not recommended
IV infusion	infuse over 1-2 hours; do not exceed a rate of 200 mg/hour
IM injection	not recommended
notes	protect from light
gentamicin	
80 mg / 2 mL ampoule	
compatible fluids	glucose 5%, glucose 10%, Hartmann's, sodium chloride 0.9%
IV injection	inject slowly over 3-5 minutes; doses > 240 mg infusion preferred
IV infusion	dilute with 50-100 mL and infuse over 15-30 minutes
IM injection	inject into a large muscle eg gluteal muscle; maximum of 4 mL at each site
notes	gentamicin is **inactivated** by penicillin and cephalosporin antibiotics; administer at separate sites if possible, if not possible, flush line well **before** and **after** giving each drug protect ampoule from light
meropenem	
500 mg vial	
compatible fluids	sodium chloride 0.9% (preferred), glucose 5%, sodium chloride and glucose solutions
IV injection	≤ 500 mg; inject over 5 minutes
IV infusion	dilute with 50-200 mL and infuse over 15-30 minutes
IM injection	not recommended

notes	different brands have different storage recommendations; check product information
metronidazole	
500 mg / 500 mL bag	
compatible fluids	glucose 5%, sodium chloride 0.9%, sodium chloride and glucose solutions
IV injection	not recommended
IV infusion	infuse 500 mg over 20 minutes; max rate 25 mg/ minute
IM injection	not recommended
notes	incompatible with aluminium containing equipment eg needles, cannula hubs protect from light; avoid direct sunlight during administration (short-term exposure to normal room light does not affect stability).
piperacillin+tazobactam	
4g+500mg vial	
compatible fluids	glucose 5%, sodium chloride 0.9%
IV injection	not recommended
IV infusion	dilute to at least 50 mL and infuse over 20-30 minutes
IM injection	not recommended
notes	reconstituted solution stable for 24 hours when refrigerated at 2-8 °C
quinine dihydrochloride	
600 mg / 10 mL ampoule	
compatible fluids	glucose 5% (preferred), sodium chloride 0.9%
IV injection	not recommended
IV infusion	dilute in 500 mL glues 5% (preferred) or sodium chloride 0.9%; infuse slowly over 4 hours

IM injection	not recommended; use only as a last resort when IV infusion not possible; quinine is irritant and painful – necrosis, abscess formation and fatal tetanus have occurred
notes	rapid infusion may causes severe and fatal cardiotoxicity; monitor pulse and blood pressure and slow the rate of infusion if dysthymias occur. monitor blood glucose concentration; glucose is the preferred diluent to reduce incidence of hypoglycaemia. protect from light.
vancomycin	
500 mg vial	
compatible fluids	glucose 5%, glucose 10%, Hartmann's, sodium chloride 0.9%
IV injection	not recommended
IV infusion	dilute to 5 mg/mL, ie dilute 1 g to at least 200 mL; infuse at a maximum rate of 10 mg/minute; if rash develops slow the infusion rate. for fluid restricted patients the maximum concentration that can be used is 10 mg/mL, however, higher concentrations increase the risk of infusion reactions (using a central line is preferred).
IM injection	contraindicated; causes ulceration and necrosis
notes	extravasation may cause tissue necrosis. may cause pain at injection site and thrombophlebitis; if possible use concentrations 2.5-5 mg/mL and rotate infusion site. **red man syndrome** presents as tingling, flushing or rash on the face, neck and upper body, muscle spasm of the chest and back and, rarely, hypotension and shock-like symptoms; if these symptoms occur **slow** the infusion rate. protect vial from light.

NB1: this table gives the maximum (fastest) safe administration rates; slower rates may be required.

NB2: check the product information as different brands may have different dilution or storage requirements.

NB3: IM route should only be used where IV route is not available for the medicines included in this table.

NB4: If fluid restriction is a concern; consider the fluid associated with administration of parenteral antimicrobials (and other medicines).

References:

Burridge, N. Symons, K (Ed). Australian Injectable Drugs Handbook, 7th Edition. Collingwood, Australia. The Society of Hospital Pharmacists Australia. 2017.

eMIMS 2019, retrieved from https://www.emims.com.au.

WHO Model Prescribing Information: Drugs used in Bacterial Infections, retrieved from https://apps.who.int/medicinedocs/en/d/Js5406e/

Appendix 7. Formulas

Assessment of renal function

Adults

For patients older than 18 years, the Cockcroft-Gault formula can be used to estimate creatinine clearance (CrCl).

$$\text{Adult males: CrCl (mL/min)} = \frac{(140 - \text{age}) \times \text{weight (kg)}}{0.814 \times \text{serum creatinine (micromol/L)}}$$

Adult females: Multiply the above formula by 0.85

Lean body weight is the preferred weight descriptor for use in the Cockcroft-Gault formula, because creatinine is a muscle breakdown product; however, it is not easily calculated manually (see formula below).

For patients who are not overweight, actual body weight can be used in place of lean body weight in the Cockcroft-Gault formula. For patients who are overweight, for practicality, ideal body weight can be used (see formula on the next page).

Children

For children, the modified Schwartz formula can be used to estimate glomerular filtration rate (eGFR).

$$\text{Child: eGFR (mL/min/1.73 m}^2\text{)} = \frac{36.5 \times \text{height (cm)}}{\text{serum creatinine (micromol/L)}}$$

Lean body weight

$$\text{Adult males: lean body weight (kg)} = \frac{9270 \times \text{weight (kg)}}{6680 + (216 \times \text{BMI})}$$

$$\text{Adult females: lean body weight (kg)} = \frac{9270 \times \text{weight (kg)}}{8780 + (244 \times \text{BMI})}$$

$$\text{body mass index (BMI) (kg/m}^2\text{)} = \frac{\text{weight (kg)}}{\text{height (m)}^2}$$

Ideal body weight

Adults

Also see IBW table page 329 or page 356.

Adult males: ideal body weight (IBW) (kg) = 50 kg + 0.9 kg per cm over 152 cm
(2.3 kg per inch over 5 feet)

Adult females: ideal body weight (IBW) (kg) = 45.5 kg + 0.9 kg per cm over 152 cm
(2.3 kg per inch over 5 feet)

Children

For children, ideal body weight can be estimated by using the corresponding weight for the height percentile on the growth chart (eg <www.cdc.gov/growthcharts>).

Body surface area

$$\text{body surface area (BSA) (m}^2\text{)} = \sqrt{\frac{\text{height (cm)} \times \text{weight kg)}}{3600}}$$

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