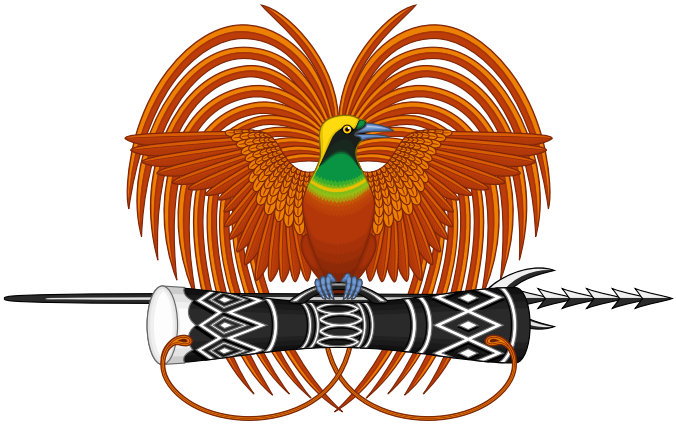
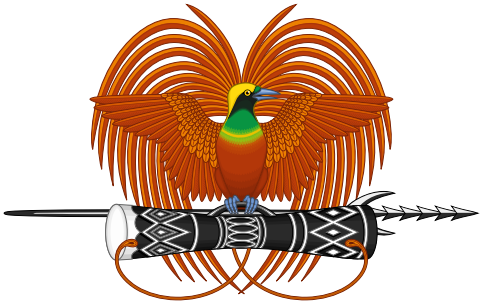


NATIONAL DEPARTMENT OF HEALTH

PAPUA NEW GUINEA ANTIMICROBIAL GUIDELINES

FIRST EDITION, 2024



National Department of Health

Papua New Guinea Antimicrobial Guidelines

First edition, 2024

World Health Organization

Burnet
reach for the many

THERAPEUTIC GUIDELINES

National Department of Health, Government of Papua New Guinea, 2024.

These *Papua New Guinea Antimicrobial Guidelines* have been endorsed by the senior executive of the National Department of Health, Government of Papua New Guinea.

Suggested citation: Papua New Guinea Antimicrobial Guidelines Writing Committee. Papua New Guinea Antimicrobial Guidelines. First edition. Port Moresby: Government of Papua New Guinea; 2024.

To provide feedback on these guidelines, contact:

Deputy Secretary National Health Standards & Compliance
National Department of Health
P. O. Box 807
Waigani
Papua New Guinea

These guidelines contain content adapted from other sources with permission, including:

Therapeutic Guidelines published by Therapeutic Guidelines Limited, an independent not-for-profit organisation which develops and publishes evidence-based, practical treatment advice to assist practitioners with decision making at the point-of-care. For more information or to discuss permission to adapt *Therapeutic Guidelines* content, email: partnershipprogram@tg.org.au.

Timor-Leste Antimicrobial Guidelines 2022 published by Ministério da Saúde, República Democrática de Timor-Leste. For more information or to discuss permission to adapt *Timor-Leste Antimicrobial Guidelines* content, contact:

Hospital Nacional Guido Valadares
Rua Bidau Toko Baru, Dili
Timor-Leste
Tel: (+670) 3311008

Fiji Antibiotic Guidelines 2019 published by the Ministry of Health and Medical Services, Government of Fiji. For more information or to discuss permission to adapt *Fiji Antibiotic Guidelines* content, email: medicinesessential@gmail.com.

Contents

Boxes

Figures

Tables

Secretary's foreword

Antimicrobial resistance (AMR) is considered one of the greatest threats to contemporary public health, especially in low- and middle-income countries, such as PNG. It occurs when bacteria, viruses, fungi and parasites change over time and no longer respond to medicines, making infections harder to treat, thereby increasing the risk of the spread of disease, severe illness and death.

AMR affects the human, animal and environmental health domains and has greater impact to our human population, with misuse and overuse of antibiotics being an important driver of AMR. Therefore, the need to have robust evidence-based antibiotic guidelines as an intervention to guide appropriate prescribing and use.

The National Antibiotic Guidelines embodies principles of antibiotic antimicrobial use towards appropriate therapy to improve patient outcomes, reduced inappropriate and unnecessary antimicrobial use, and reduced adverse consequences, such as antimicrobial resistance and toxicity.

The National Department of Health as the lead agency of the human health is very pleased and proud to have developed and refined these guidelines for PNG with the support of WHO and valuable partners. This is a milestone achievement and will go a long way towards addressing this growing and urgent health threat through a multi-sectoral One Health approach to AMR, bringing together a wide range of international and national partners across the human, animal and environmental sectors.

DR. OSBORNE LIKO
SECRETARY FOR HEALTH
CO-CHAIR NATIONAL AMR STEERING COMMITTEE

Acknowledgements

This first edition of the *Papua New Guinea Antimicrobial Guidelines* was developed by the Papua New Guinea National Department of Health (NDoH) in collaboration with the World Health Organization, Burnet Institute and Therapeutic Guidelines. The NDoH thanks the following people for their contribution to these guidelines:

- Dr Osborne Liko, Secretary for Health, NDoH and Co-Chair of the National Antimicrobial Resistance (AMR) Steering Committee
- Late Dr Goa Tau, Deputy Secretary National Health Standards and Compliance Wing, NDoH
- Dr Dora Lenturut-Katal, Acting Deputy Secretary National Health Standards and Compliance Wing, NDoH
- Dr Al Maha, Chief Physician, NDoH
- Dr Seluia Mabone, Chief Pathologist, NDoH
- Dr Cornelia Kilalang, Chief Paediatrician, NDoH
- Dr Desmond Aisi, Chief Emergency Physician, NDoH
- Dr Esther Apuahe, Chief Surgeon, NDoH
- Dr James Naipao, Chief Ear, Nose & Throat, NDoH
- Dr Ligo Augerea, Chief Obstetrician & Gynaecologist, NDoH
- Dr Simon Melengas, Chief Ophthalmologist, NDoH
- Dr Varqa Larawin, Deputy Chief Ear, Nose & Throat Surgeon, NDoH
- Dr Okti Poki, Chief Surgeon, NDoH
- Dr Takovi Maga, acting Chief Dentist, NDoH
- Dr Nora Dai, acting Chief Anaesthetist, NDoH
- Dr Arthur Elijah, Deputy Chief Obstetrician & Gynaecologist, NDoH
- Dr Robert Ko, Ophthalmologist, NDoH
- Dr Cynthia Kuanch, Dermatologist, NDoH
- Dr Ben Yapo, Highlands Regional Surgeon, NDoH
- Dr Waimbe Wahamu, Deputy Chief ophthalmologist, Highlands Region, NDoH
- Dr Damien Hasola, Surgeon, NDoH
- Mr Vali Karo, Pharmaceutical Services Standards Branch (PSSB) Manager, NDoH
- Ms Sipora Yanabis, Technical Advisor, Pharmaceutical Care Unit, PSSB, NDoH
- Ms Nancy Bala, Pharmacist, Pharmaceutical Care Unit, PSSB NDoH
- Ms Jonila Kepas, Technical Advisor and Lead Secretariat, Pharmaceutical & Medical Supplies Reform Unit, NDoH
- Ms Marlene B Lohia, Regulatory Pharmacist and Medicine Reviewer, PSSB, NDoH
- Ms Mary Keurih, Technical Advisor, Product Registration Unit, PSSB, NDoH
- Ms Judith Lizzane Nui, Quality Assurance Lead, Medicines Quality Control Laboratory, PSSB, NDoH

- Mr Graham Wavimbukie, Technical Advisor, Medicines Quality Control Laboratory, PSSB, NDoH
- Mr Dum Iwa, Momase Regional Pharmaceutical Inspector, PSSB, NDoH
- Mr Wauwa Legu, Assistant Technical Advisor, MSPDB, NDoH
- Dr Luke Anthony, Surgeon, Port Moresby General Hospital (PMGH)
- Dr Jack Mulu, Surgeon, PMGH
- Dr Garry Nou, Emergency Physician, PMGH
- Dr Aina Anota, Medical Physician, PMGH
- Dr Keno Temo, Physician, PMGH
- Dr William Toua, Physician, PMGH
- Dr Henao Asa, Orthopaedic Surgeon, PMGH
- Dr Roland Barnabas, Paediatrician, PMGH
- Dr Joel Silari, Anaesthetist and Intensivist, PMGH
- Dr Alu Kali, Anaesthetist and Intensivist, PMGH
- Dr Magdalene Mangot Ophthalmologist PMGH
- Dr Gamini Vali Paediatrician PMGH
- Dr John Kamakom TB Physician, PMGH
- Dr Nick Agebigo, Dermatologist, PMGH
- Dr Gabriella Ak, Microbiologist, PMGH
- Ms Sandy Nawara, Pharmacist, PMGH
- Mr Presley Pais, Pharmacist, PMGH
- Sister Hilda Lompu, Surgical Nurse, PMGH
- Dr Esther Gabut, Medical Physician, National Capital District Provincial Health Authority (PHA)
- Dr Scotty Kandelyo, Emergency Physician, Mount Hagen PHA
- Dr David Pahau, Ophthalmologist, Madang PHA
- Dr Dennis Tony, Physician, Milne Bay PHA
- Dr Kennan Witari, Physician, Daru PHA
- Dr Beryl Vetuna, Paediatrician, East New Britain PHA
- Dr Jambi Garap, Senior Lecturer and Ophthalmologist, Faculty of Medicine, University of PNG (UPNG)
- Dr Arnold Waine, Surgeon, Faculty of Medicine, UPNG
- Dr Pamela Toliman, Senior Research Fellow, PNG Institute of Medical Research
- Dr Polapoi Chalau, Surgeon and Director Medical Services, Paradise Private Hospital
- Dr Vincent Pyakalyia, Internal Medicine Physician, Santos Foundation
- Dr Lucy John, Manager Disease Control & Surveillance Branch, NDoH
- Ms Mary Yohogu, Technical Officer Lymphatic Filariasis, NTD Program, NDoH
- Dr Amrita Ronnachit, Infectious Diseases Physician, Senior Technical Advisor Antimicrobial Resistance and One Health working group, Burnet Institute

- Professor Rob Moulds, Medical Advisor to the Partnership Program, Therapeutic Guidelines
- Ms Mieke Hutchinson-Kern, Partnership Program Manager, Therapeutic Guidelines
- Dr Adam Jenney, Infectious Diseases Physician and Head, Microbiology Unit, Alfred Health, Melbourne; and Adjunct Professor of Internal Medicine, Fiji National University
- Associate Professor Amanda Gwee, General Paediatrician, Infectious Diseases Physician, Clinical Pharmacologist, The Royal Children's Hospital Melbourne; Leader of the Antimicrobials Group, Murdoch Children's Research Institute; and Associate Professor, Department of Paediatrics, The University of Melbourne
- Dr Angie Pinto, Infectious Diseases Physician and Clinical Microbiologist, Partners In Health
- Associate Professor John Ferguson, Senior Staff Specialist Microbiology and Infectious Diseases, Hunter New England Health, New South Wales
- Dr Chloe Story, Infectious Diseases Physician and Clinical Microbiologist, Technical Advisor Antimicrobial Resistance One Health Working Group, Burnet Institute
- Dr Mallory Morton Infectious Diseases Physician, South Western Sydney Local Health District, New South Wales
- Ms Stephanie Levy, Project Manager, Burnet Institute
- Mr Mona Kheng, Surveillance Theme Lead, Burnet Institute
- Ms Gilam Tamolsaian, Project Coordinator, Burnet Institute
- Mr Roderick L Salenga, Technical Officer (Pharmaceuticals), World Health Organization
- Mr Asaeli Raikabakaba, Technical Officer, World Health Organization.

Principles of antimicrobial use

This topic provides an overview of the principles of appropriate antimicrobial use:

The following topics are not included in this section:

- **practical information on using antibacterial drugs**, see 'Getting to know your antimicrobials,' page 9
- **'**Antimicrobial hypersensitivity,' page 27.

The principles of appropriate antimicrobial use are summarised in Figure 1 (below). Appropriate antimicrobial therapy improves patient outcomes, reduces inappropriate and unnecessary antimicrobial use, and reduces adverse consequences, such as antimicrobial resistance and toxicity.

Figure 1: The antimicrobial creed

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 medical record and/or medication chart. Documentation should include the indication and the intended duration of therapy. The patient or their carer should be provided with information about the indication and intended plan for antimicrobial therapy, and the potential adverse effects.

Antimicrobial use may be prophylactic, empirical or directed against a known pathogen.

Prophylactic therapy

Prophylactic antimicrobial therapy aims to prevent infection when there is a significant clinical risk of infection developing. Prophylaxis is of proven benefit for many surgical procedures, open fractures and in other specific circumstances. For more information, see 'Antibiotic prophylaxis in surgical procedures,' page 351.

Empirical therapy

Empirical antimicrobial therapy is used to treat an established infection when the pathogen has not been identified. When indicated, obtain specimens (e.g. blood cultures, cultures from other appropriate sites) before starting antimicrobial therapy. Antimicrobial choice should be based on the clinical presentation and the expected antimicrobial susceptibility of the most likely or important pathogen(s). Empirical therapy is reasonable in the following circumstances:

- when treatment must be started before the results of culture or susceptibility testing are available
- when the infection is not serious enough to warrant taking samples for culture
- if a sample for culture cannot be obtained.

Avoid empirical antimicrobial therapy for minor or self-limiting illnesses as it is a significant driver of antimicrobial resistance.

Review empirical therapy as soon as possible.

- If an infection has been excluded, stop antimicrobial therapy.
- If no pathogen has been identified, re-evaluate the clinical and microbiological justification for therapy. If ongoing therapy is indicated, consider de-escalation (e.g. change parenteral therapy to oral therapy, or change a broad-spectrum to a narrower-spectrum antimicrobial) for a defined duration.
- If a pathogen is identified, follow the principles of directed therapy.

Directed therapy

Directed antimicrobial therapy is used to treat an established infection when the pathogen has been identified.

Antimicrobials are chosen to ensure patients receive the most effective, least toxic and narrowest spectrum therapy 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 (e.g. in polymicrobial infection), synergy (e.g. in enterococcal endocarditis) or to minimise the development of resistance (e.g. in tuberculosis (TB) or human immunodeficiency virus (HIV) infection).

Route of administration

For the majority of infections, 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 Figure 2 (below) have good oral bioavailability and can often be given orally rather than intravenously (IV), provided they are appropriate for the specific indication, have adequate tissue penetration for the infection being treated, and the patient can tolerate oral administration. If the oral route is unsuitable, the enteral route (e.g. nasogastric) may be considered.

Figure 2: Examples of antimicrobials with good oral bioavailability

- azithromycin [Note 1]
- chloramphenicol
- ciprofloxacin
- clindamycin
- doxycycline
- fluconazole
- metronidazole
- moxifloxacin
- rifampicin
- trimethoprim+sulfamethoxazole

Note 1: Despite lower bioavailability, oral azithromycin is extensively distributed and achieves high intracellular concentrations.

Parenteral antimicrobial administration (usually intravenous, but occasionally intramuscular) is required when:

- Oral administration is not tolerated or not possible
- Gastrointestinal absorption is likely to be significantly reduced (e.g. 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 (e.g. meningitis, endocarditis)
- Urgent treatment is required for severe and rapidly progressing infection.

Unless the infection is one that requires high tissue concentrations or prolonged parenteral therapy (e.g. meningitis, endocarditis), reassess the need for ongoing intravenous therapy daily, and switch to oral or enteral therapy once the patient is clinically stable.

Figure 3: Guidance for intravenous to oral switch

It is often appropriate to switch a patient's therapy from the intravenous to oral route when all of the following apply:

- clinical improvement
- fever resolved or improving
- no unexplained haemodynamic instability
- tolerating oral intake with no concerns about malabsorption
- a suitable oral antimicrobial with the same or similar spectrum, or an oral formulation of the same drug, is available with adequate penetration to the site of infection. For children, a suitable paediatric formulation is available

Source: Nathwani D, Lawson W, Dryden M, Stephens J, Corman S, Solem C, Li J, Charbonneau C, Baillon-Plot N, Haider S, Eckmann C. Implementing criteria-based early switch/early discharge programmes: a European perspective. Clin Microbiol Infect. 2015 Sep;21 Suppl 2:S47-55.

Due to the risk of promoting resistance, the use of topical antibiotic therapy should be restricted to the few recommended indications (e.g. bacterial conjunctivitis, mild impetigo).

Optimising antimicrobial dosage regimen

When selecting a dosage regimen for antimicrobial therapy, take into account patient factors, the pharmacokinetic and pharmacodynamic properties of the drug, and potential drug interactions.

In some patients with altered pharmacokinetics, dosing may be difficult and expert advice may be required. Examples include:

- critically ill patients requiring intensive care support
- patients with severe burns
- patients with fluid sequestration into a third space (e.g. severe pancreatitis, bleeding, ascites)
- pregnant people
- obese patients.

The use of extended or continuous infusion of antimicrobials may be considered in certain circumstances to optimise the dosage regimen, for example in patients with septic shock or requiring intensive care support.

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 and glycopeptides.

Duration of antimicrobial therapy

The duration of therapy for some indications is based on clinical practice because it is not clearly defined from published studies. Prolonged duration of antimicrobial therapy is associated with an increased risk of adverse reactions, *Clostridioides* (*Clostridium*) *difficile* infection, selection of multidrug-resistant organisms, as well as increased costs. In general, use the shortest possible duration of therapy (often less than 7 days), consistent with the condition being treated and the patient's clinical response. However, there are certain indications that require a longer duration of therapy (e.g. endocarditis, osteomyelitis). Where possible, advice about duration of therapy is given in the clinical topics in these guidelines.

Adverse effects of antimicrobials

All antimicrobials can cause adverse effects, so the risk–benefit profile should be considered when deciding whether to prescribe an antimicrobial. Adverse effects are usually minor or self-limiting, but serious adverse effects, including death, can occur.

Always check whether a patient has a history of adverse drug reactions before prescribing an antimicrobial.

Adverse effects of antimicrobials can be classified as direct or indirect.

Direct adverse effects

Adverse drug reactions to antimicrobials are most commonly non–immune-mediated, pharmacologically predictable reactions (e.g. gastrointestinal upset) or immune-mediated nonsevere delayed reactions (e.g. maculopapular rash), which do not necessarily preclude further use of the drug.

Occasionally, the reaction is a severe immune-mediated hypersensitivity reaction, which can be immediate or delayed, and subsequent exposure to the drug could be fatal. For further discussion, see Antimicrobial hypersensitivity, page 17.

Indirect adverse effects

Indirect adverse effects of antimicrobials include effects on both commensal and environmental flora. *C. difficile* is a common cause of healthcare-associated and antibiotic-associated diarrhoea. *Candida* species are normal flora in the gastrointestinal and genitourinary tracts, but antibiotic therapy disrupts the normal flora, and infection caused by *Candida* species can develop. Antimicrobial use is associated with an increased risk of colonisation 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 for society. Although the mechanisms are complex, resistance usually develops due to selective pressure exerted by the widespread presence of antimicrobial drugs in the environment, together with the facilitated transfer of organisms within the environment, in both healthcare and community settings.

Antimicrobial resistance is increasing worldwide, including in Papua New Guinea. Problem organisms include *Streptococcus pneumoniae*, methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), strains of Gram-negative bacilli that produce extended-spectrum beta-lactamase (ESBL) enzymes, *Neisseria gonorrhoeae*, and multidrug-resistant *Acinetobacter* and *Pseudomonas aeruginosa*. Emergence of resistance to antibiotics such as quinolones, carbapenems, vancomycin and colistimethate sodium (colistin) is a major public health challenge.

Appropriate antimicrobial use delays the emergence of resistance and minimises the prevalence of resistance after it has emerged. To ensure that antimicrobials remain effective for the future, it is crucial to follow the principles of antimicrobial prescribing and reduce inappropriate use.

Antimicrobial stewardship

Antimicrobial stewardship (AMS) is a multifaceted approach that promotes optimal antimicrobial prescribing. The aim of an AMS program is to improve patient outcomes and reduce adverse effects associated with antimicrobial use, including antimicrobial resistance, toxicity and unnecessary costs. Effective AMS requires multidisciplinary cooperation, including pharmacy, microbiology, nursing, medical, and infection prevention and control. Evidence shows that AMS activities can reduce inappropriate antimicrobial use, which has been associated with improved patient outcomes.

Six essential strategies for effective AMS in hospitals have been recommended by the Australian Commission on Safety and Quality in Health Care[1]:

The essential strategies for effective AMS in hospitals include:

- Implementing clinical guidelines that incorporate local microbiology and antimicrobial susceptibility data
- 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
- Reviewing antimicrobial prescribing, with intervention and direct feedback to the prescriber
- Ensuring laboratories use selective reporting of susceptibility results consistent with hospital antimicrobial treatment guidelines
- Monitoring antimicrobial use and outcomes, and reporting to clinicians and management.

AWaRe antibiotic classification tool

To assist in the development of tools for AMS 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 global consumption of antibiotics most at risk of resistance.

Throughout these guidelines, antibiotics in drug recommendations are colour-coded (green, yellow or red) according to their AWaRe classification increase awareness of these classifications. The writers of these guidelines considered many factors when making each drug recommendation and prescribers are advised to select the most appropriate treatment option based on the advice provided for each specific infectious syndrome and with consideration of relevant clinical and other patient factors, even if that results in using a watch or reserve antibiotic.

1 Australian Commission on Safety and Quality in Health Care (ACSQHC). Antimicrobial Stewardship in Australian Health Care 2023. Sydney: ACSQHC; 2023. https://www.safetyandquality.gov.au/publications-and-resources/resource-library/antimicrobial-stewardship-australian-health-care

Access group antibiotics

Access antibiotics have activity against a wide range of commonly encountered pathogens while also showing lower resistance potential than antibiotics in other groups. They are essential antibiotics that should be widely available, affordable and quality assured.

These antibiotics include amoxicillin, benzylpenicillin and benzathine benzylpenicillin, cefalexin, cefazolin, chloramphenicol, clindamycin, doxycycline, flucloxacillin, gentamicin, metronidazole, nitrofurantoin, phenoxymethylpenicillin, procaine penicillin and trimethoprim+sulfamethoxazole.

Watch group antibiotics

The **watch** group includes antibiotic classes that have higher resistance potential, and includes most of the highest priority agents among the *WHO List of Critically Important Antimicrobials for Human Medicine (WHO CIA List)*. These medicines should be prioritised as key targets for monitoring and stewardship programs. Selected **watch** antibiotics are recommended in these guidelines as first- or second-line treatment options for a limited number of specific infectious syndromes.

These antibiotics include azithromycin, cefotaxime, ceftriaxone, cefuroxime, ciprofloxacin, clarithromycin, erythromycin, fusidic acid, meropenem, piperacillin+tazobactam and vancomycin.

Reserve group antibiotics

This group includes antibiotics that should be reserved for treatment of confirmed or suspected infections due to multidrug-resistant organisms. **Reserve** antibiotics should be treated as last-resort options, where all alternatives have failed or are not suitable. Access to 'reserve' antibiotics in Papua New Guinea is limited, and their use may be limited for specific indications.

These antibiotics include colistimethate sodium (colistin), linezolid and polymyxin B.

Key additional references

WHO Access, Watch, Reserve (AWaRe) classification of antibiotics for evaluation and monitoring of use, 2021. Geneva: World Health Organization; 2021 (WHO/MHP/HPS/EML/2021.04).

Getting to know your antimicrobials

This topic covers practical information on using the antibacterial drugs, focussing on those recommended in these guidelines. For comprehensive drug information, including precautions, contraindications, adverse effects and drug interactions, consult an appropriate drug information resource. When prescribing an antibacterial drug, consider the benefit–harm profile of the drug in the individual patient. Antimicrobials are listed in alphabetical order, according to class:

- **antibacterials**, page 10
  - aminoglycosides: amikacin, gentamicin and tobramycin
  - beta-lactams: penicillins, cephalosporins and carbapenems (e.g. meropenem)
  - chloramphenicol
  - fusidic acid
  - glycopeptides: vancomycin
  - lincosamides: clindamycin
  - linezolid
  - macrolides: azithromycin, clarithromycin and erythromycin
  - nitrofurantoin
  - nitroimidazoles: metronidazole and tinidazole
  - polymyxins: colistin and polymyxin B
  - quinolones: ciprofloxacin, levofloxacin and moxifloxacin
  - tetracyclines: doxycycline
  - antimycobacterials: dapsone, ethambutol, isoniazid, pyrazinamide and rifamycins
- **antifungals**, page 20
  - amphotericin B
  - azoles
  - flucytosine
  - griseofulvin
  - nystatin
  - terbinafine
- **antivirals**, page 22
  - aciclovir
  - tenofovir

cont...

- **antiparasitics**, page 22
  - anthelmintic drugs: albendazole, diethylcarbamazine, ivermectin and pyrantel
  - antimalarial drugs: artemisinin derivatives, chloroquine, primaquine, quinine, sulfadoxine-pyrimethamine
  - other antiprotozoal drugs

Also see:

- 'Appendix 1: Gentamicin dosing' (page 381) and 'Appendix 2: Vancomycin dosing' (page 386).

Antibacterials

Aminoglycosides

This group of antimicrobials includes **amikacin, gentamicin**, **kanamycin**, **streptomycin** and **tobramycin**. Aminoglycosides are rapidly bactericidal and are primarily used to treat infections caused by aerobic Gram-negative bacteria.

Gentamicin is active against most Gram-negative bacteria, including *Pseudomonas aeruginosa*. Gentamicin is the preferred aminoglycoside for empirical treatment when a serious Gram-negative infection is suspected. Gentamicin is not active against Gram-positive organisms but can be used in combination with other antibiotics for treatment of enterococcal or streptococcal endocarditis.

Amikacin, kanamycin and streptomycin are aminoglycosides reserved for second-line therapy for the treatment of *Mycobacterium tuberculosis*.

Gentamicin is the only aminoglycoside included in treatment recommendations in these guidelines. For further information about dosing, monitoring and adverse effects of gentamicin, see 'Appendix 1: Gentamicin dosing,' page 381.

Beta-lactams

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

Beta-lactams have a wide therapeutic index. In most patients, beta-lactams do not cause significant adverse effects; however, some patients are hypersensitive to one or more beta-lactams (see **cross-reactivity between beta-lactams** (page 32) in 'Antimicrobial hypersensitivity').

Penicillins

Narrow-spectrum penicillins

Narrow-spectrum penicillins are mainly active against Gram-positive organisms, including streptococci, some anaerobes and a few other organisms including *Neisseria* species and spirochaetes. However, penicillinase-producing *Neisseria gonorrhoeae* is common, and *Streptococcus pneumoniae* (pneumococcal) strains with decreased susceptibility to penicillin have been reported.

Narrow-spectrum penicillins are inactivated by beta-lactamase enzymes. Most *Staphylococcus aureus* strains will produce beta-lactamase enzymes, so isolates should only be considered penicillin-susceptible if susceptibility is confirmed by a microbiologist.

Phenoxymethylpenicillin (penicillin V) is only given orally. It should be taken on an empty stomach as food impairs absorption. It is intrinsically less active than benzylpenicillin.

Benzylpenicillin (penicillin G or crystalline penicillin) is given intravenously.

Benzathine benzylpenicillin and **procaine benzylpenicillin** are formulated to allow for less frequent administration and are hydrolysed to benzylpenicillin in the body. Benzathine benzylpenicillin is given intramuscularly and results in low blood concentrations of benzylpenicillin for up to 4 weeks. Procaine penicillin is also given intramuscularly and absorbed slowly into circulation but is not on the Papua New Guinea Medical and Dental Catalogue.

Antistaphylococcal penicillins

Flucloxacillin is a narrow-spectrum penicillin that is stable to staphylococcal beta-lactamases. Flucloxacillin is also active against streptococci, so is recommended as first-line therapy for skin and soft tissue infections.

Food impairs the absorption of flucloxacillin so it should be given on an empty stomach, ideally at 6-hourly intervals. However, for practical purposes four-times-daily dosing, evenly spaced during waking hours, is often used.

Flucloxacillin is usually well tolerated but can rarely cause interstitial nephritis and cholestatic jaundice, particularly in older patients on prolonged therapy.

Moderate-spectrum penicillins

Amoxicillin and **ampicillin** 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. However, they are inactivated by beta-lactamase enzymes, and resistance among *E. coli* and *H. influenzae* is now widespread.

They are the drugs of choice for enterococcal infections. Amoxicillin is preferred to phenoxymethylpenicillin for oral treatment of *Streptococcus pneumoniae* infections because it has a longer half-life.

Broad-spectrum penicillins

The beta-lactamase enzyme inhibitors, clavulanate and tazobactam, have little inherent antibacterial activity; they inhibit the beta-lactamase enzymes produced by *S. aureus*, *Bacteroides fragilis* and *H. influenzae*, and some of the beta-lactamase enzymes produced by *E. coli* and *Klebsiella* species. They are used in combination with amoxicillin (**amoxicillin+clavulanate**) or piperacillin (**piperacillin+tazobactam**) to significantly broaden the spectrum of activity of these antibiotics.

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

Piperacillin is only available in combination with tazobactam, and is the only penicillin with activity against *P. aeruginosa*. When used to treat *P. aeruginosa*, piperacillin+tazobactam must be dosed **6-hourly**.

Cephalosporins

Widespread use of cephalosporins is linked to an increasing prevalence of infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), multidrug-resistant Gram-negative bacteria and *Clostridioides difficile*.

All cephalosporins lack activity against enterococci and *Listeria monocytogenes*.

Cephalosporins are grouped into generations according to their spectrum of activity. Currently, there are five generations of cephalosporins; however, only the first three generations are available in Papua New Guinea.

First-generation cephalosporins (moderate-spectrum cephalosporins)

Cefalexin and **cefazolin** have a similar spectrum of antibacterial activity. They are 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 any Gram-negative anaerobic organisms.

Cefalexin is dosed 6-hourly due to a relatively short half-life. However, different dosing frequencies are recommended in these guidelines for some indications. For cystitis, a 12-hourly dosing frequency is recommended due to concentration in the bladder. In children, a 45 mg/kg dose 8-hourly is recommended for the treatment of some bone and joint infections to improve compliance. This is supported by pharmacokinetic, pharmacodynamic and clinical data.

Second-generation cephalosporins (moderate-spectrum cephalosporins with anti-Haemophilus activity)

Cefuroxime has marginally broader Gram-negative activity than cefalexin and cefazolin. Cefuroxime is preferred to cefalexin for the oral treatment of respiratory tract infections because of superior activity against *S. pneumoniae*, *H. influenzae* and *Moraxella catarrhalis*.

Third-generation cephalosporins (broad-spectrum cephalosporins)

Cefotaxime and **ceftriaxone** are broad-spectrum cephalosporins with activity against most enteric Gram-negative bacilli, but they are **not** active against *P. aeruginosa*. Cefotaxime and ceftriaxone are less active against staphylococci than cefazolin, and are inactive against MRSA, but retain excellent activity against streptococci. A major advantage of these antibiotics is that they achieve therapeutic concentrations in the cerebrospinal fluid, making them effective for treatment of meningitis.

Cefotaxime is usually preferred for use in neonates because of the potential risk of bilirubin encephalopathy with ceftriaxone.

Cefixime is an oral third-generation cephalosporin, although its spectrum of activity is not quite as broad as other third-generation cephalosporins. It has little activity against staphylococci but good activity against *N. gonorrhoeae*. It is primarily used as an oral option to treat genitourinary and sexually transmissible infections where gonorrhoea may be involved.

Ceftazidime is a third-generation cephalosporin with activity against *P. aeruginosa*. It is indicated for treatment of suspected or confirmed *P. aeruginosa* infections and melioidosis.

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

Carbapenems

Carbapenems include **meropenem**, **imipenem** and **ertapenem**. They are broad-spectrum antibacterials with activity against many Gram-negative bacteria that are resistant to other classes of antibiotics, including organisms which produce extended-spectrum beta-lactamase (ESBL) enzymes and *P. aeruginosa*. Carbapenems also have excellent activity against anaerobic organisms (including *Bacteroides fragilis*) and many Gram-positive organisms (including streptococci, methicillin-sensitive staphylococci and *Nocardia* species).

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

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

Chloramphenicol

Chloramphenicol is a potent, broad-spectrum antibiotic active against many Gram-positive and Gram-negative bacteria, including anaerobes, *Rickettsia* species and *Chlamydia/Chlamydophila* species. However, it is not effective against *P. aeruginosa*.

Chloramphenicol can be used topically, orally or parenterally. Bioavailability after oral administration is very high. It readily diffuses into many body tissues including pleural and ascitic fluids. Unlike many antibiotics, it penetrates well into all parts of the eye and into the cerebrospinal fluid (CSF) even in the absence of meningitis.

Chloramphenicol is generally well tolerated, but its use has been restricted in many countries due to the risk of 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 to 40 000 courses). Chloramphenicol is safe to use in the first and second trimesters of pregnancy; however, the oral and intravenous formulations should be avoided during the third trimester, while breastfeeding and in neonates due to the risk of grey baby syndrome. Grey baby syndrome (a type of circulatory collapse that can occur in newborn infants, characterised by hypotonia, lethargy, unresponsiveness and peripheral hypoperfusion).

When administered orally or intravenously, where possible, perform baseline complete blood count (CBC), liver and renal function, and serum iron level tests (if available), followed by reticulocyte count and CBC twice weekly while on therapy.

Chloramphenicol inhibits the activity of several liver enzymes and interferes with the biotransformation of phenytoin and warfarin, leading to increased serum levels and potential toxicity, so its use with these drugs should be avoided. Consult an appropriate drug interactions resource when starting macrolides in patients taking other drugs.

Folic acid antagonists

Trimethoprim and **sulfamethoxazole** (a sulfonamide) act by inhibiting bacterial folate production, which is essential for bacterial DNA synthesis. Trimethoprim+sulfamethoxazole is a synergistic combination of these two antimicrobials which act on different stages of the bacterial folate pathway. It is active against a wide variety of aerobic Gram-positive and Gram-negative organisms, including most non–multidrug-resistant MRSA, *Burkholderia* species, *S. maltophilia* and *Nocardia* species, as well as *Pneumocystis jirovecii* and some protozoa. It is not active against most anaerobes.

Trimethoprim (including when used in combination with sulfamethoxazole) 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. Serum potassium should be monitored after 3 days of treatment with trimethoprim in patients at increased risk of hyperkalaemia (e.g. patients with renal impairment, patients taking a high dose of trimethoprim or other drugs that can cause hyperkalaemia).

Trimethoprim+sulfamethoxazole should generally be avoided in the first trimester of pregnancy due to the risk of congenital malformation. It should also be avoided in the last month of pregnancy and in infants younger than 1 month due to the risk of kernicterus.

Oral bioavailability is excellent. Trimethoprim+sulfamethoxazole penetrates well into most tissues and body fluids including sputum, pleural fluid, middle ear fluid and CSF even in the absence of inflamed meninges.

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

Fusidic acid

Fusidic acid (fusidate sodium) has a narrow spectrum of activity. It is active against *S. aureus*, including MRSA. Resistance develops readily, so oral fusidic acid should always be used concomitantly with other antibiotics.

Fusidic acid cream is used to treat superficial staphylococcal soft tissue infection.

Glycopeptides

Vancomycin is a glycopeptide that is active against a wide range of Gram-positive organisms. However, it is usually reserved for treating Gram-positive infections resistant to beta-lactams, particularly MRSA and ampicillin-resistant enterococci, and for patients with immediate hypersensitivity to beta-lactams. Gram-negative organisms are not susceptible to vancomycin. Vancomycin is not absorbed orally; it is only used orally to treat *C. difficile*-associated diarrhoea refractory to treatment with metronidazole. For further information about vancomycin use and monitoring, please see ‘Appendix 2: ‘Principles of vancomycin use’ page 386.

Lincosamides

Clindamycin is active against most Gram-positive aerobic organisms, including streptococci and staphylococcus species (but not enterococci), and most anaerobic bacteria. Clindamycin is not active against Gram-negative organisms.

Clindamycin is commonly used, particularly in skin and soft tissue infections, as second-line therapy for patients with hypersensitivity to penicillins and cephalosporins. Although limited clinical evidence is available, clindamycin is also used in combination with beta-lactams to reduce bacterial toxin production in necrotising skin and soft tissue infections and toxic shock syndromes.

Clindamycin commonly causes antibiotic-associated diarrhoea.

Linezolid

Linezolid is active against Gram-positive bacteria including MRSA, methicillin-resistant coagulase-negative staphylococci, VRE and penicillin-resistant strains of *S. pneumoniae*. In Papua New Guinea, linezolid is reserved for the treatment of multidrug-resistant TB.

Bone marrow suppression and peripheral neuropathy can occur in patients taking linezolid for longer than 14 days, so haematological and neurological monitoring is required.

Linezolid is a weak monoamine oxidase inhibitor, so it significantly interacts with some foods and drugs. Consult an appropriate resource on drug interactions when starting linezolid in patients taking other drugs.

Macrolides

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

Clarithromycin is active against nontuberculous mycobacteria, including *Mycobacterium avium* complex (MAC), and is used in combination with other drugs for treatment of 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 has a broader range of activity against Gram-negative organisms (e.g. *Salmonella* species). Azithromycin is also active against nontuberculous mycobacteria, including MAC, and some parasites (e.g. *Toxoplasma gondii*).

Macrolides attain high intracellular concentrations, which 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 may have significant drug interactions. Consult an appropriate drug interactions resource when starting macrolides in patients taking other drugs. Macrolides can also prolong the QT interval.

Roxithromycin is not recommended for any indication in these guidelines.

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. Therefore, the use of erythromycin in clinical practice is limited. Erythromycin is not recommended for neonates because of the risk of pyloric stenosis.

Nitrofurantoin

Nitrofurantoin is active against organisms that commonly cause urinary tract infection, including many Gram-negative bacilli (e.g. *E. coli*) and Gram-positive cocci (e.g. *Enterococcus faecalis*).

Nitrofurantoin is indicated for the treatment of uncomplicated lower urinary tract infections (e.g. cystitis). **Do not** use it to treat pyelonephritis as it does not achieve adequate concentrations in kidney tissue.

Nitrofurantoin is excreted by the kidneys. Effective treatment of urinary tract infection relies on achieving an adequate concentration of nitrofurantoin in the urine, so treatment is less effective in those with even mild renal impairment.

Nitroimidazoles

Metronidazole and tinidazole have activity against almost all Gram-negative anaerobic bacteria (e.g. *B. fragilis*) and most Gram-positive anaerobic bacteria (*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 intravenously, orally or rectally. Metronidazole crosses the blood–brain barrier, and it is usually well tolerated. Common side effects include nausea, vomiting and a metallic taste in the mouth.

For the treatment of mixed aerobic and anaerobic infections in these guidelines, the recommended dosage of metronidazole is 400 mg orally or 500 mg intravenously, **12-hourly**. The 12-hourly dosing regimen is based on pharmacokinetic data and minimum inhibitory concentrations of the pathogens involved, in addition to limited clinical studies and extensive clinical experience with its use.

Tinidazole has a longer half-life than metronidazole, so it requires less frequent dosing and often a shorter treatment course.

The nitroimidazoles may cause a disulfiram-like reaction when taken with alcohol, resulting in flushing, tachycardia, nausea, vomiting and palpitations. Patients should be advised to avoid alcohol during treatment and for at least 24 hours after completing a course of metronidazole or 72 hours after completing a course of tinidazole.

Caution should be used when giving a prolonged (> 14 days) course of a nitroimidazole due to the risk of peripheral neuropathy.

Polymyxins

Colistimethate sodium (commonly referred to as colistin) and **polymyxin B** are polymyxin antibiotics with activity against many Gram-negative bacteria that are resistant to other drug classes, including *P. aeruginosa* and *Acinetobacter baumannii*.

Polymyxins should only be used with specialist supervision. Their use is associated with severe adverse effects, including renal toxicity and neurotoxicity.

Dosing of polymyxins is complex and dosing recommendations in product information are not appropriate. Seek advice from a clinical microbiologist or infectious disease physician.

Quinolones

Quinolones, including **ciprofloxacin**, **levofloxacin** and **moxifloxacin**, are generally reserved for treatment of infections resistant to other drugs or when alternative antibiotics are contraindicated. Resistance to quinolones is now widespread, particularly in enteric Gram-negative bacilli, *P. aeruginosa*, *Campylobacter* species and *N. gonorrhoeae*.

Ciprofloxacin has a broad spectrum of activity, which includes activity against aerobic Gram-negative bacteria (including *H. influenzae*, enteric Gram-negative bacilli, *P. aeruginosa* and Gram-negative cocci) and some Gram-positive cocci. It is also active against intracellular bacteria, including *Legionella* species and some mycobacteria. Ciprofloxacin has poor activity against anaerobic bacteria and streptococci.

Moxifloxacin has increased activity against Gram-positive aerobic bacteria (including staphylococci and streptococci) compared to ciprofloxacin. Activity against MRSA is variable. Moxifloxacin is active against many aerobic Gram-negative bacteria but has poor activity against *Pseudomonas aeruginosa*. Moxifloxacin has good activity against anaerobic bacteria and most atypical bacteria that cause pneumonia. It is also used for the management of some mycobacterial infections.

Levofloxacin is primarily used as part of second-line regimens for treatment of TB.

Quinolones should be used with caution in children younger than 14 years due to concerns for adverse effects on cartilage development. Quinolones should also be avoided, where possible, during pregnancy and lactation.

Quinolones can cause tendinitis, commonly involving the Achilles tendon, though other tendons can be affected. Risk factors for tendinitis include concomitant corticosteroid use, advanced age, renal impairment and prolonged therapy.

Quinolones have many clinically significant drug interactions. An appropriate resource on drug interactions should be consulted prior to starting quinolones in patients taking other drugs. Quinolones can prolong the QT interval.

Tetracyclines

Doxycycline is a tetracycline with 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 (e.g. *Plasmodium* species).

Unlike older tetracyclines, doxycycline has not been associated with tooth discolouration, enamel hyperplasia or bone deposition, even in children younger than 8 years, so is increasingly used in this age group. However, use is limited by the lack of a suitable commercially available formulation (e.g. an oral liquid formulation).

Oesophagitis can occur with oral doxycycline. It should be taken with food and a full glass of water, and the patient should remain upright for at least an hour after administration. Photosensitivity reactions can also occur, and patients should be warned to avoid sun exposure.

Antimycobacterials

Dapsone

Dapsone is used for the treatment of leprosy and toxoplasmosis and for the treatment and prevention of *P. jirovecii* infection. Glucose-6-phosphate dehydrogenase (G6PD) deficiency should be excluded before starting treatment because patients who are deficient are at risk of severe haemolytic anaemia. Peripheral neuropathy can occur, particularly with daily doses exceeding 200 mg.

Dapsone is structurally similar to sulfonamides. Cross-reactivity between dapsone and sulfamethoxazole is 9 to 12%. Do not use dapsone in patients with immediate hypersensitivity or another severe reaction (e.g. drug rash with eosinophilia and systemic symptoms (DRESS) or Stevens–Johnson syndrome) to sulfonamides.

Ethambutol

Ethambutol is used to treat TB and nontuberculous mycobacterial infections. Ethambutol can cause optic neuritis – check visual acuity (clarity of vision) and colour vision before starting treatment and instruct patients to report any changes in vision. Stop ethambutol immediately if visual symptoms develop.

Isoniazid

Isoniazid is used as part of combination treatment for *M. 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, excessive alcohol consumption and pre-existing liver disease.

Pyrazinamide

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

Rifamycins

Rifampicin is used in the treatment of TB and for some *S. aureus* infections. It is also used as prophylaxis for contacts of patients with *H. influenzae* type B infection and meningococcal disease. Since resistance emerges rapidly, it should always be used in combination with other antibiotics (except when used as prophylaxis).

Rifampicin may cause hepatitis, so liver function tests should be monitored regularly. Patients should be warned that rifampicin will cause orange discolouration of body fluids, including urine, sweat and tears.

Rifampicin has many clinically significant drug interactions. Consult an appropriate drug interaction resource prior to commencing rifampicin in patients taking other drugs. Commonly used drugs that interact with rifampicin include the oral contraceptive pill, warfarin, glucocorticoids and statins.

Antifungals

Amphotericin B

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

Amphotericin B is associated with significant toxicity, including infusion-related ‘flu-like’ reactions, nephrotoxicity, electrolyte abnormalities and anaemia. Adverse

reactions are particularly common with amphotericin B deoxycholate (the conventional form of amphotericin B); the liposomal formulation is generally better tolerated.

To minimise toxicity with amphotericin B deoxycholate, prehydrate the patient with sodium chloride 0.9% (0.5 to 1 L intravenously) prior to infusion, and consider pretreatment with hydrocortisone, an antihistamine, an antiemetic, an analgesic or an antipyretic.

The dosage and infusion rates for each amphotericin B formulation is significantly different.

Exercise caution when prescribing and administering amphotericin B as errors have caused fatalities.

Azoles

Fluconazole is active against most yeasts, including *Candida* species (but not *Candida krusei*), and *Cryptococcus* species. Fluconazole has no activity against moulds. It is well absorbed after oral administration and has good central nervous system penetration.

Fluconazole interacts with many other drugs (including commonly prescribed drugs such as amiodarone, clopidogrel, phenytoin and warfarin). It is generally well tolerated but can cause gastrointestinal upset and hepatic dysfunction. Fluconazole may prolong the QT interval.

Ketoconazole, clotrimazole and miconazole are available in PNG as topical preparations for the treatment of superficial fungal infections.

Flucytosine

Flucytosine is used in combination with amphotericin B for synergistic activity for cryptococcal infections. Use with caution in patients with renal impairment as high plasma concentrations of flucytosine are associated with bone marrow toxicity. All patients receiving flucytosine should have a full blood count monitored regularly to monitor for adverse events.

Griseofulvin

Griseofulvin is used for the treatment of tinea capitis and kerion. When given orally, it concentrates in keratinised tissues and prevents further invasion by dermatophytes.

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.

Terbinafine

Terbinafine is available in oral and topical formulations for the treatment of fungal skin infections and onychomycosis. Taste disturbance is an uncommon adverse effect of terbinafine; resolution of the disturbance can be delayed (several weeks up to a year) and is rarely permanent.

Antivirals

Aciclovir

Aciclovir is active against herpes virus infections, particularly herpes simplex virus (HSV) (types I and II) and varicella-zoster virus. Aciclovir is available in oral, intravenous and topical formulations. It is poorly and erratically absorbed orally.

Oral aciclovir is used for skin, mucous membrane and eye infections. Intravenous aciclovir is used for the treatment of HSV encephalitis and disseminated shingles. Renal function should be monitored closely during treatment.

Tenofovir

Tenofovir is a nucleotide reverse transcriptase inhibitor which is used for the treatment of chronic hepatitis B virus (HBV) infection and HIV (in combination with other agents). Two formulations of tenofovir are available; tenofovir disoproxil fumarate and tenofovir alafenamide (which is the preferred formulation for patients with renal impairment).

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.

For practical information on using antiretrovirals, see *Papua New Guinea National Guidelines for HIV Care and Treatment*.

Antiparasitic drugs

Anthelmintic drugs

Albendazole

Albendazole is primarily used to treat intestinal worm infections, such as roundworm (*Ascaris lumbricoides*), threadworm (or pinworm) (*Enterobius vermicularis*), hookworm (*Ancylostoma duodenale* and *Necator americanus*), dog hookworm (*Ancylostoma caninum*), whipworm (*Trichuris trichiura*) and strongyloidiasis (*Strongyloides stercoralis*). Albendazole is also used for community deworming programs.

Albendazole is used as an adjunct to surgery or percutaneous drainage for treatment of hydatid disease (*Echinococcus* species) and for treatment of neurocysticercosis. It is used as an alternative to ivermectin for treatment of cutaneous larva migrans.

The main adverse effects of albendazole are elevated liver transaminases, gastrointestinal upset and haematological abnormalities (e.g. leucopenia). Albendazole should be avoided in the first trimester of pregnancy and in children less than 6 months.

For treatment of systemic infections, albendazole should be taken with a fatty meal to improve absorption. In contrast, when treating intestinal worms, it should be taken on an empty stomach to limit systemic absorption.

Diethylcarbamazine

Diethylcarbamazine (DEC) is used for the treatment of lymphatic filariasis. Adverse effects of DEC are usually attributable to the host's response to the death of microfilariae; common symptoms include nausea, headache, fever and arthralgias.

Ivermectin

Ivermectin is used to treat filariasis, strongyloidiasis, scabies, head lice and cutaneous larva migrans. It is not currently licensed for use in children weighing less than 15 kg because of a lack of safety data. However, limited data suggest that oral ivermectin in children weighing less than 15 kg is well tolerated with no serious or long-term adverse effects.

Absorption of ivermectin is improved when taken with food.

Ivermectin can cause hypersensitivity reactions when used for filarial infections. These reactions are usually transient and respond to analgesics and antihistamines.

Pyrantel

Pyrantel can be given for intestinal worm infections as an alternative to albendazole for women in the first trimester of pregnancy and in infants < 6 months. Adverse effects are uncommon.

Antimalarial 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 the lumefantrine.

Chloroquine

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, including Papua New Guinea. Chloroquine is therefore no longer recommended as a first-line treatment option for malaria. It may be used as prophylaxis or treatment in some cases. Common side effects include headache, skin eruptions, itch and gastrointestinal disturbance. It should be taken with food to reduce stomach upset.

The dose is sometimes provided in mg of chloroquine base and sometimes chloroquine phosphate. Check if the product is available before prescribing or administering. 250 mg chloroquine phosphate is equivalent to 155 mg chloroquine base.

Primaquine

Primaquine is essential for the treatment of malaria caused by *P. vivax* and *P. ovale* because it eradicates dormant parasites (hypnozoites) in the liver that can reactivate, resulting in relapsed malaria.

Exclude glucose-6-phosphate dehydrogenase (G6PD) deficiency prior to starting treatment with primaquine as patients who are deficient are at risk of developing severe haemolysis. Adverse effects of primaquine include gastrointestinal disturbances and methaemoglobinaemia.

Quinine

Quinine is used orally to treat uncomplicated malaria and intravenously to treat severe 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, hypoglycaemia, electrocardiogram (ECG) changes and, in patients with G6PD deficiency, haemolytic anaemia. Monitor blood glucose concentration, blood pressure and ECG during intravenous treatment.

Sulfadoxine-pyrimethamine

Sulfadoxine-pyrimethamine is a combination agent of two folic acid antagonists which is used for the prevention and treatment of acute uncomplicated *Plasmodium falciparum* malaria and toxoplasmosis.

Gastrointestinal upset and headache are common. Bone marrow suppression can occur, and haemolytic anaemia may occur in patients with G6PD deficiency. The sulfonamide component may be associated with severe cutaneous allergic reactions (e.g. Stevens–Johnson syndrome). It should be used with caution in those with renal or hepatic dysfunction.

Other antiprotozoal drugs

Benzyl benzoate

Benzyl benzoate is an alternative to permethrin for the treatment of scabies and lice. Skin irritation is common. It should be diluted with water before application in children, and it can be diluted in adults who experience excessive stinging with the undiluted preparation.

Gamma benzene hexachloride

Gamma benzene hexachloride (also known as GBH or lindane) lotion is not on the Papua New Guinea Medical and Dental Catalogue but is widely available in the community as a treatment for scabies. However, it has been associated with neurotoxicity, including seizures. It should be used with caution in infants, children, pregnancy, the elderly and people with other skin conditions (e.g. atopic dermatitis, psoriasis), and in those who weigh less than 50 kg as they are at increased risk of neurotoxicity. It is contraindicated in premature infants and for people with an uncontrolled seizure disorder.

Permethrin

Permethrin is a topical insecticide used for the treatment of scabies and lice. It is generally well tolerated and is the treatment of choice for scabies because of its low toxicity and high efficacy. It is available as a lotion and a cream; a higher strength (5%) is required for scabies treatment. Itch, redness and swelling, which often accompany lice infestations, may be temporarily increased by permethrin.

Key additional references

Jittamala P, Monteiro W, Smit MR, Pedrique B, Specht S, Chaccour CJ, Dard C et al. A systematic review and an individual patient data meta-analysis of ivermectin use in children weighing less than fifteen kilograms: Is it time to reconsider the current contraindication? PLoS Negl Trop Dis. 2021 Mar 17;15(3):e0009144.

Wilkins AL, Steer AC, Cranswick N, Gwee A. Question 1: Is it safe to use ivermectin in children less than 5 years of age and weighing less than 15 kg? Archives of Disease in Childhood 2015; 103:514-519.

Antimicrobial hypersensitivity

This topic includes information and advice on antimicrobial hypersensitivity:

The following topic is not included in this section:

- **adverse effects of antimicrobials**, see page 5 in 'Principles of antimicrobial use.'

Introduction to antimicrobial hypersensitivity

'Hypersensitivity' is a broad term for unpredictable adverse drug reactions, which can be caused by immune-mediated or other mechanisms. 'Allergy' refers to an immune-mediated hypersensitivity.

It is common for patients to report a history of allergy to an antimicrobial (usually penicillin), and this can present a dilemma. If the antimicrobial is administered to a patient who is truly allergic, a serious reaction can occur. However, many patients who report an allergy will tolerate the drug when it is administered again. A history of antimicrobial allergy often dates back to a suspected reaction that occurred in childhood, and it is commonly described as a rash with vague features not typical of an immune-mediated hypersensitivity reaction. Few childhood reactions are reproducible in adulthood, and over 90% of reported penicillin allergies can be excluded by antibiotic allergy testing.

Careful assessment of antimicrobial hypersensitivity ensures that patients are not unnecessarily denied the most effective treatment or treated unnecessarily with broad-spectrum antibiotics. Recent research has found that when an antimicrobial allergy is documented in the medical record, patients are more likely to receive inappropriate antibiotic therapy and have inferior clinical and microbiological outcomes.

Antimicrobial hypersensitivity reactions are classified by timing and severity. The classifications outlined in Figure 4 (next page) will be used throughout these guidelines.

Figure 4: Examples of antimicrobial allergy, classified by severity and timing

	Severe	Nonsevere
Immediate	Anaphylaxis, angioedema, airway compromise, hypotension, extensive urticaria	Mild urticaria or mild immediate rash
Delayed	Severe cutaneous adverse drug reactions (e.g. DRESS, SJS/TEN), or significant internal organ involvement (e.g. acute interstitial nephritis)	Benign childhood rash or maculopapular rash

DRESS = drug rash with eosinophilia and systemic symptoms; SJS/TEN = Stevens–Johnson syndrome / toxic epidermal necrolysis.

Types of antimicrobial hypersensitivity

The most common types of immune-mediated hypersensitivity reactions are immediate immune-mediated (IgE) and delayed immune-mediated (T-cell) reactions. Immediate or acute reactions that are not IgE-mediated can also occur, for example vancomycin infusion-related 'red man' syndrome. These are usually caused by mast-cell degranulation and may be ameliorated by prophylactic antihistamines and slowing the infusion rate. Antibiotic allergies can be classified as immediate or delayed, severe or nonsevere (see Figure 4 above).

Immediate immune-mediated (IgE) 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, airway compromise, angioedema, hypotension or anaphylaxis. The reaction occurs up to 2 hours after exposure to the drug. Anaphylaxis is more likely with parenteral rather than oral administration.

A clear history of an IgE-mediated reaction means the drug (and sometimes related drugs) should not be administered again unless appropriate precautions have been taken (e.g. desensitisation).

Delayed immune-mediated (T-cell) hypersensitivity reactions

Delayed immune-mediated hypersensitivity reactions 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 onset days after starting treatment. However, they can occur more rapidly on rechallenge (within 6 hours).

Delayed hypersensitivity reactions are much more common than immediate reactions, and the majority are not severe. They often occur in patients with a viral infection and can be due to the infection itself or a drug–virus interaction. Such reactions are often not reproducible upon supervised challenge when the patient is well.

Severe delayed hypersensitivity

Severe delayed reactions are uncommon but serious. They include severe cutaneous adverse reactions (SCAR), a group of T-cell mediated hypersensitivities with cutaneous plus internal organ or mucous membrane involvement.

Examples of delayed severe reactions include:

- DRESS: characterised by fever, eosinophilia, desquamative dermatitis and liver or kidney dysfunction.
- SJS/TEN: a rare, acute and potentially fatal skin reaction caused by acute keratinocyte death, resulting in sheet-like skin and mucosal loss similar to burn injuries.
- acute generalised exanthematous pustulosis: characterised by pin-sized pustules on a background of erythema, often with fever and leucocytosis, and rarely, organ involvement. Can have an onset within 1 day of drug administration.
- acute interstitial nephritis: most commonly associated with penicillins. Causes kidney dysfunction and can include eosinophilia, fever and exanthematous rash.
- serum sickness: characterised by vasculitic rash, arthralgia/arthritis, influenza-like symptoms and sometimes fever and proteinuria.
- drug-induced liver injury.

A delayed severe hypersensitivity reaction is a contraindication to further drug exposure (including desensitisation) as this can be fatal.

Diagnosis of antimicrobial hypersensitivity

Clinical history is the single most important component in the diagnosis of antimicrobial hypersensitivity. If hypersensitivity is reported, ask about the nature and severity of the reaction, timing of the reaction in relation to the drug exposure, how it was managed and whether the patient has tolerated any other antibiotics since the reaction. Accurate and detailed documentation of antimicrobial hypersensitivity in the patient record is essential.

Isolated intolerances such as gastrointestinal upset or headache are commonly reported with antimicrobials and do not indicate hypersensitivity. A family history of antimicrobial allergy does not justify avoidance of the implicated drug.

The PEN-FAST penicillin allergy risk tool (see Figure 5 below) is a simple, validated tool that enables point-of-care risk assessment of patients with reported penicillin allergies. A patient with a PEN-FAST score less than 3 may be able to have their penicillin allergy directly de-labelled or undergo a drug challenge.

Figure 5: PEN-FAST penicillin allergy risk tool

PEN	*P*enicillin allergy reported by patient	☐ *If yes, proceed with assessment*
F	*F*ive years or less since reaction[Note 1]	☐ **2 points**
A	*A*naphylaxis or angioedema	
	OR	☐ **2 points**
S	Severe cutaneous adverse reaction[Note 2]	
T	*T*reatment required for reaction[Note 1]	☐ **1 point**
		☐ **Total points**

Interpretation

Points	
0	**Very low risk** of positive penicillin allergy test <1% (<1 in 100 patients reporting penicillin allergy)
1-2	**Low risk** of positive penicillin allergy test 5% (1 in 20 patients)
3	**Moderate risk** of positive penicillin allergy test 20% (1 in 5 patients)
4-5	**High risk** of positive penicillin allergy test 50% (1 in 2 patients)

Adapted with permission from: Trubiano JA, Vogrin S, Chua KYL, Bourke J, Yun J, Douglas A, Stone CA, Yu R, Groenendijk L, Holmes NE, Phillips EJ. Development and Validation of a Penicillin Allergy Clinical Decision Rule. JAMA Intern Med. 2020 May 1;180(5):745-752. doi: 10.1001/jamainternmed.2020.0403.

Note 1: Includes unknown.

Note 2: Forms of severe delayed reactions include potential Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms, and acute generalised exanthematous pustulosis. Patients with a severe delayed rash with mucosal involvement should be considered to have a severe cutaneous adverse reaction. Acute interstitial nephritis, drug induced liver injury, serum sickness and isolated drug fever were excluded phenotypes from the derivation and validation cohorts.

If after detailed history taking, a reported allergy is subsequently excluded, the patient's medical record should be updated, including information about how the allergy was excluded.

Allergy testing for assessing patients with a history of immune-mediated hypersensitivity is offered in specialist centres internationally, but it is not currently available in Papua New Guinea.

Drug provocation testing

Drug provocation testing, also called drug challenge, is the controlled administration of a drug in order to diagnose hypersensitivity. It is often used to confirm tolerance to an antimicrobial when skin-prick testing is negative or allergy history means that hypersensitivity is very unlikely.

Drug provocation testing should only be performed under medical supervision, after consultation with a specialist, in a safe environment where severe allergic reactions such as anaphylaxis can be managed, and after obtaining informed consent from the patient.

Desensitisation

Drug desensitisation renders mast cells temporarily unresponsive so that a patient with a history of antimicrobial hypersensitivity can receive the drug. Desensitisation remains effective while the patient is continuously exposed to the drug, but hypersensitivity will return soon after the drug is cleared.

Desensitisation is predominantly used in patients with a history of IgE-mediated immediate hypersensitivity for whom there are no appropriate alternative antimicrobials, or when a particular antimicrobial is the preferred drug (e.g. benzylpenicillin for streptococcal endocarditis).

Desensitisation has been best validated for penicillins, but it has also been described for other antimicrobials.

Desensitisation should be performed in a hospital setting, where the patient can be closely monitored and resources to manage anaphylaxis and threatened airway are available. Seek expert advice prior to performing drug desensitisation on a patient.

Desensitisation is contraindicated in patients with a history of delayed severe immune-mediated hypersensitivity.

Cross-reactivity between beta-lactams

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

It is a common misconception that cephalosporin allergy occurs in approximately 10% of patients who are allergic to a penicillin. However, a recent review found that only 1 to 2% of patients with confirmed penicillin allergy have a cephalosporin allergy. Cefazolin has no common side-chains with other beta-lactams so is often tolerated in patients with a penicillin or cephalosporin allergy.

In settings where allergy testing is not available and a beta-lactam antibiotic is the preferred drug, antimicrobials to avoid based on potential cross-reactivity due to identical or similar R1 side-chains are:

- amoxicillin or ampicillin allergy: avoid cefalexin or cefaclor (except in delayed nonsevere hypersensitivity)
- ceftriaxone allergy: avoid cefotaxime and cefuroxime.

Cross-reactivity between penicillins and carbapenems is approximately 1%.

In patients with a history of an **immediate severe** reaction to penicillins, penicillins and cephalosporins should be avoided in most situations. However, in a critical situation when a beta-lactam is the preferred drug, a cephalosporin can be considered after undertaking a risk–benefit analysis, assessment of potential side-chain cross-reactivity and seeking expert advice.

In patients with a **delayed severe** penicillin hypersensitivity, **do not use cross-reactivity to guide treatment** and avoid all penicillins and cephalosporins.

Cross-reactivity between sulfonamides

Antibiotic sulfonamides (e.g. sulfamethoxazole, sulfadiazine, dapsone) are often avoided in patients who are allergic to nonantibiotic sulfonamides (e.g. frusemide [furosemide]). However, this is usually not necessary because, with one exception, there is no cross-reactivity between antibiotic and nonantibiotic sulfonamides. The exception is sulfasalazine, a nonantibiotic sulfonamide that is structurally similar to sulfonamide antibiotics. Avoid sulfasalazine in patients with antibiotic sulfonamide allergy, and vice versa.

Evidence shows that the rate of immune-mediated cross-reactivity within the antibiotic sulfonamide group (e.g. between sulfamethoxazole and dapsone) is lower (9 to 12%) than previously thought (20%), and therefore these antibiotics could be used in a patient with a history of nonsevere allergy to another antibiotic sulfonamide. However, this does not apply in patients with anaphylaxis or a severe cutaneous adverse reaction such as drug rash with eosinophilia and systemic symptoms (DRESS) or Stevens–Johnson syndrome/toxic epidermal necrolysis (SJS/TEN).

Differential diagnosis of infectious conditions

This topic includes advice on differentiating and diagnosing generalised or systemic infectious conditions.

For information on managing these conditions, see:

- **bacterial sepsis (empirical management of sepsis or septic shock)** page 247 in 'Sepsis and bloodstream infections'
- **typhoid fever** page 148 in 'Gastrointestinal tract infections'
- **dengue** - refer to local treatment protocols
- **malaria** refer to the *National Malaria Treatment Protocol*
- **leptospirosis** page 345 in 'Miscellaneous infections'
- **spotted fever** (rickettsial infections) page 346 in 'Miscellaneous infections'
- **murine typhus** page 346 in 'Miscellaneous infections'
- **scrub typhus** page 346 in 'Miscellaneous infections'
- **Japanese encephalitis** page 87 in 'Central nervous system infections'
- **acute rheumatic fever** page 341 in 'Miscellaneous infections.'

The table on the following pages was developed to assist clinicians in differentiating generalised or systemic infectious disease conditions and the recommended confirmatory tests. Note that clinical presentations can be variable and all features described might not be present; this table is just a guide.

Table 1: Differential diagnosis of generalised or systemic infectious disease conditions

Disease	Risk factors	Clinical characteristics
bacterial sepsis [Note 1]	indwelling device, recent surgery or wound, re-presentation to emergency department, immune compromise, age > 65 years or < 3 months, fall, deterioration despite treatment	fever / rigors, hypotension, low oxygen saturation, tachycardia, raised respiratory rate, hypothermia, altered level of consciousness, non-blanching rash site specific: dysuria, cough, dyspnoea, abdominal pain / distension/ peritonism, recent delivery or miscarriage
typhoid fever	endemic typhoid known in that area patient resides in an urban settlement with poor water	fever (high and persistent), abdominal cramps, constipation, anorexia +/- nausea and vomiting, head and body aches, weakness /fatigue, +/- confusion +/- enlarged liver and spleen, hypotension, tachycardia
dengue	known cases occurring in locality / outbreaks	fever, myalgia and arthralgia, rash, nausea and vomiting, bleeding manifestations (e.g. petechiae, easy bruising), hypotension, tachycardia
malaria	known cases occurring in locality traditional or other basic housing and no use of bed nets	fever (may exhibit cycles every 48 to 72 hours), headache, fatigue, nausea and vomiting, jaundice, anaemia, hypotension, tachycardia
leptospirosis	river water exposure other known local cases	fever, headache, myalgia, conjunctival suffusion (redness without discharge), jaundice, abdominal pain, renal failure, hypotension, tachycardia
spotted fever (rickettsial infections)	tick bite	fever, rash (may develop petechiae), with or without eschar (blackish scab) at the site of the tick bite, arthralgia, headache
murine typhus	patient resides in an urban settlement (PNG epidemiology uncertain)	fever, headache, rash (may develop petechiae), myalgia, nausea and vomiting, abdominal pain
scrub typhus	rural setting (PNG epidemiology uncertain)	fever, eschar (blackish scab) at the site of the tick bite, headache, myalgia, rash (may develop petechiae), lymphadenopathy
Japanese encephalitis (JE)	coastal location other known local cases/outbreak	fever, headache, altered mental status, seizures, rash
acute rheumatic fever [Note 2]	age 5 to 16 years (but can occur in adults)	fever, joint pain and swelling, chest pain, shortness of breath, rash, heart murmur

Continued on next page.

Note 1: For further advice, see Australia Sepsis Kills Program pathways (adult, paediatric, perinatal and neonatal versions): www.cec.health.nsw.gov.au/keep-patients-safe/sepsis/sepsis-tools

Note 2: RHD Australia has an app for diagnostic guidance. https://www.rhdaustralia.org.au/apps

cont...

Table 1: Differential diagnosis of generalised or systemic infectious disease conditions (continued)

Disease	WCC / other	Platelets	CRP [Note 3]	Confirmatory test(s)
bacterial sepsis	leucocytosis high venous or arterial lactate (> 4) and/or low base excess (< negative 5.0)	variable	high (may take 8-12 hrs to rise)	blood culture culture of specific sites e.g. CSF, urine, joint, peritoneal or pleural fluid
typhoid fever	leucocytosis	variable	high	blood culture, stool culture Widal test **not** recommended (poor specificity)
dengue	leucopenia or normal	low	normal to moderate elevation	RDT – NS1 antigen
malaria	variable	low	normal to moderate elevation	RDT- malaria microscopy - thick film
leptospirosis	leucocytosis	low	normal to moderate elevation	no testing currently available [Note 4]
spotted fever (rickettsial infections)	leucocytosis	low	mild elevation	no testing currently available [Note 4]
murine typhus	leucocytosis	low	mild elevation	no testing currently available [Note 4]
scrub typhus	leucocytosis	low	high	no testing currently available [Note 4]
Japanese encephalitis (JE)	normal or mild elevation	normal or mild reduction	normal to mild elevation	send CSF sample to CPHL for testing by ELISA
acute rheumatic fever	variable	normal or mild reduction	moderate to high	no testing currently available [Note 5]

CPHL = Central Public Health Laboratory, CRP = C-reactive protein, CSF = cerebrospinal fluid, ELISA = enzyme-linked immunosorbent assay, RDT = rapid diagnostic test, WCC = white cell count

Note 3: CRP is the recommended assay for detecting an acute phase reaction to infection. While it is more specific than erythrocyte sedimentation rate (ESR) for infection, it is also elevated in a range of noninfective syndromes.

Note 4: Retrospective diagnosis may be possible – seek advice from PMGH Pathology.

Note 5: See acute rheumatic fever, page 341 in 'Miscellaneous infections' for further information.

Bone and joint infections

This topic includes advice on the management of the following conditions in adults and children 3 months and older:

- **osteomyelitis**, page 39
  - adults: long-bone, page 40 and vertebral, page 42
  - children (long-bone and vertebral), page 48
- **septic arthritis**, page 51
- infection of **bone and joint prostheses**, page 56
- **open fractures**, page 56
- **maxilla or mandible fractures**, page 60.

The following topics are not included in this section:

- **mandibular osteomyelitis** (page 100) in 'Dental infections'
- **septic arthritis** in neonates and infants younger than 3 months (page 207) in 'Infections in neonates and young infants.'

Osteomyelitis

Osteomyelitis is an infection involving bone. Osteomyelitis is classified by its anatomical location (long bone or vertebral) and time course (acute or chronic).

Long-bone osteomyelitis most commonly occurs in children, with haematogenous seeding of bacteria to the well-vascularised metaphyseal bone adjacent to the physis (growth plate).

Acute osteomyelitis is when bone infection symptoms are present for less than 2 weeks. Chronic osteomyelitis is bone infection with symptoms over months to years. The presence of a sinus tract is pathognomonic (distinctively characteristic) for chronic osteomyelitis. Unlike in other settings, osteomyelitis occurs following trauma more frequently than haematogenous spread in Papua New Guinea.

The most likely causative agents are *Staphylococcus aureus* for long-bone osteomyelitis or TB for vertebral osteomyelitis but occasionally *Streptococcus* species and *Salmonella* species are causes. Chronic infections are often polymicrobial, involving Gram-positive and Gram-negative aerobic and anaerobic bacteria.

Consider methicillin-resistant *S. aureus* (MRSA) in patients not improving with empirical therapy if microbiology is not available to confirm diagnosis.

Chronic osteomyelitis will require surgical debridement in addition to antibiotics for cure.

Take blood cultures and/or collect pus or a bone specimen for microscopy and undertake culture and susceptibility testing and histology before starting therapy, if available. Tailor antibiotic therapy to the results of culture and susceptibility testing.

For information on duration of therapy, including timing of switch to oral therapy, see Table 3 for osteomyelitis in adults (page 47) and Table 4 for osteomyelitis in children (page 50).

For patients with bacteraemia (i.e. positive blood cultures), a longer duration of intravenous antibiotics is needed; see 'Sepsis and bloodstream infections,' page 245.

Long-bone osteomyelitis in adults

The affected limb is usually hot, swollen and tender. The ends of the long bones are commonly affected. Pathologically, there is low-grade inflammation, and the presence of sequestra or an involucrum (new bone) formation adjacent to a sequestrum.

The alternative diagnosis of cellulitis should also be considered, but only made with caution.

Management of long-bone osteomyelitis in adults

Empirical therapy for long-bone osteomyelitis in adults

For information on duration of therapy, including timing of switch to oral therapy, see Table 3 (page 47).

For initial empirical therapy, use:

flucloxacillin *2 g IV, 6-hourly.*

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

cefazolin *2 g IV, 8-hourly.*

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

chloramphenicol *1 g IV, 6-hourly.*

Selection of ongoing therapy for long-bone osteomyelitis in adults

For patients improving on initial empirical therapy

Switch to oral therapy when appropriate (see Table 3, page 47) based on the identified organism (see directed therapy and IV to oral switch below).

For patients **not** improving on initial empirical therapy

For patients on flucloxacillin or cefazolin who do not clinically improve within 3 to 4 days, **add** chloramphenicol to cover potential MRSA:

chloramphenicol *1 g IV, 6-hourly.*

For all cases, consider infection caused by TB or Gram-negative pathogens. Take open tissue specimens or needle biopsy for microscopy and culture, and GeneXpert testing for TB, if possible.

Directed therapy and IV to oral switch for long-bone osteomyelitis in adults

For patients with positive blood cultures, see the relevant section in **directed therapy for bloodstream infections** (page 253) in 'Sepsis and bloodstream infections,' for ongoing management.

For information on duration of therapy, including timing of switch to oral therapy, see Table 3 (page 47).

Methicillin-susceptible *Staphylococcus aureus* (MSSA)

For infection caused by methicillin-susceptible *S. aureus* (MSSA), continue intravenous flucloxacillin (or alternative in patients with penicillin hypersensitivity) until it is appropriate to switch to oral antibiotics (see Table 3, page 47).

For oral therapy, use:

flucloxacillin *1 g orally, 6-hourly.*

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

cefalexin *1 g orally, 6-hourly.*

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

chloramphenicol *500 mg orally, 6-hourly.*

Methicillin-resistant *Staphylococcus aureus* (MRSA)

For patients with proven methicillin-resistant *S. aureus* (MRSA), use initially:

vancomycin *slow IV infusion,* ***consider a loading dose in critically ill adults****. See 'Appendix 2: Vancomycin dosing' (page 386) for information on loading dose, dosing frequency and infusion time.*

adult ≥ 40 years: 15 mg/kg, see Table 18 for dosing frequency (page 390)

adult < 40 years 20 mg/kg, see Table 17 for dosing frequency (page 389).

When it is appropriate to switch to oral antibiotics, based on the results of susceptibility testing, use:

trimethoprim+sulfamethoxazole *320+1600 mg orally, 12-hourly*

OR

clindamycin *450 mg orally, 8-hourly.*

Gram-negative bacteria

Ciprofloxacin is the drug of choice for susceptible Enterobacterales and *Pseudomonas* species. Use:

ciprofloxacin *750 mg orally, 12-hourly.*

Organism unknown

If the results of susceptibility testing are not available, use:

flucloxacillin *1 g orally, 6-hourly*

PLUS

chloramphenicol *500 mg orally 6-hourly.*

Vertebral osteomyelitis in adults

Tuberculosis infection is the most common cause of vertebral osteomyelitis in Papua New Guinea – see Table 2 (page 43) for differences between spinal TB and pyogenic infection. If spinal TB is suspected or proven, see the *National Tuberculosis Management Protocol* for management.

The next most common causative pathogen is *Staphylococcus aureus*. Gram-negative organisms (e.g. *Escherichia coli* and *Klebsiella pneumoniae*) and enterococci are less common pathogens.

Other causes of vertebral pain and erosion, such as malignancy, should also be considered.

After evaluating the clinical presentation and radiological findings (see Table 2 below), decide whether tuberculosis or pyogenic infection is more likely. If the diagnosis is unclear, obtain a timely open or needle biopsy for microscopy, culture and GeneXpert testing, if possible.

Monitor clinical response and inflammatory markers (e.g. C-reactive protein or erythrocyte sedimentation rate). If the patient is not improving on initial empirical treatment, consider the following pathogens and alternative causes and seek appropriate advice:

- TB
- MRSA
- multidrug-resistant Gram-negative organisms
- noninfective diagnosis e.g. malignancy or multiple myeloma.

Table 2: Clinical and radiological differences between spinal TB and vertebral pyogenic infection in adults and children

	Tuberculous spondylitis	**Vertebral pyogenic infection**
Age	younger	older
Risk factors	n/a	intravenous drug use documented prior bacteraemia (usually *Staphylococcus aureus*)
Clinical symptoms	longer duration and intermittent fever	shorter duration and high fever
Commonly involved region	thoracolumbar spine	lumbar spine
Levels	frequently multilevel, more severe destruction	≤2 levels, mild to moderate destruction
Disc involvement	normal to mild destruction	involved early; moderate to severe destruction
Spread beneath the anterior longitudinal spinal ligament	frequently extensive	limited
Skip lesions	frequent	rare
Paraspinal soft tissue/ abscess	well-defined, large	less well defined, small

cont...

Enhancement of abscess wall	thin, smooth	thick, irregular, nodular
Calcification on CT	may be present	absent

Sources:

Chaudhary, K. Dhawale, A. Chaddha, R. Laheri, V. Spinal tuberculosis – an Update. Bombay Orthopaedic Society. Vol 2; issue 1. Jan-June 2017.

Kritsaneepaiboon, S. Skeletal Involvement in Pediatric Tuberculosis. WFPI TB Corner 2016; 2 (2):1-6.

Non-tuberculous vertebral osteomyelitis in adults who have a normal neurological examination

Empirical therapy

Use:

flucloxacillin *2 g IV, 6-hourly.*

For adults with **immediate nonsevere** or **delayed nonsevere** hypersensitivity to penicillins, use:

cefazolin *2 g IV, 8-hourly.*

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

vancomycin *slow IV infusion,* ***consider a loading dose in critically ill adults****. See 'Appendix 2: Vancomycin dosing' (page 386) for information on loading dose, dosing frequency and infusion time.*

adult ≥ 40 years: 15 mg/kg, see Table 18 for dosing frequency (page 390)

adult < 40 years 20 mg/kg, see Table 17 for dosing frequency (page 389).

If vancomycin is not available, use:

chloramphenicol *1 g IV, 6-hourly.*

Monitor clinical response and inflammatory markers (e.g. CRP or ESR).

If the patient is **not** improving, consider alternative pathogens (TB, MRSA, multidrug-resistant Gram-negative organisms) and seek appropriate advice.

Modify therapy according to the results of culture and susceptibility testing, if available.

Ongoing management

Modify therapy according to the results of culture and susceptibility testing, if available. For information on duration of therapy, including timing of switch to oral therapy, see Table 3 (page 47).

If the results of culture and susceptibility testing are **not** available, for patients who improved on initial empirical therapy, when appropriate, switch to:

flucloxacillin *1 g orally, 6-hourly.*

For adults with **immediate nonsevere** or **delayed nonsevere** hypersensitivity to penicillins, use:

cefalexin *1 g orally, 6-hourly.*

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

trimethoprim+sulfamethoxazole *320+1600 mg orally, 12-hourly.*

For information on duration of therapy, see Table 3 (page 47).

Non-tuberculous vertebral osteomyelitis in adults associated with epidural abscess or progressive neurological compromise

Empirical therapy

As a three-drug regimen, use initially:

flucloxacillin *2 g IV, 6-hourly*

PLUS

vancomycin *slow IV infusion,* ***consider a loading dose in critically ill adults****. See 'Appendix 2: Vancomycin dosing' (page 386) for information on loading dose, dosing frequency and infusion time.*

adult ≥ 40 years: 15 mg/kg, see Table 18 for dosing frequency (page 390)

adult < 40 years 20 mg/kg, see Table 17 for dosing frequency (page 389)

PLUS

ceftriaxone *2 g IV, 12-hourly.*

cont...

For adults with **immediate nonsevere** or **delayed nonsevere** hypersensitivity to penicillins, as a two-drug regimen, use initially:

vancomycin *slow IV infusion,* ***consider a loading dose in critically ill adults****. See 'Appendix 2: Vancomycin dosing' (page 386) for information on loading dose, dosing frequency and infusion time.*

adult ≥ 40 years: 15 mg/kg, see Table 18 for dosing frequency (page 390)

adult < 40 years 20 mg/kg, see Table 17 for dosing frequency (page 389)

PLUS

ceftriaxone *2 g IV, 12-hourly.*

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

vancomycin *slow IV infusion,* ***consider a loading dose in critically ill adults****. See 'Appendix 2: Vancomycin dosing' (page 386) for information on loading dose, dosing frequency and infusion time.*

adult ≥ 40 years: 15 mg/kg, see Table 18 for dosing frequency (page 390)

adult < 40 years 20 mg/kg, see Table 17 for dosing frequency (page 389)

PLUS

ciprofloxacin *400 mg IV, 8-hourly.*

For any of the above regimens, if vancomycin is not available, substitute with:

chloramphenicol *1 g IV, 6-hourly.*

Ongoing management

Monitor clinical response and inflammatory markers (e.g. CRP or ESR).

Modify therapy according to the results of culture and susceptibility testing, if available.

If microbiological diagnosis cannot be achieved, but the patient is improving with initial intravenous therapy, use an oral regimen as for empirical therapy for adults with vertebral osteomyelitis who have a normal neurological examination.

If the patient is **not** improving, consider surgical options, alternative pathogens (e.g. TB, MRSA, resistant Gram-negative organisms) or malignancy, and seek appropriate advice.

Duration of therapy for non-tuberculous osteomyelitis in adults

Table 3: Suggested duration of antibiotic therapy for osteomyelitis in adults

Adults with acute osteomyelitis usually require a minimum of 7 days intravenous therapy, except where the patient has a concomitant infection that requires a longer course of intravenous therapy e.g. *S. aureus* bacteraemia (see page 253). Adults with chronic osteomyelitis may not require initial intravenous therapy but may require a longer total duration of therapy – seek appropriate advice.	
Location of infection	**Suggested total duration of antibiotic therapy (IV + oral) [Note 1]**
Long-bone osteomyelitis	6 weeks
Vertebral osteomyelitis	12 weeks
Osteomyelitis contiguous with leg or foot ulcers [Note 2]	If infected bone is entirely removed (i.e. total amputation of all infected tissue), antibiotic therapy can be stopped 2 to 5 days after surgery In patients who have undergone debridement of all necrotic tissue but have residual osteomyelitis, continue for 6 weeks.
Osteomyelitis complicating sacral pressure ulcers	6 weeks
Mandibular osteomyelitis	see **mandibular osteomyelitis** (page 100) in 'Dental infections.'
Osteomyelitis of the hand [Note 2]	6 weeks although shorter course of therapy may be considered
CRP = C-reactive protein; ESR = erythrocyte sedimentation rate Note 1: The durations of therapy suggested in this table are a guide only—modify according to clinical stability and response, appropriate surgical management (where relevant), location of infection and presence of concurrent conditions (e.g. infective endocarditis). Note 2: A shorter duration may be appropriate in the postoperative setting where the infected tissue has been removed (e.g. total amputation of infected tissue) or debrided (e.g. diabetic foot osteomyelitis).	

Long-bone and vertebral osteomyelitis in children

In children, vertebral osteomyelitis is most commonly associated with TB. See Table 2 (page 43) for further information on differentiating TB from pyogenic osteomyelitis. If history and clinical findings are suggestive of TB, start TB treatment; see the *National Tuberculosis Management Protocol* for recommended therapy.

S. aureus is the most common pathogen identified in long-bone osteomyelitis (and second most common for vertebral osteomyelitis), although *Kingella kingae* is an increasingly recognised cause of osteomyelitis, particularly in infants and children younger than 4 years.

Cefazolin is preferred as empirical therapy for both long-bone and non-tuberculous vertebral osteomyelitis in children, as it targets both *S. aureus* and *K. kingae*. If a child does not improve on standard empirical therapy, consider MRSA.

Management of non-tuberculous long-bone and vertebral osteomyelitis in children

Empirical therapy

Use:

cefazolin *50 mg/kg up to 2 g IV, 8-hourly.*

Cefazolin is the preferred drug for empirical therapy in children as it is targets both *S. aureus* and *K. kingae*. If cefazolin is not available, use:

flucloxacillin *50 mg/kg up to 2 g IV, 6-hourly.*

For children with **immediate severe** or **delayed severe** hypersensitivity to penicillins:

vancomycin *slow IV infusion, child 3 months and older: 15 mg/kg, 6-hourly. Consider a* ***loading dose*** *in critically ill children. See page 392 in 'Appendix 2: Vancomycin dosing' for information on loading dose, dosing frequency and infusion time in children.*

Based on local susceptibility data, the following may be appropriate alternatives to vancomycin:

clindamycin *15 mg/kg up to 600 mg IV, 8-hourly*

OR

trimethoprim+sulfamethoxazole *320+1600 mg (child ≥1 month: 8+40 mg/kg up to 320+1600 mg) orally, 12-hourly.*

Directed therapy and IV to oral switch

For information on duration of therapy, including timing of switch to oral therapy, see Table 4 (page 50).

Modify therapy according to the results of culture and susceptibility testing, if available.

Methicillin-susceptible *Staphylococcus aureus* (MSSA)

When appropriate to switch to oral therapy (see Table 4, page 50), use:

flucloxacillin *25 mg/kg up to 1 g orally, 6-hourly.*

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

cefalexin *45 mg/kg up to 1.5 g orally, 8-hourly.*

Cefalexin may also be preferred in infants and young children without penicillin hypersensitivity as the liquid formulation is better tolerated.

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

trimethoprim+sulfamethoxazole *320+1600 mg (child ≥1 month: 8+40 mg/kg up to 320+1600) mg orally, 12-hourly.*

Methicillin-resistant *Staphylococcus aureus* (MRSA)

For proven/suspected MRSA, use:

vancomycin *slow IV infusion, child 3 months and older: 15 mg/kg, 6-hourly. Consider a* ***loading dose*** *in critically ill children. See page 392 in 'Appendix 2: Vancomycin dosing' for information on loading dose, dosing frequency and infusion time in children.*

Based on susceptibility results (or local susceptibility data where MRSA is suspected but not confirmed), the following may be appropriate alternatives to vancomycin:

clindamycin *15 mg/kg up to 600 mg IV, 8-hourly*

When appropriate, switch to:

clindamycin *10 mg/kg up to 450 mg orally, 8-hourly*

OR

trimethoprim+sulfamethoxazole *320+1600 mg (child ≥1 month: 8+40 mg/kg up to 320+1600 mg) orally, 12-hourly.*

Gram-negative organisms

Ciprofloxacin should be reserved for patients where a susceptible Gram-negative organism is identified from cultures. Use:

ciprofloxacin *20 mg/kg up to 750 mg orally, 12-hourly.*

Organism unknown

If culture results are not available, for patients who improved on initial empirical therapy, (when appropriate) switch to:

cefalexin *45 mg/kg up to 1.5 g orally, 8-hourly.*

Cefalexin is preferred to flucloxacillin for oral therapy because it is active against *K. kingae,* and the liquid formulation is better tolerated. If cefalexin is not available, use:

flucloxacillin *25 mg/kg up to 1 g orally, 6-hourly.*

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

trimethoprim+sulfamethoxazole *320+1600 mg (child ≥1 month: 8+ 40mg/kg up to 320+1600 mg) orally, 12-hourly.*

Duration of therapy for non-tuberculous osteomyelitis in children

Children usually require a shorter duration of therapy for osteomyelitis than adults. In children with acute osteomyelitis, intravenous therapy should generally be continued until the child is afebrile and has clinically improved. Some children need a longer duration of intravenous therapy than recommended in Table 4.

Table 4: Suggested duration of antibiotic therapy for osteomyelitis in children 3 months and older

Type of infection	Suggested duration of antibiotic therapy [Note 1]	
	Intravenous	Total (IV + oral)
Acute osteomyelitis—uncomplicated infection	2 days or until the child is afebrile and has clinically improved	minimum 2 to 3 weeks (exception: vertebral osteomyelitis – 6 weeks)

cont...

Acute osteomyelitis—complicated infection (e.g. delayed presentation, associated with wound or abscess)	minimum 4 days, although longer duration is likely to be required, depending on whether there was surgical intervention – seek appropriate advice	minimum 3 weeks, although a longer duration is likely to be required – seek appropriate advice. (exception: vertebral osteomyelitis – 6 weeks)
Chronic osteomyelitis	may not be necessary	minimum 6 weeks
Note 1: The durations of therapy suggested for osteomyelitis in this table are a guide only and should be modified according to clinical response, concurrent conditions (eg *S. aureus* bacteraemia, infective endocarditis, spinal epidural abscess) and, in some circumstances, the pathogen and the antibiotic(s) used – seek appropriate advice.		

Septic arthritis

Septic arthritis usually presents as a monoarticular arthritis, spontaneously or following trauma.

Infection is most commonly caused by Gram-positive organisms—*S. aureus* (including MRSA) and *Streptococcus* species. *K. kingae* is an increasingly recognised cause of septic arthritis in infants and children, particularly those younger than 4 years.

Diagnostic specimens should include blood for culture and a joint aspirate taken under sterile conditions, so that alternative or coexisting diagnoses, such as an acute crystal arthropathy (in adults) or inflammatory arthritis, can be excluded and antibiotic therapy can be directed. Where possible, take specimens before starting antibiotic therapy.

Rule out TB by sending aspirate of joint fluid for GeneXpert testing.

In children and young adults, consider acute rheumatic fever and other types of inflammatory arthritis (e.g. reactive arthritis). In older adults, differential diagnoses include acute gout.

Early orthopaedic consult is desirable. Early surgical intervention is essential for source control of septic arthritis and multiple joint washouts may be needed.

See Table 5 (page 56) for duration of therapy.

Septic arthritis in adults

Urgent surgical drainage and microbiological examination of pus may be required. Modify therapy according to the results of culture and susceptibility testing.

Neisseria gonorrhoeae is a common cause of native joint septic arthritis in sexually active adults which may involve multiple joints. A disseminated (bacteraemic) form of infection also occurs with the classic triad of dermatitis (tiny maculopapular, pustular, or vesicular lesions), tenosynovitis and migratory polyarthritis. Send urine and synovial fluid for analysis. While gonococcal polymerase chain reaction (PCR) is currently not available in Papua New Guinea, most laboratories are able to distinguish gonococcus on microscopy of joint fluid.

Management of septic arthritis in adults

Empirical therapy

Use:

flucloxacillin *2 g IV, 6-hourly.*

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

cefazolin *2 g IV, 8-hourly.*

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

vancomycin *slow IV infusion,* ***consider a loading dose in critically ill adults****. See 'Appendix 2: Vancomycin dosing' (page 386) for information on loading dose, dosing frequency and infusion time*

adult ≥ 40 years: 15 mg/kg, see Table 18 for dosing frequency (page 390)

adult < 40 years 20 mg/kg, see Table 17 for dosing frequency (page 389).

Monitor clinical response and ensure surgical review.

Ongoing therapy

For patients improving on initial empirical therapy

Modify therapy according to the results of culture and susceptibility testing when available.

If culture results are not available, switch to empirical oral therapy oral therapy when appropriate as per osteomyelitis, see directed therapy and IV to oral switch for long-bone osteomyelitis in adults, page 41 in this topic.

For information on timing of oral switch and duration of therapy, see Table 5 (page 56).

For patients **not** improving on initial empirical therapy

Escalation may be required in patients with poor response despite surgical intervention (i.e. two or more surgical washouts); consider **adding**:

chloramphenicol *1 g IV, 6-hourly*

PLUS

ciprofloxacin *400 mg IV, 8-hourly.*

Gonococcal septic arthritis

If there is high clinical or microbiological suspicion of gonococcal arthritis (see introductory text for septic arthritis in adults on the previous page), use:

ceftriaxone *2 g IM/IV, daily for 48 hours or until afebrile*

Then switch to

doxycycline *100 mg orally, 12-hourly for a further 7 days.*

Septic arthritis in infants (> 3 months) and children

For septic arthritis in neonates and infants younger than 3 months, see page 207 in 'Infections in neonates and young infants.'

Consider acute rheumatic fever as a differential diagnosis.

In infants and children, septic arthritis is an emergency and requires urgent drainage.

Management of septic arthritis in infants and children

Empirical therapy

Use:

cefazolin *50 mg/kg up to 2 g IV, 8-hourly.*

Cefazolin is preferred first-line treatment in children as it targets both *S. aureus* and *K. kingae*. If cefazolin is not available, use:

flucloxacillin *50 mg/kg up to 2 g IV, 6-hourly.*

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

vancomycin *slow IV infusion, child 3 months and older: 15 mg/kg, 6-hourly. Consider a* ***loading dose*** *in critically ill children. See page 392 in 'Appendix 2: Vancomycin dosing' for information on loading dose, dosing frequency and infusion time in children.*

Modify therapy according to the results of culture and susceptibility testing and switch to oral antibiotics when appropriate (see Table 5, page 56).

Directed therapy and IV to oral switch for septic arthritis in infants and children

Modify therapy according to the results of culture and susceptibility testing.

For information on duration of therapy, including timing of switch to oral therapy, see Table 5, page 56.

Methicillin-susceptible *Staphylococcus aureus* (MSSA)

When appropriate to switch to oral therapy, use:

flucloxacillin *25 mg/kg up to 1 g orally, 6-hourly.*

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

cefalexin *45 mg/kg up to 1.5 g orally, 8-hourly.*

Cefalexin may also be preferred in infants and young children without penicillin hypersensitivity as the liquid formulation is better tolerated.

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

trimethoprim+sulfamethoxazole *320+1600 mg (child ≥1 month: 8+40 mg/kg up to 320+1600) mg orally, 12-hourly.*

Methicillin-resistant *Staphylococcus aureus* (MRSA)

If MRSA is identified, switch to intravenous vancomycin:

vancomycin *slow IV infusion, child 3 months and older: 15 mg/kg, 6-hourly. Consider a* ***loading dose*** *in critically ill children. See page 392 in 'Appendix 2: Vancomycin dosing' for information on loading dose, dosing frequency and infusion time in children.*

When it is appropriate to switch to an oral agent, select treatment based on the results of culture and susceptibility testing. Suitable options may include:

clindamycin *10 mg/kg up to 450 mg orally, 8-hourly*

OR

trimethoprim+sulfamethoxazole *320+1600 mg (child ≥1 month: 8+40 mg/kg up to 320+1600 mg) orally, 12-hourly.*

Organism unknown

If culture results are not available, for patients who improved on initial empirical therapy, when appropriate, switch to:

cefalexin *45 mg/kg up to 1.5 g orally, 8-hourly.*

Cefalexin is preferred to flucloxacillin for oral therapy because it is active against *K. kingae*, and the liquid formulation is better tolerated. If cefalexin is not available, use:

flucloxacillin *25 mg/kg up to 1 g orally, 6-hourly.*

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

trimethoprim+sulfamethoxazole *320+1600 mg (child ≥1 month: 8+40 mg/kg up to 320+1600) mg orally, 12-hourly.*

Duration of therapy for septic arthritis in adults and children

Table 5: Suggested duration of antibiotic therapy for septic arthritis in a native joint (adults and children)

Patient age	Suggested duration of antibiotic therapy [Note 1]	
	Intravenous (minimum) [Note 2]	Total (IV + oral)
Child	2 days	3 weeks
Adult	1 week	4 weeks

Note 1: The durations of therapy suggested in this table are a guide and should be modified according to source control, clinical response, pathogen isolated, location of infection and the presence of conditions requiring a longer course of therapy. These treatment durations do not apply to *Neisseria gonorrhoeae* (gonococcal) arthritis, which should be treated for a total of 7 days. Shorter duration of therapy may also be considered in other circumstances (e.g. septic arthritis involving the hand with adequate surgical source control).

Note 2: Seek appropriate advice to guide the route and duration of antimicrobial therapy. This may involve multidisciplinary specialist discussion, as appropriate. If the patient has had joint drainage and irrigation and is clinically improving with no evidence of sepsis or other condition requiring longer intravenous therapy, switching to oral therapy may be possible, as long as there is an appropriate oral antimicrobial available. Conversely, some patients need a longer duration of intravenous therapy than recommended in this table.

Infection of bone and joint prostheses

Bone and joint infections involving the presence of prosthetic material are extremely complex to manage. Management of infected material is complicated by the formation of biofilm on foreign material. Extensive debridement, with or without removal of prosthetic material, should be considered.

Combined specialist surgical and medical input is important.

Prolonged duration of antibiotic therapy and removal of prosthetic material, where feasible, are often required.

Open fractures

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 external means) are critical for preventing infection. Ascertain the tetanus immunisation status of all

patients with an open fracture and give tetanus toxoid if indicated – see Table 13: Guide to tetanus prophylaxis in wound management, page 378 in 'Prevention of infection for medical conditions.'

The Gustilo–Anderson system classifies injury severity of open fractures as follows:

- **Type I:** a < 1 cm low-energy wound with no signs of infection
- **Type II:** a > 1 cm low-energy wound with moderate soft tissue damage
- **Type III:** a high-energy wound
  - **IIIa:** with adequate soft tissue cover
  - **IIIb:** with inadequate soft tissue cover
  - **IIIc:** with neurovascular compromise requiring repair.

The choice and duration of antibiotic therapy for open fracture depends on the nature and extent of injury severity, and the timeliness of debridement.

For late presentations (i.e. presentation 24 hours or more after the injury) or where infection is established, treat as **osteomyelitis** (see page 39 in this topic).

Table 6: Presumptive antibiotic therapy for open fractures

Gustilo–Anderson type I or II (acute presentation, i.e. within 24 hours of injury) Administer antibiotics as soon as possible, ideally within 6 hours of injury. Cease antibiotics 24 hours after wound closure.		
Absence of potential soil or water contamination	**Presence of potential soil contamination (in the absence of water contamination)**	**Presence of water contamination**
Use: ***cefazolin*** *2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly.* For patients with **immediate severe** or **delayed severe** hypersensitivity to penicillins, use: ***vancomycin*** *slow IV infusion, consider a loading dose in critically ill adults and children. See 'Appendix 2: Vancomycin dosing' (page 386) for information on dosing.*	Use: ***cefazolin*** *2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly.* *PLUS* ***metronidazole*** *500 mg (child: 12.5 mg/kg up to 500 mg) IV, 12-hourly [Note 1].* For patients with **immediate severe** or **delayed severe** hypersensitivity to penicillins, use: ***clindamycin*** *600 mg (child: 15 mg/kg up to 600 mg) IV, 8-hourly.*	No modification needed

cont...

Gustilo–Anderson type III (acute presentation, i.e. within 24 hours of injury) Administer antibiotics as soon as possible, ideally within 6 hours of injury. Cease antibiotics after 72 hours or within a day after soft tissue injuries have been closed.		
Absence of potential soil or water contamination	**Presence of potential soil contamination (in the absence of water contamination)**	**Presence of water contamination**
Use: ***gentamicin*** *IV, see 'Appendix 1: Gentamicin dosing' (page 381) for information on dosing.* *PLUS* ***cefazolin*** *2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly.* For patients with **immediate severe** or **delayed severe** hypersensitivity to penicillins, use: ***gentamicin*** *IV, see 'Appendix 1: Gentamicin dosing' (page 381) for information on dosing.* *PLUS* ***clindamycin*** *600 mg (child: 15 mg/kg up to 600 mg) IV, 8-hourly.*	Use: ***gentamicin*** *IV, see 'Appendix 1: Gentamicin dosing' (page 381) for information on dosing* *PLUS* ***cefazolin*** *2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly.* *PLUS* ***metronidazole*** *500 mg (child: 12.5 mg/kg up to 500 mg) IV, 12-hourly [Note 1].* For patients with **immediate severe** or **delayed severe** hypersensitivity to penicillins, use: ***gentamicin*** *IV, see 'Appendix 1: Gentamicin dosing' (page 381) for information on dosing* *PLUS* ***clindamycin*** *600 mg (child: 15 mg/kg up to 600 mg) IV, 8-hourly.*	For fresh water contamination, use: ***ciprofloxacin*** *500 mg (child: 12.5 mg/kg up to 500 mg) orally, 12- hourly* *PLUS* ***metronidazole*** *500 mg (child: 12.5 mg/kg up to 500 mg) IV, 12-hourly [Note 1].* For patients with hypersensitivity to penicillins, use: ***meropenem*** *1 g (child: 20 mg/kg up to 1 g) IV, 8-hourly* For sea water contamination, use: ***piperacillin+tazobactam*** *4+0.5 g (child: 100+12.5 mg/kg up to 4+0.5 g) IV, 6-hourly* *PLUS* ***doxycycline*** *100 mg (child: 2 mg/kg up to 100 mg, rounded to the nearest 25 mg) orally, 12-hourly.*[2]

cont...

2 Unlike older tetracyclines, doxycycline has not been associated with tooth discolouration, enamel hypoplasia or bone deposition with short-term use (< 21 days), even in children younger than 8 years, so is increasingly used in this age group. However, use may be limited by the lack of a suitable paediatric formulation.

		For patients with hypersensitivity to penicillins, use: ***meropenem*** *1 g (child: 20 mg/kg up to 1 g) IV, 8-hourly* *PLUS* ***doxycycline*** *100 mg (child: 2 mg/kg up to 100 mg, rounded to the nearest 25 mg) orally, 12-hourly.*
Gustilo–Anderson any type (chronic presentation, i.e. more than 24 hours after injury, or established infection)		
Treat as osteomyelitis, see **long-bone osteomyelitis in adults** (page 40) and **long-bone and vertebral osteomyelitis in children** (page 48) in this topic.		
Note 1: Switch to oral metronidazole when the patient can tolerate oral therapy, use: metronidazole 400 mg (child: 10 mg/kg up to 400 mg) orally, 12-hourly.		

Maxilla or mandible fractures

Refer patients with maxillofacial trauma to an oral maxillofacial specialist as soon as possible for further review and management.

Empirical therapy for maxilla or mandible fractures

Facial fractures requiring surgical management may require additional surgical antibiotic prophylaxis, see Table 11: Surgical antibiotic prophylaxis for specific procedures, page 355 in 'Antibiotic prophylaxis in surgical procedures.'

Presumptive treatment for patients without systemic features of infection

Use:

amoxicillin+clavulanate *500+125 mg (child: 15 mg/kg amoxicillin component up to 500 mg) orally, 8-hourly for up to 72 hours.*

For patients with hypersensitivity to penicillins, use:

clindamycin *450 mg (child: 10 mg/kg up to 450 mg orally, 8-hourly for up to 72 hours.*

Alternatively, including for patients with **immediate nonsevere** or **delayed nonsevere** hypersensitivity to penicillins, use (as a two-drug regimen):

cefalexin *1 g (child: 25 mg/kg up to 1 g) orally, 8-hourly for up to 72 hours*

PLUS

metronidazole *400 mg (child: 10 mg/kg up to 400 mg) orally, 12-hourly for up to 72 hours.*

Empirical therapy for patients with systemic features of infection

Use:

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

PLUS either

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 severe** or **delayed severe** hypersensitivity to penicillins, or with proven or suspected MRSA (e.g. suspected because of lack of treatment response to the above regimen at 72 hours), use (as a single agent):

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

OR

vancomycin *slow IV infusion,* ***consider a loading dose in critically ill adults and children****. See* 'Appendix 2: Vancomycin dosing' *(page 386) for information on loading dose, dosing frequency and infusion time*

adult ≥ 40 years: 15 mg/kg, see Table 18 for dosing frequency (page 390)

adult < 40 years 20 mg/kg, see Table 17 for dosing frequency (page 389)

child 3 months and older: 15 mg/kg, 6-hourly

OR

trimethoprim+sulfamethoxazole *320+1600 mg (child ≥1 month: 8+40 mg/kg up to 320+1600 mg) orally, 12-hourly (oral-only option).*

For patients on an intravenous regimen, switch to an appropriate oral regimen as for presumptive therapy when the patient has clinically improved.

Duration

7 to 10 days total (IV and oral). Delayed presentations usually require 10 days of therapy.

Key additional references

Chaudhary, K. Dhawale, A. Chaddha, R. Laheri, V. Spinal tuberculosis – an Update. Bombay Orthopaedic Society. Vol 2; issue 1. Jan-June 2017.

Gwee A, Autmizguine J, Curtis N, Duffull SB. Twice- and Thrice-daily Cephalexin Dosing for Staphylococcus aureus Infections in Children. Pediatr Infect Dis J. 2020 Jun;39(6):519-522. doi: 10.1097/INF.0000000000002646. PMID: 32412727.

Kritsaneepaiboon, S. Skeletal Involvement in Pediatric Tuberculosis. WFPI TB Corner 2016; 2 (2):1-6.

Cardiovascular infections

This topic includes advice on the management of the following conditions in adults and children 3 months and older:

- **infective endocarditis**
  - assessment and diagnosis, page 63
  - empirical therapy, page 66
  - directed therapy, page 68
- **bacterial pericarditis**, page 74.

Infective endocarditis

Assessment of infective endocarditis

Infective endocarditis may be **acute** (symptoms often less than 1 week's duration, including being unwell with fever, rigors, with or without shock, with or without cardiac failure due to valvular destruction, new cardiac murmur, embolic and vascular phenomena, embolic stroke, or secondary abscess) or **subacute** (low-grade symptoms for weeks to months including fatigue, fever, embolic and vascular phenomenon, embolic stroke, or changing cardiac murmur). Patient risk factors include pre-existing valvular disease (e.g. rheumatic heart disease), a prosthetic valve, recent dental or other procedure, or a history of intravenous drug use.

Patients who present with stroke or acute limb ischaemia should always be carefully evaluated for the presence of underlying endocarditis – taking blood for culture is usually indicated. Fever may be absent on presentation in these circumstances.

If bacterial endocarditis is suspected:

- take **3 sets of blood for culture** (from separate venepuncture sites) before initiating antibiotic therapy. Multiple sets for culture increase the likelihood of detecting bloodstream infection; when three sets of blood samples are taken before antibiotic administration, the pathogen is identified in about 90% of cases
- perform an echocardiogram
- measure white cell count (WCC), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP); ESR and/or CRP is elevated in almost all cases of endocarditis
- perform liver and renal function tests.

Diagnostic criteria for endocarditis

Diagnostic criteria are specified by the modified Duke criteria[3] (see the reference for a full description or the online calculator 'Duke Criteria for Infective Endocarditis' from mdcalc.com). A definitive diagnosis requires 2 major or 1 major + 3 minor or 5 minor criteria.

Major criteria include isolation of typical microorganisms associated with infective endocarditis (e.g. *Staphylococcus aureus*, viridans streptococci, enterococci or the HACEK group of oral Gram-negative bacilli) and echocardiographic evidence for infective endocarditis (e.g. vegetation, abscess or new valvular regurgitation), noting that echocardiogram is not a fully sensitive detection method.

Minor criteria include the presence of risk factors (e.g. pre-existing valvular disease such as rheumatic heart disease, a prosthetic valve, recent dental or other procedure, or a history of intravenous drug use), fever (temperature ≥38 °C), vascular phenomena (major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial haemorrhage, conjunctival haemorrhages, or Janeway lesions) or immunologic phenomena (glomerulonephritis, Osler nodes, Roth spots).

Approach to managing infective endocarditis

General approach

Seek expert advice for both suspected and proven infective endocarditis cases. Consult a medical microbiologist or infectious diseases physician and a cardiologist, where possible, as management of these patients is complex and requires a prolonged duration of treatment. In certain low risk situations, it is safe to switch treatment to an oral antibiotic; this possibility can be discussed with the available expert(s) on an individual case basis. A collaborative, multidisciplinary approach has been shown to reduce infective endocarditis mortality.

If culture and susceptibility testing is available and the results are positive, tailor the treatment against the specific pathogen identified (see page 68 for pathogen-specific regimens). Acute cases are usually caused by methicillin-susceptible *Staphylococcus aureus* (MSSA) or methicillin-resistant *S. aureus* (MRSA) infection, whereas subacute cases are usually associated with infection due to enterococci (e.g. *Enterococcus faecalis*) or streptococci (*Streptococcus* 'viridans' species).

If culture and susceptibility testing is not available or the results of testing are negative, treatment should be based on whether the presentation is acute or subacute. If the presentation is acute, treat as per MSSA see ***Staphylococcus aureus* native valve endocarditis**, page 70. If the presentation is subacute, treat as per uncomplicated streptococcal or enterococcal disease, see **streptococcal endocarditis**, page 68 or **enterococcal endocarditis**, page 72 in this topic.

3 Li JS, Sexton DJ, Mick N, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clin Infect Dis 2000;30:633-8.

Principles of antimicrobial therapy for infective endocarditis

General approach and duration of therapy

- treatment must be given intravenously to ensure adequate drug concentrations, except in specific circumstances as described in these guidelines and under the guidance of an appropriate specialist.
- the treatment duration is usually 4 to 6 weeks (see recommendations).
- cases with an acute presentation (as described under 'assessment of infective endocarditis') should start treatment without delay.
- obtain input from medical microbiologist or infectious diseases physician, and a cardiologist where possible (see 'general approach' on the previous page).
- in patients who are haemodynamically stable, with a subacute or indolent presentation and who have had bloods taken for culture, delay antibiotics until the results are available.

Gentamicin for the treatment of infective endocarditis

Gentamicin is recommended as part of the empirical therapy regimen for native valve and prosthetic valve endocarditis to cover the possibility of Gram-negative sepsis. For empirical treatment, gentamicin should be given once daily as outlined in 'Appendix 1: Gentamicin dosing,' page 381.

For confirmed enterococcal endocarditis, gentamicin is often continued at a lower dose for synergistic therapy, see Box 1 below.

Box 1: Synergistic gentamicin therapy

Synergistic gentamicin therapy is the use of low-dose gentamicin in combination with a beta-lactam antibiotic to enhance the beta-lactam's bactericidal activity. In these guidelines, synergistic gentamicin therapy is recommended for enterococcal endocarditis only.

The duration of synergistic gentamicin therapy is a maximum of two weeks.

Do not use synergistic gentamicin therapy in patients with a contraindication to gentamicin, see Appendix 1: Gentamicin dosing (page 381) **or in locations where creatinine cannot be monitored**.

For patients treated with synergistic gentamicin therapy, monitor renal function (creatinine) every 3 days and regularly ask the patient about symptoms of ototoxicity such as vertigo or hearing loss. If symptoms occur, cease gentamicin and switch to an alternative regimen, if provided, and/or seek appropriate advice.

Empirical therapy for infective endocarditis

Empirical therapy for community-acquired native valve endocarditis

For management of native valve infective endocarditis cases presenting from the community, **without** septic shock and where MRSA is **not** suspected, select the treatment approach based on the patient's presentation:

- **acute cases**: use directed therapy as for *Staphylococcus aureus* native valve endocarditis (see page 70 in this topic) – **start treatment without delay**.
- **subacute cases**: await the results of culture and susceptibility testing before commencing treatment. If testing has not been done or is not available, treat as for streptococcal endocarditis (see page 68 in this topic).

Empirical therapy for prosthetic valve endocarditis, endocarditis associated with septic shock, healthcare-associated endocarditis or where MRSA is suspected

Use:

vancomycin *slow IV infusion, see 'Appendix 2: Vancomycin dosing' (page 386) for information on timing of next dose after loading dose, dosing frequency and infusion time*

adults ≥ 40 years: ***loading dose 25 mg/kg up to 3 g*** *then 15 mg/kg, see Table 18 for dosing frequency (page 390)*

adults < 40 years: ***loading dose 25 mg/kg up to 3 g*** *then 20 mg/kg, see Table 17 for dosing frequency (page 389)*

children 3 months and older: ***loading dose 25 mg/kg up to 3 g*** *then 15 mg/kg, 6-hourly*

PLUS

flucloxacillin *2 g (child: 50 mg/kg) IV, 6-hourly*

PLUS

gentamicin *IV, see Appendix 1: Gentamicin dosing (page 381) for information on dosing frequency, maximum dose and maximum number of doses.*

adults: 5 mg/kg (7 mg/kg in critical illness), see Table 14 for dosing frequency (page 384)

children 3 months and older: 7 mg/kg up to 560 mg, once daily.

Flucloxacillin is used in addition to vancomycin as it is more effective than vancomycin for MSSA.

cont...

Modify treatment based on culture and susceptibility results when available, see directed therapy for infective endocarditis on the next page.

A suitable alternative in patients **immediate nonsevere** or **delayed nonsevere** hypersensitivity to penicillins is:

cefazolin *2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly; for adults with septic shock or requiring intensive care support, use 6-hourly dosing*

PLUS

vancomycin *slow IV infusion, see 'Appendix 2: Vancomycin dosing' (page 386) for information on timing of next dose after loading dose, dosing frequency and infusion time*

- *adults ≥ 40 years:* ***loading dose 25 mg/kg up to 3 g*** *then 15 mg/kg, see Table 18 for dosing frequency (page 390)*
- *adults < 40 years:* ***loading dose 25 mg/kg up to 3 g*** *then 20 mg/kg, see Table 17 for dosing frequency (page 389)*
- *children 3 months and older:* ***loading dose 25 mg/kg up to 3 g*** *then 15 mg/kg, 6-hourly*

PLUS

gentamicin *IV, see 'Appendix 1: Gentamicin dosing' (page 381) for information on dosing frequency, maximum dose and maximum number of doses.*

- *adults: 5 mg/kg (7 mg/kg in critical illness), see Table 14 for dosing frequency (page 384)*
- *children 3 months and older: 7 mg/kg up to 560 mg, once daily.*

For patients with **immediate severe** or **delayed severe** hypersensitivity to penicillins, use vancomycin plus gentamicin.

Modify treatment based on culture and susceptibility results when available, see directed therapy for infective endocarditis on the next page.

Ongoing empirical therapy where culture and susceptibility testing is unavailable or the results of testing are negative

If culture and susceptibility testing is unavailable (e.g. at sites without access to a microbiology service) or the results of testing are negative, ongoing empirical management is required. Select an ongoing treatment regimen based on the patient's clinical presentation:

- For **acute, severe, hospital-acquired cases**, continue treatment as for staphylococcal endocarditis (MSSA) for at least 6 weeks, and seek advice from multidisciplinary specialists, where available
- For **subacute cases**, continue directed therapy for native valve streptococcal endocarditis for at least 4 weeks.

Culture-negative endocarditis is commonly due to prior antibiotic therapy but can also be caused by unusual pathogens including *Bartonella*, *Coxiella burnetii*, *Legionella*, *Mycoplasma* and *Tropheryma whipplei*; however, these cannot currently be diagnosed in Papua New Guinea.

Monitoring response to therapy

Monitor clinical response closely. If available, measure CRP or ESR every 72 hours. If the patient is deteriorating or not improving, then reconsider the diagnosis and treatment – consult an appropriate specialist.

Directed therapy for infective endocarditis

Streptococcal endocarditis

Endocarditis caused by viridans streptococci and *Streptococcus bovis* group (now classified as *Streptococcus gallolyticus* or *Streptococcus infantarius*).

Also use this regiment for **subacute presentations** of suspected endocarditis if culture and susceptibility testing is unavailable or the results of testing are negative.

Use:

benzylpenicillin *1.8 g (child 50 mg/kg up to 1.8 g), IV 4-hourly*

For patients with **immediate nonsevere** or **delayed nonsevere** hypersensitivity to penicillins or if gentamicin is contraindicated or inappropriate, use ceftriaxone as a single agent:

ceftriaxone

adult: 2 g daily

child: 100 mg/kg up to 4 g IV, daily or 50 mg/kg up to 2 g 12-hourly.

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

vancomycin *slow IV infusion,* ***consider a loading dose in critically ill adults and children****. See 'Appendix 2: Vancomycin dosing' (page 386) for information on loading dose, dosing frequency and infusion time*

adult ≥ 40 years: 15 mg/kg, see Table 18 for dosing frequency (page 390)

adult < 40 years 20 mg/kg, see Table 17 for dosing frequency (page 389)

child 3 months and older: 15 mg/kg, 6-hourly.

IV to oral switch

Switching to an oral antibiotic after a period of IV therapy may be feasible for **uncomplicated native valve disease** – discuss options with the available expert(s).

Duration of treatment

Monitor clinical response closely. Measure CRP or ESR every 72 hours. For patients who are deteriorating or not improving, consult an appropriate specialist.

For **uncomplicated native valve endocarditis**, treat for a total of 4 weeks.

For patients with **complicated disease** (large vegetation, slow response to treatment, extra-cardiac infection), treat for a total of 6 weeks.

For patients with **prosthetic valves**, treat for 6 weeks.

Staphylococcal endocarditis

Staphylococcus aureus native valve endocarditis

See also *Staphylococcus aureus* bacteraemia (page 253) in 'Sepsis and bloodstream infections.'

Also use this regimen for **acute presentations** of suspected endocarditis if culture and susceptibility testing is unavailable or the results of testing are negative.

Rationale for antibiotic selection:

- flucloxacillin is more effective than vancomycin for MSSA
- clindamycin or chloramphenicol should not be used for staphylococcal endocarditis because rates of treatment failure are unacceptably high.

For native valve endocarditis caused by **MSSA**, use:

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

Alternatively, for patients **immediate nonsevere** or **delayed nonsevere** hypersensitivity to penicillins, use:

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

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

vancomycin *slow IV infusion, see 'Appendix 2: Vancomycin dosing' (page 386) for information on timing of next dose after loading dose, dosing frequency and infusion time*

adults ≥ 40 years: ***loading dose 25 mg/kg up to 3 g*** *then 15 mg/kg, see Table 18 for dosing frequency (page 390)*

adults < 40 years: ***loading dose 25 mg/kg up to 3 g*** *then 20 mg/kg, see Table 17 for dosing frequency (page 389)*

children 3 months and older: ***loading dose 25 mg/kg up to 3 g*** *then 15 mg/kg, 6-hourly.*

For native valve endocarditis caused by **MRSA**, use vancomycin as per regimen for immediate severe or delayed severe hypersensitivity to penicillins, above.

Monitoring response to therapy

Repeat blood cultures 72 to 96 hours after commencing treatment (20 mL of blood divided between 2 bottles). If cultures remain positive, evaluate the patient for an undiagnosed deep source (e.g. abscess), including a repeat echocardiography.

Monitor clinical response closely. Measure CRP or ESR every 72 hours, if available. If the patient deteriorates or does not improve, seek appropriate advice.

IV to oral switch

Switching to oral therapy after a period of IV therapy may be feasible for uncomplicated native valve disease – seek appropriate advice from the available expert(s).

Duration of treatment

MSSA: For uncomplicated infection, treat for 4 weeks. For patients with complicated infections (e.g. perivalvular abscess, septic embolic complications), treat for 6 weeks.

MRSA: Treat for 6 weeks.

Prosthetic valve endocarditis with *Staphylococcus aureus* or coagulase-negative *Staphylococcus*

Coagulase-negative staphylococci are an important cause of prosthetic valve endocarditis, particularly in the first year after insertion of the valve.

For prosthetic valve endocarditis caused by MSSA or a susceptible coagulase-negative staphylococci, use:

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

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

cefazolin *2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly; for adults with septic shock or requiring ICU support, use 6-hourly dosing.*

For MRSA or methicillin-resistant coagulase-negative staphylococci, or for MSSA in patients with **immediate severe** or **delayed severe** hypersensitivity to penicillins, use:

cont...

vancomycin *slow IV infusion, see 'Appendix 2: Vancomycin dosing' (page 386) for information on timing of next dose after loading dose, dosing frequency and infusion time*

adults ≥ 40 years: ***loading dose 25 mg/kg up to 3 g*** *then 15 mg/kg, see Table 18 for dosing frequency (page 390)*

adults < 40 years: ***loading dose 25 mg/kg up to 3 g*** *then 20 mg/kg, see Table 17 for dosing frequency (page 389)*

children 3 months and older: ***loading dose 25 mg/kg up to 3 g*** *then 15 mg/kg, 6-hourly.*

IV to oral switch

Use IV antibiotics for the total duration of treatment. Switching to oral antibiotic therapy is **not** advisable.

Duration of treatment

Treat for 6 weeks.

Enterococcal endocarditis

For enterococcal endocarditis **susceptible to penicillin**, use:

benzylpenicillin *2.4 g (child: 60 mg/kg up to 2.4 g), IV 4-hourly*

PLUS

gentamicin *(adult and child)* ***3 mg/kg*** *daily.*

Alternatively, use:

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

PLUS

gentamicin *(adult and child)* ***3 mg/kg*** *IV, daily.*

If gentamicin is contraindicated or inappropriate (e.g. if creatinine cannot be monitored), **replace** gentamicin in the above regimens with:

ceftriaxone *2 g (child: 50 mg/kg up to 2 g) IV, 12-hourly.*

cont...

For endocarditis caused by a **penicillin-resistant** enterococci, or for patients with **immediate severe** or **delayed severe** hypersensitivity to penicillins, use:

vancomycin *slow IV infusion, see 'Appendix 2: Vancomycin dosing' (page 386) for information on timing of next dose after loading dose, dosing frequency and infusion time*

adults ≥ 40 years: ***loading dose 25 mg/kg up to 3 g*** *then 15 mg/kg, see Table 18 for dosing frequency (page 390)*

adults < 40 years: ***loading dose 25 mg/kg up to 3 g*** *then 20 mg/kg, see Table 17 for dosing frequency (page 389)*

children 3 months and older: ***loading dose 25 mg/kg up to 3 g*** *then 15 mg/kg, 6-hourly*

PLUS

gentamicin *(adult and child)* ***3 mg/kg*** *IV, daily.*

In patients treated with gentamicin, monitor renal function (creatinine) every 3 days and regularly ask about symptoms of ototoxicity, such as vertigo or hearing loss. If symptoms occur, cease gentamicin and switch to an appropriate alternative regimen and/or seek appropriate advice.

IV to oral switch

Use IV antibiotics for the total duration of treatment. Switching to oral antibiotic therapy is **not** advisable.

Duration of treatment

Beta-lactam susceptible enterococci

- for uncomplicated native valve disease, if there is rapid response to therapy treat for 4 weeks but stop gentamicin after 2 weeks (if used).
- for complicated native valve disease, prosthetic valve disease, or slow response to treatment, treat for 6 weeks but stop gentamicin after 2 weeks (if used).

Beta-lactam resistant enterococci

- treat with vancomycin for 6 weeks and gentamicin for 2 weeks.

Monitor clinical response closely. Measure CRP or ESR every 48 to 72 hours, if available. If the patient is deteriorating or not improving, seek advice from available expert(s).

Endocarditis caused by HACEK group

Haemophilus parainfluenzae, *Aggregatibacter* species, *Cardiobacterium* species, *Eikenella corrodens*, and *Kingella* species

Use:

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

Duration of treatment

Discuss the duration of therapy for individual patients with appropriate expert(s); 4 to 6 weeks of IV antibiotics is usually required.

Bacterial pericarditis

Causes of pericarditis can be:

- **infective**: most commonly viral (including enteroviruses, human immunodeficiency virus [HIV] and COVID-19) but also bacterial (most commonly TB, but rarely other organisms [e.g. *Haemophilus influenzae*])
- **noninfective**: commonly autoimmune, but may be neoplastic, metabolic (e.g. uraemia), traumatic, post–acute myocardial infarction (e.g. Dressler syndrome), or iatrogenic.

Bacterial pericarditis may occur because of direct spread from an intrathoracic focus, haematogenous spread or extension from a subdiaphragmatic focus.

Tuberculosis is a common cause of bacterial pericarditis in Papua New Guinea. It may present as acute (chest pain, pericardial friction rub and widespread ST elevation without effusion), subacute, or chronic presentations (heart failure and/or cardiac tamponade due to moderate-to-large pericardial effusion, or symptoms of pericardial constriction). If an effusion is present, aspiration will reveal a protein-rich lymphocytic exudate that is frequently macroscopically bloodstained. Cell count, Gram stain, microscopy for acid-fast bacilli (AFB) and GeneXpert (TB) testing should be performed, however neither AFB microscopy nor GeneXpert are sensitive tests. If available, blood and pericardial fluid should be taken for culture to rule out another bacterial cause.

For suspected or confirmed TB pericarditis, refer to the *National Tuberculosis Management Protocol* for management advice.

If routine bacterial cultures return positive results, seek advice from a clinical microbiologist or infectious disease physician for directed treatment against the identified pathogen.

Key additional references

Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta J-P, Del Zotti F, et al., ESC Scientific Document Group, 2015 ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC) Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM), Eur Heart J 2015; 36 (44): 3075–3128. https://doi.org/10.1093/eurheartj/ehv319

Li JS, Sexton DJ, Mick N, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clin Infect Dis 2000;30:633-8.

Isiguzo G, Du Bruyn E, Howlett P, Ntsekhe M. Diagnosis and Management of Tuberculous Pericarditis: What Is New? Curr Cardiol Rep. 2020 Jan 15;22(1):2. doi: 10.1007/s11886-020-1254-1. PMID: 31940097; PMCID: PMC7222865.

Lazarou E, Tsioufis P, Vlachopoulos C, Tsioufis C, Lazaros G. Acute Pericarditis: Update. Curr Cardiol Rep. 2022 Aug;24(8):905-913. doi: 10.1007/s11886-022-01710-8. Epub 2022 May 20. PMID: 35595949; PMCID: PMC9122084.

McDonald EG, Aggrey G, Tarık Aslan A, et al. Guidelines for Diagnosis and Management of Infective Endocarditis in Adults: A WikiGuidelines Group Consensus Statement. JAMA Netw Open. 2023;6(7):e2326366. doi:10.1001/jamanetworkopen.2023.26366

Central nervous system infections

This topic includes advice on the management of the following conditions in adults and children 3 months and older:

- **meningitis**
  - clinical presentation and principles of management, page 77
  - empirical management, page 78
  - directed therapy, page 80
- **meningitis following penetrating head trauma or neurosurgery**, page 86
- **encephalitis**, page 87
- **brain abscess and subdural empyema**, page 89
- **epidural abscess**, page 91
- **neurocysticercosis**, page 92.

The following topics are not included in this section:

- meningitis or encephalitis in neonates and infants younger than 3 months, see **sepsis, septic shock and meningitis in neonates and young infants** (page 199) in 'Infections in neonates and young infants.'
- chemoprophylaxis for patients and close contacts after meningococcal meningitis, see **prophylaxis for exposure to infectious conditions: invasive meningococcal disease** (page 377) in 'Prevention of infection for medical conditions.'

Meningitis

Clinical presentation and aetiology of meningitis

Meningitis is a severe, potentially life-threatening infection. It typically presents with an acute fever, neck stiffness and altered conscious state. Other common symptoms include headache, photophobia, and nausea or vomiting.

The most common pathogens in bacterial meningitis are *Streptococcus pneumoniae*, *Neisseria meningitidis* and *Haemophilus influenzae*. *Listeria monocytogenes* is more common in adults older than 50 years and immunocompromised patients.

Key principles in managing meningitis

The key principles in managing meningitis are as follows:

- Clinical differentiation of bacterial meningitis from other diagnoses (such as aseptic meningitis, encephalitis or subarachnoid haemorrhage) can be difficult.
- Lumbar puncture to obtain cerebrospinal fluid (CSF) for examination (protein, glucose, microscopy) and culture is key to diagnosis and directed therapy for bacterial meningitis.
- Ideally, obtain microbiological samples (e.g. CSF, blood) before starting empirical antibiotic therapy.
- Early empirical antibiotic therapy, ideally within 60 minutes of presentation to hospital, when clinical suspicion of bacterial meningitis is high. Do not withhold treatment if there is a significant delay in performing investigations.

Defer lumbar puncture if there are focal neurological signs, reduced Glasgow coma scale (GCS) score, cardiovascular compromise or coagulopathy. Exclude raised intracranial pressure with fundoscopy and computed tomography (CT) prior to lumbar puncture. Raised intracranial pressure may cause coma or focal neurological signs. Do not conduct lumbar puncture through infected skin.

Corticosteroids (e.g. dexamethasone) are used as an adjunct in the treatment of bacterial meningitis and have been shown to improve mortality in adults with pneumococcal meningitis. Current evidence for use in children with meningitis is mixed but suggests that steroids may reduce hearing loss in children with *H. influenzae* type b (Hib) meningitis.

Corticosteroids can be administered up to 4 hours after starting antibiotic therapy.

Do not delay administration of antibiotics if corticosteroids are not available.

Consider stopping antibiotics and dexamethasone if the CSF examination is consistent with viral meningitis.

Central nervous system (CNS) tuberculosis is an important differential diagnosis. See tuberculosis meningitis (page 85) later in this topic for further detail on clinical features, and the *National Tuberculosis Management Protocol* for management.

If a patient has chronic meningitis symptoms with a persistent headache or is immunocompromised, consider cryptococcal meningitis and request cryptococcal antigen testing on CSF and/or blood specimens.

Empirical management of meningitis

Empirical therapy should ideally be commenced within 60 minutes of presentation to a healthcare facility.

Do not withhold treatment if there is a significant delay in performing investigations.

Empirical therapy for meningitis in adults and children older than 3 months

Use:

dexamethasone 10 mg (child: 0.15 mg/kg up to 10 mg) IV, 6-hourly for 4 days

PLUS

ceftriaxone

Adults: 2 g IV, 12-hourly

Child: 100 mg/kg up to 4 g IV, daily

Alternatively, if ceftriaxone is unavailable, use:

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

In patients with **immediate severe** or **delayed severe** hypersensitivity to penicillins (or if neither ceftriaxone nor cefotaxime are available), use:

***chloramphenicol** 1 g (child: 25 mg/kg up to 1 g) IV, 6-hourly.*

L. monocytogenes is intrinsically resistant to cephalosporins. For patients who are immunocompromised, older than 50 years, or are pregnant, to cover the possibility of *Listeria*, **add** to any of the above regimens:

***benzylpenicillin** 2.4 g (child: 60 mg/kg up to 2.4 g) IV, 4-hourly.*

Duration

Following identification of the pathogen, choose the appropriate directed regimen – see directed therapy for meningitis on the next page.

If a pathogen is not isolated, but there is pleocytosis on CSF examination, continue the empirical antibiotic regimen for 10 days. Dexamethasone should be stopped after 4 days.

If the CSF examination is consistent with viral meningitis, consider stopping antibiotics and dexamethasone.

Directed therapy for meningitis (organism and susceptibility known)

N. meningitidis (meningococcal) meningitis

Stop dexamethasone.

Use:

ceftriaxone *2 g (child: 50 mg/kg) IV, 12-hourly for 5 days.*

In children, a single daily dose of ceftriaxone (100 mg/kg up to 4 g IV, daily) can be continued if this was started empirically.

S. pneumoniae (pneumococcal) meningitis

Continue dexamethasone for 4 days.

Use:

ceftriaxone *2 g (child: 50 mg/kg up to 2 g) IV, 12-hourly for 10 to 14 days.*

In children, a single daily dose of ceftriaxone (100 mg/kg up to 4 g IV, daily) can be continued if this was started empirically.

H. influenzae meningitis

Continue dexamethasone for 4 days.

Use:

ceftriaxone *2 g (child: 50 mg/kg up to 2 g) IV, 12-hourly for 7 to 10 days.*

In children, a single daily dose of ceftriaxone (100 mg/kg up to 4 g IV, daily) can be continued if this was started empirically.

L. monocytogenes meningitis

Stop dexamethasone.

Use:

benzylpenicillin *2.4 g (child: 60 mg/kg up to 2.4 g) IV, 4-hourly for 3 weeks.*

In patients who are immunocompromised, treat for an additional 3 weeks with:

trimethoprim+ sulfamethoxazole *(adult > 60 kg: 320mg+1600 mg; adult 40 to 60kg: 240mg+1200 mg; child > 1 month: 6+30mg/kg up to 240+1200 mg) orally, 12-hourly for 3 weeks.*

***Streptococcus agalactiae* (group B streptococcus) meningitis**
Stop dexamethasone. Switch initial empirical therapy to: ***benzylpenicillin*** *2.4 g (child: 60 mg/kg up to 2.4 g) IV, 4-hourly for 14 days.* Extend the duration of therapy to 21 days (3 weeks) for complicated infection.

***Streptococcus suis* meningitis**
S. suis is a cause of acute bacterial meningitis. It is associated with substantial morbidity (hearing loss).
Continue dexamethasone for 4 days. Give directed therapy as for pneumococcal meningitis for 10 to 14 days, see *Streptococcus pneumoniae* (pneumococcal) meningitis on the previous page.

Cryptococcal meningitis

For primary prophylaxis in people living with human immunodeficiency virus (HIV), see page 376 in 'Prevention of infection for medical conditions.'

Clinical presentation and diagnosis

Cryptococcus species are a major cause of meningitis in people living with HIV. The presentation may be subacute, and fever may be absent. Diagnosis is confirmed by India Ink staining of CSF, raised opening CSF pressures during lumbar puncture, rapid CSF cryptococcal antigen (CrAg) assay or rapid serum CrAg results.

Patients with undiagnosed HIV infection may present initially with cryptococcal meningitis, therefore it is important to screen all patients with cryptococcal meningitis for HIV. In patients with cryptococcal meningitis and newly diagnosed HIV, the timing of antiretroviral therapy initiation is complex – see *National Guidelines for HIV Care and Treatment* and seek appropriate advice.

Approach to management of cryptococcal meningitis

Antifungal therapy for cryptococcal meningitis is administered in consecutive phases—induction, consolidation and maintenance/eradication (or suppression in patients who do not have HIV infection but are persistently immunocompromised).

There is no role for corticosteroids or diuretics (e.g. acetazolamide or mannitol) in reducing intracranial pressure in cryptococcal meningitis, except in the setting of immune reconstitution inflammatory syndrome (IRIS) or cerebral oedema surrounding a cryptococcoma.

Prevention, monitoring and management of amphotericin B toxicity

Amphotericin B and flucytosine are associated with significant toxicity; for advice on administration and monitoring, see page 20 in 'Getting to know your antimicrobials' and page 409 in 'Appendix 6: Parenteral administration of antimicrobials.'

Assess baseline renal function for all patients commencing on amphotericin B.

Regularly monitor patients for adverse effects such as anaemia, hypertension or hypotension, hypoxia, metabolic derangements such as hypokalaemia, hypomagnesaemia and nephrotoxicity.

Adverse reactions are more common with amphotericin B desoxycholate than with liposomal amphotericin, but the liposomal formulation was not available in Papua New Guinea at the time of writing. To minimise the risk of toxicity, administer pre- and post-treatment hydration and oral electrolyte supplementation, for details see page 20 in 'Getting to know your antimicrobials.'

Management of cryptococcal disease in people living with HIV

These recommendations apply to the treatment of cryptococcal disease (meningeal and disseminated non-meningeal) in people living with HIV (adults, adolescents and children).

Induction therapy	
Preferred induction regimen	Use: *amphotericin B deoxycholate 1 mg/kg IV, once daily for 7 days* *PLUS* *flucytosine 25 mg/kg orally, 6-hourly for 7 days* Followed by: *fluconazole 1200 mg (child or adolescent: 12 mg/kg up to 800 mg) orally/IV, daily for 7 days (days 8 to 14 of induction regimen)*
Alternative induction regimen (if no amphotericin formulation is available).	Use: *fluconazole 1200 mg (child: 12 mg/kg up to 1200 mg) orally/IV, daily for 14 days* *PLUS* *flucytosine 25 mg/kg orally, 6-hourly for 14 days.*

Alternative induction regimen (if flucytosine is not available). Note: flucytosine-containing regimens are superior.	If flucytosine is unavailable, use: *amphotericin B deoxycholate 1 mg/kg IV, daily for 14 days* *PLUS* *fluconazole 1200 mg (child or adolescent: 12 mg/kg up to 800 mg) orally/IV, daily for 14 days.*
Consolidation and maintenance/eradication therapy	
Consolidation therapy	Following completion of an induction regimen, use: *fluconazole 400 mg to 800 mg (child: 12 mg/kg up to 800 mg) orally, daily for 8 weeks.* Fluconazole can cause nausea at higher doses. A dose at the lower end of the range (e.g. 400 mg) is suitable for most patients but higher doses may be required for heavier patients.
Maintenance / eradication therapy	Following the completion of consolidation therapy, use: *fluconazole 200 mg to 400 mg (child: 6 mg/kg up to 200 mg) orally, daily.* The dose varies depending on patient tolerance, response to treatment and the susceptibility of the pathogen
Duration of maintenance (eradication) therapy In patients with HIV infection who respond to antiretroviral therapy, continue eradication therapy for at least 1 year and until CD4 count is more than 100 cells/microlitre for 3 months or longer. If CD4 count is not available, continue for at least 1 year and until the patient has achieved a suppressed viral load. In children with HIV infection aged between 2 and 5 years with successfully treated cryptococcal disease (meningeal and non-meningeal), discontinuation of antifungal treatment maintenance is recommended if the child is stable and adherent to antiretroviral therapy (ART) and antifungal maintenance treatment for at least 1 year. Maintenance therapy for cryptococcal disease should **not** be discontinued in children aged less than 2 years.	

Management of cryptococcal meningitis in people without HIV

Antifungal therapy is in consecutive phases—induction, consolidation and eradication; ongoing suppression therapy may be required in patients who are persistently immunocompromised.

Induction regimen	Use: *amphotericin B deoxycholate 1 mg/kg IV, daily* *PLUS* *flucytosine 25 mg/kg orally, 6-hourly.* **Duration of induction regimen** Continue the induction regimen for 2 to 6 weeks, depending on culture conversion, the presence of neurological dysfunction or cerebral cryptococcomas, whether the patient is immunocompromised, and the species of *Cryptococcus* (*gattii* or *neoformans*). Seek advice from a clinical microbiologist and/or infectious disease physician.
Consolidation regimen	Following the induction regimen, use: *fluconazole 400 to 800 mg (child: 6 to 12 mg/kg up to 800 mg) orally, daily.* **Duration of consolidation regimen** Patients should receive a minimum of 10 weeks therapy (induction and consolidation) before starting eradication therapy.
Eradication regimen	Following the consolidation regimen, use: *fluconazole 200 to 400 mg (child: 6 to 12 mg/kg up to 800 mg) orally, daily.* **Duration of eradication regimen** The total duration of therapy is 12 to 18 months, depending on whether the patient remains immunocompromised, and the presence or resolution of cerebral cryptococcomas. For persistently immunocompromised patients (e.g. transplant recipients), it may be necessary to continue fluconazole as long-term suppression therapy.

Eosinophilic meningitis

Eosinophilic meningitis is usually caused by *Angiostrongylus cantonensis* and sometimes by *Gnathostoma* species. Confirm the presence of eosinophils in the CSF by Giemsa stain – standard CSF stains cannot distinguish eosinophils from neutrophils.

There is conflicting evidence about the treatment of *A. cantonensis* meningoencephalitis – seek appropriate advice. Corticosteroid therapy improves symptoms. The benefits of anthelmintic treatment (usually in combination with corticosteroids) are thought to outweigh the risks if started within 3 weeks of exposure.

Tuberculoma / tuberculous meningitis (TB meningitis)

Presentation of TB meningitis may be acute or chronic varying from 1 day to 9 months. It may present with cranial nerve deficits, meningismus (which includes symptoms such as headache and neck stiffness) and altered mental status. The initial symptoms are usually nonspecific, including headache, vomiting, photophobia and fever.

Consider tuberculous meningitis if:

- fever has persisted for 14 days
- fever has persisted for > 7 days, and a family member has TB
- a chest X-ray suggests TB
- the patient is unconscious and remains so despite treatment for bacterial meningitis
- the patient is known to have HIV infection or is exposed to HIV
- the CSF has a moderately high white blood cell count (typically < 500 white cells per mL, mostly lymphocytes), elevated protein (0.8 to 4 g/L) and low glucose (< 1.5 mmol/L), or this pattern persists despite adequate treatment for bacterial meningitis.

TB meningitis requires corticosteroids in addition to standard anti-tuberculosis therapy, seek appropriate advice and refer to the *National Tuberculosis Management Protocol* and the *Standard Treatment for Common Illnesses in Children in Papua New Guinea* for management details.

Test all patients for HIV.

In patients with TB who test positive to HIV, monitor patients closely when initiating early ART as high rates of adverse events (e.g. IRIS) and deaths have been reported in a randomised trial.

Meningitis following penetrating head trauma or neurosurgery

Common organisms include *Staphylococcus aureus*, coagulase-negative staphylococci, and Gram-negative bacilli including *Pseudomonas aeruginosa*.

Perform blood culture testing on all patients and obtain CSF where possible.

Remove temporary external ventricular catheters (used for drainage and management of intracranial pressure) that become infected. Whenever possible, remove permanent shunts that are infected.

Empirical therapy for meningitis following penetrating head trauma or neurosurgery

Use:

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

PLUS

vancomycin *slow IV infusion, see 'Appendix 2: Vancomycin dosing' (page 386) for information on timing of next dose after loading dose, dosing frequency and infusion time*

- *adults ≥ 40 years:* ***loading dose 25 mg/kg up to 3 g*** *then 15 mg/kg, see Table 18 for dosing frequency (page 390)*
- *adults < 40 years:* ***loading dose 25 mg/kg up to 3 g*** *then 20 mg/kg, see Table 17 for dosing frequency (page 389)*
- *children 3 months and older:* ***loading dose 25 mg/kg up to 3 g*** *then 15 mg/kg, 6-hourly.*

In patients with **immediate severe** or **delayed severe** hypersensitivity to penicillins, **replace** ceftazidime in the above regimen with:

meropenem *2 g (child: 40 mg/kg up to 2 g) IV, 8-hourly.*

Modify therapy based on the results of culture and susceptibility testing, when available.

Duration

The duration of therapy usually ranges from 10 to 21 days, depending on the pathogen and clinical response.

Encephalitis

For infants < 3 months, see 'Infections in neonates and young infants,' page 199.

Clinical presentation and diagnosis of encephalitis

Encephalitis often presents with symptoms similar to meningitis such as acute onset of fever and headache. Suspect encephalitis in patients with acute fever and focal neurological symptoms and signs, including seizures, behavioural changes, personality change, and emotional lability and coma. Examination of the patient may reveal focal neurological deficits.

In the setting of meningoencephalitis, it can often be difficult to distinguish encephalitis from viral and bacterial meningitis, particularly if there are no typical associated features.

Start aciclovir therapy in all patients with suspected acute encephalitis while further investigations are underway because herpes simplex virus (HSV) is the most common treatable cause.

If bacterial meningitis or sepsis is possible, also commence empirical antibiotics as for meningitis (see page 78 in this topic).

As it is difficult to differentiate clinically between viral and bacterial causes of CNS infection, perform blood cultures and lumbar puncture, where safe to do so. Defer lumbar puncture if there are focal neurological signs, reduced GCS, cardiovascular compromise, or coagulopathy.

Aetiology of encephalitis

Likely causes of encephalitis are HSV, *Mycoplasma pneumoniae*, Epstein-Barr virus (EBV), cytomegalovirus (CMV), human herpesvirus 6 (HHVS6), influenza and arboviruses.

Unrecognised HSV encephalitis is a devastating illness with significant morbidity and mortality. Treatment with aciclovir can lead to full recovery, therefore empirical therapy with aciclovir should be started in all patients while further investigations are underway.

Japanese encephalitis and Nipah virus cannot be treated with antivirals; if a diagnosis is confirmed, the patient should be managed with supportive care alone.

Listeria monocytogenes infection may present with meningoencephalitis, especially in the elderly, immunocompromised patients and neonates. *Toxoplasma gondii* can also be a cause of encephalitis, particularly in people living with HIV and in other immunocompromised patients.

Many other disorders can mimic viral encephalitis and are also worth considering. This may include cerebral toxoplasmosis (particularly in people living with HIV), tuberculosis or anti-N-methyl-D-aspartate-receptor (anti-NMDAR) encephalitis. Also consider eosinophilic meningitis, which is usually caused by *Angiostrongylus cantonensis* and sometimes by *Gnathostoma* species, see **eosinophilic meningitis**, page 85 in this topic.

Varicella-zoster virus encephalitis should be suspected if associated with a typical rash see varicella-zoster virus infections (page 281) in 'Skin infections.'

See *Papua New Guinea National Guidelines for HIV Care and Treatment* for treatment of CMV and toxoplasma encephalitis.

Management of encephalitis

Empirical therapy for encephalitis in adults and children > 3 months

Use:

aciclovir IV, 8-hourly

adult or child older than 12 years: 10 mg/kg

child younger than 5 years: 20 mg/kg or 500 mg/m^2

child 5 to 12 years: 15 mg/kg or 500 mg/m^2.

If a parenteral formulation of aciclovir is not available, use oral aciclovir:

aciclovir 400 mg orally, 5 times a day.

Consider adding empirical treatment for *Listeria* if at risk (patients who are immunocompromised, older than 50 years, or are pregnant) – see **empirical therapy for meningitis** (page 79) earlier in this topic for appropriate regimens.

Note: steroids are **not** recommended in the treatment of HSV encephalitis.

Mycoplasma pneumoniae is a possible cause of meningoencephalitis in children. For severe cases of encephalitis in children, to treat *M. pneumoniae,* consider **adding** azithromycin to aciclovir, use:

azithromycin *10 mg/kg up to 500 mg orally/IV on the first day, followed by 5 mg/kg up to 250 mg orally/IV, daily for the next four days.*

Duration of treatment

If HSV encephalitis is confirmed, or cannot be ruled out, treat with aciclovir for 14 to 21 days.

Brain abscess and subdural empyema

Brain abscess or subdural empyema usually cause persistent fever plus focal neurological signs and often a reduced level of consciousness. If brain abscess or subdural empyema is suspected, refer the patient to a hospital with specialised facilities for further investigation and surgical management.

Potential sources of these infections include paranasal sinusitis, otitis media, malignant otitis externa, dental infection, endocarditis or penetrating trauma. Subdural empyema commonly occurs as a consequence of bacterial meningitis or frontal sinus infection. Determining the source of infection is helpful to guide management, but not always successful.

These conditions are often polymicrobial. Organisms may include anaerobes, *Streptococcus* species or Gram-negative bacteria.

Surgical drainage is required, where possible. If present, an infected sinus or ear should be drained and infected bone removed where possible. Send blood cultures, pus swabs and tissue for culture, TB and cryptococcal antigen testing. Modify antibiotic therapy according to the results of culture and susceptibility testing.

In immunocompromised patients, consider other diagnoses including toxoplasmosis, *Cryptococcosis* species, *Nocardiosis* species and TB. In patients with multiple abscesses, test for HIV. Malignancy should also be considered as an alternative diagnosis if there is no improvement with empiric therapy.

For brain abscess after penetrating trauma or neurosurgery, treat as for **meningitis following penetrating head trauma or neurosurgery** (page 86), but use the duration for brain abscess and subdural empyema (see next section).

Empirical therapy for brain abscess and subdural empyema

Seizures are frequent, give prophylactic anticonvulsants in addition to antibiotics.

Use:

ceftriaxone *2 g (child: 50 mg/kg up to 2 g) IV, 12-hourly*

PLUS

metronidazole *500 mg (child: 12.5 mg/kg up to 500 mg) IV, 8-hourly.*

If there are multiple abscesses or for probable haematogenous spread, **add**:

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

For patients who are at increased risk of methicillin-resistant *Staphylococcus aureus* (MRSA) (e.g. recent prolonged or frequent hospital admission, prior colonisation with MRSA), instead of flucloxacillin, add:

vancomycin *slow IV infusion,* ***consider a loading dose in critically ill adults and children****. See 'Appendix 2: Vancomycin dosing' (page 386) for information on loading dose, dosing frequency and infusion time*

adult ≥ 40 years: 15 mg/kg, see Table 18 for dosing frequency (page 390)

adult < 40 years 20 mg/kg, see Table 17 for dosing frequency (page 389)

child 3 months and older: 15 mg/kg, 6-hourly.

IV to oral switch

It may be appropriate to switch to oral antibiotics following surgical drainage and clinical improvement for some patients. If used, oral antibiotics should have good CNS penetration (e.g. trimethoprim+sulfamethoxazole, fluoroquinolones). Do not use oral beta-lactams because these have poor CSF penetration in the absence of meningeal inflammation.

Intravenous treatment should be extended if surgical drainage cannot be performed.

Duration: The total duration of therapy (IV + oral) is usually 4 to 8 weeks, with a minimum of 2 weeks of IV treatment, depending on whether surgical drainage was performed, the clinical response, and radiological evidence of resolution.

Epidural abscess

Also see: vertebral osteomyelitis (for adults, see page 42 and for children, see page 48) in 'Bone and joint infections.'

Epidural abscesses are most commonly caused by *Staphylococcus aureus.*

Tuberculosis is an important differential diagnosis in high-prevalence settings like Papua New Guinea.

Empirical therapy for epidural abscess

Take two sets of blood for culture prior to commencing antibiotics.

For diagnosis, perform MRI or, if not available, CT (MRI is preferred, if available, as abscesses may be missed with CT).

Use:

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

PLUS

ceftriaxone *2 g (child: 50 mg/kg up to 2 g) IV, 12-hourly.*

If there is an increased risk of methicillin-resistant *S. aureus* (MRSA) (recent prolonged or frequent hospital admission, or prior colonisation with MRSA), **add**:

vancomycin *slow IV infusion,* ***consider a loading dose in critically ill adults and children****. See 'Appendix 2: Vancomycin dosing' (page 386) for information on loading dose, dosing frequency and infusion time*

adult ≥ 40 years: 15 mg/kg, see Table 18 for dosing frequency (page 390)

adult < 40 years 20 mg/kg, see Table 17 for dosing frequency (page 389)

child 3 months and older: 15 mg/kg, 6-hourly.

For patients with hypersensitivity to penicillins, use vancomycin as a single agent (however, note that this will only be active against Gram-positive organisms).

Modify therapy according to the results of culture and susceptibility testing. If microbiological diagnosis is not obtained, modify antibiotic therapy (ideally to a single agent) based on the most likely cause of infection.

It may be appropriate to switch to oral therapy after 2 to 4 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.

Duration

Treat for at least 6 weeks, with a minimum of 2 to 4 weeks IV.

Neurocysticercosis

Neurocysticercosis is caused by the larval stage of the pork tapeworm *Taenia solium*.

Diagnosis is based on a consistent clinical picture and radiology (CT and MRI). Serologic testing is not currently available in Papua New Guinea. All patients with neurocysticercosis should be evaluated for ocular cysticercosis by ophthalmology.

Antiparasitic therapy plus adjunctive corticosteroids are indicated for patients with active lesions. Patients with calcified cysts but no active lesions do not benefit from antiparasitic treatment. Differentiation of active lesions from inactive lesions requires imaging.

Patients with neurocysticercosis often present with seizures. Use of albendazole reduces long-term seizure frequency in patients with active lesions.

Corticosteroids should always be administered with antiparasitic therapy. Corticosteroids should also be used in the treatment of cysticercal encephalitis.

Oedema surrounding active lesions may cause raised intracranial pressure; this should be managed with corticosteroids.

Treatment for neurocysticercosis with active lesions

For more detailed information on management, see *WHO Guidelines on Management of Taenia solium Neurocysticercosis*.

Consider antiseizure medications to manage acute symptoms.

Begin steroids one day before antiparasitic treatment, use:

dexamethasone 0.1 mg/kg orally, daily for a minimum of 10 days

OR

prednisone 1 mg/kg orally, daily for a minimum of 10 days

Then add:

albendazole 7 mg/kg (maximum dose 600 mg) orally, 12-hourly for 10 days.

Do not give antiparasitic therapy to patients with untreated hydrocephalus, ocular cysticercosis or high–cyst-burden disease with diffuse cerebral oedema, as inflammation around the degenerating cysts may worsen symptoms. For the management of these patients, seek appropriate advice.

Duration: The optimal duration of corticosteroid treatment depends on the number and size of the lesions and the clinical response. Longer dosing with corticosteroids (i.e. 28 days) has been associated with better clinical outcomes than shorter schedules (e.g. 10 days). Corticosteroids used for treatment durations of 3 weeks or more will require tapering.

Key additional references

'Meningitis and Encephalitis' [published March 2020] in: Clinical Practice Guidelines. The Royal Children's Hospital Melbourne. Available from: https://www.rch.org.au/clinicalguide/guideline_index/Meningitis_encephalitis/

Guidelines for diagnosing, preventing and managing cryptococcal disease among adults, adolescents and children living with HIV. Geneva: World Health Organization; 2022.

WHO consolidated guidelines on tuberculosis. Module 4: treatment - drug-susceptible tuberculosis treatment. Geneva: World Health Organization; 2022.

WHO guidelines on management of Taenia solium neurocysticercosis. Geneva: World Health Organization; 2021.

Dental infections

This topic includes advice on the management of the following conditions in adults and children 3 months and older:

- **dental caries**, page 95
- **acute odontogenic infections** (including Ludwig angina), page 95
- **periodontal disease** including periodontitis, alveolar osteitis (dry socket), pulpitis, localised pericoronitis, chronic gingivitis and necrotising gingivitis, page 98
- **mandibular osteomyelitis**, page 100.

The following topics are not included in this section:

- **peritonsillar abscess** (page 116) and **salivary gland infections** (page 121) in 'Ear, nose and throat infections.'

Dental caries

Systemic antibiotic use is **not** recommended. Refer the patient to a dentist for dental treatment.

Acute odontogenic infections

If an odontogenic infection is ignored or not appropriately treated, it can progress to a localised abscess or spread to the soft tissues of the face or neck. Rare but serious complications include Ludwig angina, airway compromise, sepsis, or spread to the bone, brain, neck or mediastinum.

The most important element of management is surgical drainage and removal of necrotic tissue with dental extraction, where indicated. If necrotising infection is present, see **necrotising soft tissue infection** (page 307) in 'Soft tissue infections.'

Persistent dental pain and swelling after dentoalveolar surgery could be due to alveolar osteitis or a postoperative infection.

Osteomyelitis of the jaw is an important differential diagnosis in patients with an unresolved oral infection with systemic features and localised bone pain or tenderness.

Most **infections following dentoalveolar surgery** can be managed by dental treatment alone. If there are systemic features of infection or the patient is immunocompromised, treat as spreading odontogenic infection with or without severe or systemic symptoms, depending on severity (see recommendations in this topic).

Features of odontogenic infections

Localised odontogenic infections cause dental pain and abscesses (localised swelling on the gum or fluctuant tissue) with or without visible pus but **without** facial swelling or systemic features.

Spreading odontogenic infection without severe or systemic features can cause facial swelling, dental or facial pain, and abscesses with or without visible pus

Spreading odontogenic infection with severe or systemic features cause severe features such as significant facial swelling and pain, neck swelling, trismus, dysphagia (difficulty swallowing) and difficulty breathing. Systemic features include fever > 38°C, tachycardia, pallor and diaphoresis (excessive sweating).

Treatment of odontogenic infections

Localised odontogenic infection
Antibiotic use is not recommended.
Refer to dentist for prompt dental treatment (e.g. extraction, root canal) or surgical intervention to address the source of the infection.

Spreading odontogenic infections

Spreading odontogenic infection without severe or systemic features
Use: ***amoxicillin*** *500 mg (child 25 mg/kg up to 500 mg) orally, 8-hourly for 5 days* *PLUS* ***metronidazole*** *400 mg (child 10 mg/kg up to 400 mg) orally, 12-hourly for 5 days.* Alternatively, as a single agent, use: ***amoxicillin+clavulanate*** *500+125 mg (child 25+5 mg/kg) orally, 12-hourly for 5 days.* In patients with hypersensitivity to penicillins, use: ***clindamycin*** *300 mg (child: 7.5 mg/kg up to 300 mg) orally, 8-hourly for 5 days.*

Spreading odontogenic infection with severe or systemic features

Including Ludwig angina.

Arrange urgent transfer to hospital. In conjunction with surgical intervention, use:

benzylpenicillin *1.8 g (if in ICU 2.4 g) (child: 50 mg/kg up to 1.8 g [or 2.4 g if in ICU]) IV, 4-hourly*

PLUS

metronidazole *500 mg (child: 12.5 mg/kg up to 500 mg) IV, 12-hourly.*

For patients with **immediate nonsevere** or **delayed nonsevere** hypersensitivity to penicillins, replace benzylpenicillin with:

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

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

chloramphenicol *1 g (child: 25 mg/kg up to 1 g) IV, 6-hourly.*

Consider a single dose of hydrocortisone if the patient's airway is obstructed.

Switch to oral therapy once swelling and trismus subside (and the patient can swallow), and purulent discharge from drains slows.

Duration of therapy

Continue antibiotics until signs and symptoms of infection have resolved, usually 10 to 14 days (IV + oral).

Periodontal disease

Periodontitis (including rapidly progressing periodontitis)

First-line treatment is mechanical plaque control with scaling and root debridement. Antibiotics are rarely needed for periodontitis.

Only consider antibiotics in patients with the following:

- rapidly progressing periodontitis
- periodontitis that has not responded to dental treatment
- immunocompromised patients (including patients with poorly controlled diabetes).

If antibiotics are indicated, use:

amoxicillin+clavulanate *500+125 mg (child: 25+5 mg/kg up to 500+125 mg) orally, 8-hourly for 7 to 10 days.*

In patients with hypersensitivity to penicillins, use:

clindamycin *300 mg (child: 7.5 mg/kg up to 300 mg) orally, 8-hourly for 7 to 10 days.*

Patients with trismus may require IV therapy – treat as for spreading odontogenic infections.

Alveolar osteitis (dry socket)

Antibiotics are **not** recommended.

Treatment should involve saline irrigation, antiseptic/analgesic dressings, and symptomatic relief of pain.

Pulpitis (reversible and irreversible)

Antibiotics are **not** recommended.

Use analgesic dressings and symptomatic relief of pain.

Localised pericoronitis

Antibiotics are **not** recommended.

Treatment should involve antiseptic irrigation, mouthwash and symptomatic relief of pain.

Gingivitis

Chronic gingivitis

Antibiotics are **not** recommended.

First-line treatment involves scaling and chemical plaque control.

Consider short-term use of a mouthwash to reduce plaque formation; use:

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.

Necrotising gingivitis (previously known as acute necrotising ulcerative gingivitis [ANUG])

Necrotising 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
- the patient mechanically cleaning their teeth
- counselling and lifestyle adjustment (including smoking or betel nut cessation)
- analgesics.

Treatment failure is usually due to inadequate debridement or poor oral hygiene, rather than ineffective antibiotic therapy.

For antibiotic therapy for necrotising gingivitis, use:

metronidazole *400 mg orally, 12-hourly for 3 to 5 days*

PLUS short-term use of a mouthwash to prevent plaque formation:

chlorhexidine 0.2% mouthwash 10 mL rinsed in the mouth for 1 minute then spat out, 8- to 12-hourly until pain has reduced.

Mandibular osteomyelitis

Treatment of mandibular osteomyelitis of dental origin

Surgical debridement with dental extraction where indicated is important.

Culture and susceptibility testing is necessary to guide antibiotic treatment. Send tissue specimens from debridement for culture. If systemically unwell, send blood specimens for culture.

For **chronic osteomyelitis**, this usually resolves on extraction of the affected tooth. Only commence antibiotics when causative organisms are identified following debridement, using culture and susceptibility results to guide antibiotic selection.

For **acute osteomyelitis**, use:

amoxicillin+clavulanate *500+125 mg (child: 25+5 mg/kg up to 500+125 mg) orally, 8-hourly.*

In patients with hypersensitivity to penicillins, use:

clindamycin *300 mg (child: 7.5 mg/kg up to 300 mg) orally, 8-hourly.*

Patients with difficulty swallowing (e.g. trismus) or airway compromise require hospitalisation and IV antibiotics, seek appropriate advice and start:

amoxicillin+clavulanate

adult: 1+0.2 g IV, 6-hourly

child 3 months or older: 25+5 mg/kg up to 1+0.2 g IV, 6-hourly

OR

benzylpenicillin *1.8 g (if in ICU 2.4 g) (child: 50 mg/kg up to 1.8 g or 2.4 g if in ICU) IV, 4-hourly*

PLUS

metronidazole *500 mg (child: 12.5 mg/kg up to 500 mg) IV, 12-hourly*

OR including for patients with penicillin hypersensitivity

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

Modify antibiotics according to the results of culture and susceptibility testing, when available.

Duration

Acute osteomyelitis: Treat for 6 weeks (IV + oral)

Chronic osteomyelitis: Treat for 3 months.

Key additional references:

Johnston DT, Phero JA, Hechler BL. Necessity of antibiotics in the management of surgically treated mandibular osteomyelitis: A systematic review. Oral Surg Oral Med Oral Pathol Oral Radiol. 2023 Jan;135(1):11-23. doi: 10.1016/j.oooo.2022.05.001. Epub 2022 May 13. PMID: 35863960.

Ear, nose and throat (ENT) infections

This topic includes advice on the management of the following conditions in adults and children 3 months and older:

- **otitis media** including acute otitis media without effusion, acute otitis media with effusion, chronic suppurative otitis media and recurrent otitis media, page 103
- **otitis externa** including acute diffuse otitis externa and necrotising otitis externa, page 108
- **mastoiditis**, page 110
- **rhinosinusitis / sinusitis** including acute bacterial sinusitis, page 113
- **sore throat** (pharyngitis and tonsillitis), page 115
- **peritonsillar abscess** (quinsy), page 116
- **retropharyngeal and parapharyngeal abscesses**, page 118
- **epiglottitis**, page 119
- **salivary gland infections**, page 121.

The following topics are not included in this section:

- **cervical lymphadenitis** (page 315) in 'Soft tissue infections.'

Otitis media

Otitis media refers to inflammation and infection of the middle ear space and is best regarded as a spectrum of disease that ranges from mild (otitis media with effusion) to severe (chronic suppurative otitis media [CSOM]).

Nearly all children will experience at least one episode of acute otitis media, and most children will improve spontaneously. Concerns arise for children who suffer frequent episodic acute otitis media or persistent otitis media with effusion as this can lead to permanent hearing loss.

Acute otitis media (AOM) is a common paediatric presentation. Viral upper respiratory tract infections are often accompanied by mild inflammation of the middle ear.

AOM is very likely if there is an acute onset of symptoms such as pain alone, usually preceded by coryzal symptoms, hearing loss with or without otorrhoea (pus draining from the ear). Signs include an erythematous, bulging, immobile tympanic membrane or pus draining from the ear for less than 2 weeks.

Pain alone is not sufficient for a diagnosis of otitis media.

Adequate and regular pain relief is the mainstay of AOM treatment. Provide pain relief (e.g. paracetamol and/or ibuprofen) and advise the patient or carer to return for follow-up if the child's symptoms worsen or if there is no improvement in 2 to 3 days. Review all children after 4 to 7 days.

Most cases do not require antibiotics and recover with supportive therapy alone within 3 to 7 days.

Antibiotic therapy is required in the following groups:

- infants younger than 6 months
- children younger than 2 years with bilateral infection
- children who are systemically unwell (e.g. high fever [39°C or higher], severe pain, vomiting or lethargy)
- children with otorrhea (indicative of tympanic membrane perforation)
- children at high risk of complications (e.g. immunocompromised children).

Do not use lower amoxicillin doses than recommended in this topic because they will not achieve adequate plasma and tissue concentrations to treat resistant *Streptococcus pneumoniae* strains.

Treatment of acute otitis media

Acute otitis media (AOM) without effusion (otorrhoea)

Avoid routine antibiotic use.

If antibiotics are indicated (see comments above), use:

amoxicillin *30 mg/kg up to 1 g orally,* ***12-hourly*** *for 7 days.*

Review all children at 4 to 7 days; if the eardrum bursts, treat as for AOM with otorrhoea, if the eardrum is bulging, increase the dose of amoxicillin:

amoxicillin *30 mg/kg up to 1 g orally,* ***8-hourly*** *for a further 7 days.*

Review again after 1 week. If bulging eardrum persists, review adherence and change to:

amoxicillin+clavulanate *22.5+3.2 mg/kg up to 875+125 mg orally, 12-hourly for 7 days.*

OR

amoxicillin+clavulanate *15+3.75 mg/kg up to 500+125 mg orally, 8-hourly for 7 days.*

Continue to review weekly.

cont...

In place of amoxicillin or amoxicillin+clavulanate, for patients with **delayed nonsevere** hypersensitivity to penicillins, use:

cefuroxime *(child 3 months or older) 15 mg/kg up to 500 mg orally, 12-hourly for 7 days.*

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

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

Acute otitis media (AOM) with effusion (otorrhoea)

Gentamicin ear drops are contraindicated in the setting of otorrhoea due to risk of ototoxicity.

Ear toileting involves dry mopping the ear with rolled tissue spears or similar, performed 6-hourly until the ear is dry. Perform prior to instilling ear drops.

Consider sending middle ear fluid for culture if poor response to empiric therapy.

Use:

amoxicillin *1 g (child: 45 mg/kg up to 1 g) orally, 12-hourly*

PLUS

ear toileting.

Review at 7 days, or earlier if no better. If discharge or bulging eardrum persists, change to:

amoxicillin+clavulanate *22.5+3.2 mg/kg up to 875+125 mg orally, 12-hourly*

OR

amoxicillin+clavulanate *15+3.75 mg.kg up to 500+125 mg orally, 8-hourly*

PLUS

ciprofloxacin *0.3% ear drops, 2-5 drops instilled into the affected ear 2 to 4 times per day.*

Alternatively, if ciprofloxacin ear drops are not available, use:

chloramphenicol *0.5% ear/eye drops, 5 drops instilled into the affected ear(s), twice a day.*

Continue to review weekly.

Duration: Treat for 14 days. Continue ear drops until ear dry for at least 3 days (this may require prolonged treatment).

Chronic suppurative otitis media (CSOM)

CSOM is an infection of the middle ear with a perforated eardrum and discharge for at least 6 weeks.

Send a swab for culture in all patients with CSOM.

Occasionally, serious complications can occur, such as intracranial infection and acute mastoiditis.

Gentamicin ear drops are contraindicated in the setting of a perforated tympanic membrane due to risk of ototoxicity.

CSOM can cause hearing impairment and disability.

Refer any child with CSOM to ENT for hearing assessment.

Advise patients/carers to keep the ear as dry as possible and perform ear toileting (mopping the ear with rolled tissue spears or similar), 6-hourly until the ear is dry. Perform ear toileting prior to instilling ear drops.

Use:

> ***ciprofloxacin*** *0.3% ear drops 5 drops into the affected ear(s) 2 to 4 times a day after ear toilet until ear dry for at least 3 days up to a maximum of 2 weeks.*

Alternatively, if ciprofloxacin ear drops are not available, use:

> ***chloramphenicol*** *0.5% ear/eye drops, 5 drops instilled into the affected ear(s), twice a day after ear toilet, until ear dry for at least 3 days to a maximum of 2 weeks.*

Review weekly. If effusion continues for more than 2 weeks, continue aural toilet and ensure the child is under the care of an ENT specialist.

If persistent CSOM after 4 months of treatment, **add**:

> ***trimethoprim+sulfamethoxazole*** *4+20 mg/kg (maximum 160+800 mg) orally, 12-hourly for 6 to 12 weeks.*

If otorrhea continues for more than 3 weeks after commencement of therapy, treatment is considered to have failed.

For children that are not improving, escalation to cover *Pseudomonas aeruginosa* may be required, use:

> ***ciprofloxacin*** *10 mg/kg up to 750 mg orally, 12-hourly.*

Other causes of treatment failure include poor adherence to treatment, cholesteatoma, antimicrobial resistance and underlying immunodeficiency.

Recurrent otitis media

Recurrent AOM should be diagnosed in children who have documented AOM (with or without effusion/otorrhoea) more than three times in 6 months or four times in 12 months.

Accurate diagnosis of AOM requires assessment of the appearance of tympanic membrane by otoscope plus compliance or mobility of the tympanic membrane by pneumatic otoscopy or tympanometry.

Ensure the current episode of otitis media has been treated appropriately. If bulging eardrum or discharge has not resolved, treat as per AOM without perforation or AOM with perforation as appropriate.

Assess the child's risk factors. A child is at high risk of AOM with perforation or CSOM if they have one or more of the following risk factors:

- live in a remote community
- is younger than 2 years
- had their first episode of OM before 6 months of age
- has a family history of CSOM
- has a current or previous tympanic membrane perforation
- has craniofacial abnormalities
- has a cleft palate, Down Syndrome, immunodeficiency or cochlear implants
- has developmental delay, with hearing loss
- has severe visual impairment.

If a child is not at high risk, review monthly for 3 months.

For a child with one or more risk factors, use prophylactic antibiotics:

amoxicillin 25 to 50 mg/kg orally, 1 to 2 times a day for 3 to 6 months.

Consider referral to ENT for potential surgical options of recurrent AOM and **continue to review monthly**.

Duration: Continue prophylaxis until no AOM for 3 months and no persistent bilateral otitis media with effusion.

Otitis externa

Acute diffuse otitis externa

Otitis externa is often caused by skin breakdown in the external auditory canal following excessive water exposure. *Pseudomonas aeruginosa* and *Staphylococcus aureus* are the most common causes of acute diffuse otitis externa.

Topical therapy alone is sufficient in most cases of acute diffuse otitis externa.

Ear toileting involves dry mopping the ear with rolled tissue spears or similar, performed 6-hourly until the ear is dry. Perform prior to instilling ear drops.

Collect swabs for microscopy and culture in patients with severe or recurrent otitis externa, and in patients who are immunocompromised.

The ear canal must be kept as dry as possible during treatment and for 2 weeks afterwards.

Note that acute otitis externa may present similarly to AOM with perforation.

If AOM with perforation is excluded, use:

dexamethasone+framycetin+gramicidin 0.05%+0.5%+0.005% ear drops (e.g. Otodex, Sofradex), 3 drops instilled into the affected ear(s) after ear toilet, 3 times daily for 5 to 7 days.

If AOM with perforation cannot be excluded (e.g. obscured tympanic membrane), avoid ototoxic preparations and use:

ciprofloxacin *0.3% ear drops, 5 drops instilled into the affected ear(s), 2 to 4 times daily after ear toileting.*

Ear drops are the most effective treatment for otitis externa, as they deliver a high concentration of medication to the infected and inflamed external tissue. If ear drops are not available, oral corticosteroids can be considered for patients with severe symptoms:

prednisolone 40 mg (child: 1 mg/kg up to 40 mg) orally, daily for 3 to 7 days, then taper dose according to response.

cont...

For otitis externa with systemic symptoms or spread of inflammation to the pinna, **add** to topical treatment:

flucloxacillin *1 g (child: 25 mg/kg up to 1 g) orally, 6-hourly*

PLUS

ciprofloxacin *750 mg (child: 20 mg/kg up to 750 mg) orally, 12-hourly.*

If intravenous therapy is required, use:

flucloxacillin *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.*

Consider the possibility of necrotising otitis externa in patients who fail to improve with the above treatment, see the next section.

Duration

For otitis externa with systemic symptoms or spread of inflammation to pinna, treat for 7 to 10 days (IV + oral).

Necrotising otitis externa

Necrotising otitis externa is a rare complication of acute diffuse otitis externa, involving spread of infection to cartilage and bone in the external ear canal and base of skull. It mostly occurs in elderly, immunocompromised or diabetic patients. The most common causative pathogen is *P. aeruginosa*.

Features include fever, severe persistent pain, visible granulation tissue and progressive cranial neuropathies.

Consider CT and/or MRI to detect bone involvement or intracranial complications.

Urgently refer to an ENT specialist.

Collect swabs and tissue samples for microscopy and culture prior to administering antibiotics. Collect blood for cultures if the patient is systemically unwell or immunocompromised. Consider biopsy if no pathogen is isolated from other cultures and the patient fails to improve with empirical therapy.

Suctioning may be needed in an ENT setting.

cont...

Until the results of culture and susceptibility testing are available, use an antipseudomonal regimen:

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

If piperacillin+tazobactam is unavailable or for patients with hypersensitivity to penicillins, use:

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

Change to oral antibiotic therapy when improving, according to the results of culture and susceptibility testing, if available.

If culture and susceptibility results are not available, use:

ciprofloxacin *750 mg (child: 20 mg/kg up to 750 mg) orally, 12-hourly.*

In patients who do not improve with empirical management, consider fungal infection, particularly in diabetic patients. Seek appropriate advice.

Duration: Prolonged treatment is required because the infection involves bone or cartilage, treat for a total of 6 to 8 weeks (IV + oral). The patient should receive close clinical follow up to ensure clinical improvement.

Mastoiditis

Mastoiditis is a suppurative infection of the mastoid air cells of the temporal bone. Acute mastoiditis refers to infection with symptoms of less than 1 month's duration, while chronic mastoiditis refers to an infection with a duration of months to years.

In children, acute mastoiditis is a rare complication of AOM. It presents with a high fever and a tender swelling behind the ear. Symptoms include conductive hearing loss and tenderness, swelling, and pain behind the ear. Complications include subperiosteal, subcutaneous, intratemporal or intracranial collections, and facial nerve palsy.

In adults, mastoiditis can be a complication of chronic suppurative otitis media or cholesteatoma.

Consider CT and/or MRI to detect bone involvement or intracranial complications.

Management is usually surgical – refer the patient to an ENT specialist. Surgical procedures for consideration include aspiration and drainage of the middle ear, ventilation tube placement, incision and drainage of subperiosteal abscess, and mastoidectomy. Send operative samples for culture and susceptibility testing.

Treatment of mastoiditis in children

Consult ENT urgently and collect specimens for culture and susceptibility testing, if possible.

For empirical treatment, use:

amoxicillin+clavulanate *IV:*

child younger than 3 months and less than 4kg: 25+5 mg/kg, 12-hourly

child younger than 3 months and 4 kg or more: 25+5 mg/kg, 8-hourly

child 3 months or older: 25+5 mg/kg 6-hourly.

If a parenteral formulation of amoxicillin+clavulanate is not available, use:

flucloxacillin *50 mg/kg up to 2 g orally, 6-hourly*

PLUS

cefotaxime *50 mg/kg up to 2 g IV, 8-hourly.*

For children with otorrhoea (effusion), use as a **single agent**:

ceftazidime *50 mg/kg up to 2 g IV, 8-hourly.*

For patients with hypersensitivity to penicillins, use as a single agent:

ciprofloxacin *10 mg/kg up to 400 mg IV, 8-hourly.*

Change to oral antibiotics when appropriate (see comments under duration), according to susceptibility results.

If susceptibility results are not available, use:

amoxicillin+clavulanate *22.5+3.2 mg/kg up to 875+125 mg orally, 12-hourly*

OR

amoxicillin+clavulanate*15+3.75 mg.kg up to 500+125 mg orally, 8-hourly.*

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

cefuroxime *15 mg/kg up to 500 mg orally, 12-hourly.*

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

azithromycin *10 mg/kg up to 500 mg orally, daily.*

cont...

For children who received ceftazidime due to otorrhoea, but susceptibility results are not available, step down to:

ciprofloxacin *20 mg/kg up to 750 mg orally, 12-hourly*

PLUS

flucloxacillin *12.5 mg/kg up to 500 mg orally, 6-hourly.*

Duration

For acute mastoiditis, treat with IV antibiotics for at least 5 days. Switch to oral antibiotics when improving and continue for a total duration of 12 to 15 days (IV + oral).

Longer antibiotic treatment is required for chronic mastoiditis, if surgical drainage was not completed or if there are intracranial complications. Seek appropriate advice.

Treatment of mastoiditis in adults

Consult ENT urgently and collect specimens for culture and susceptibility testing, if possible.

For empirical treatment, use:

flucloxacillin *2 g IV, 6-hourly*

PLUS

chloramphenicol *1 g IV, 6-hourly.*

If there is no improvement on initial therapy, ensure the patient receives a surgical review and switch chloramphenicol to:

ceftazidime *2 g IV, 8-hourly.*

Switch to oral antibiotics when appropriate (see comments under duration), according to the results of culture and susceptibility testing.

If culture and susceptibility results are not available, use:

amoxicillin+clavulanate *500+125 mg orally, 8-hourly.*

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

cefuroxime *500 mg orally, 12-hourly.*

cont...

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

azithromycin *500 mg orally, daily.*

For patients who received ceftazidime, but for whom the results of culture and susceptibility testing are not available, step down to:

ciprofloxacin *750 mg orally, 12-hourly*

PLUS

flucloxacillin *500 mg orally, 6-hourly.*

Duration

For acute mastoiditis, usually 1 week of intravenous therapy is required initially, then switch to oral antibiotics to complete a total duration of 2 weeks (IV + oral).

Longer antibiotic treatment may be required if surgical drainage was not done or if there are intracranial complications.

For chronic mastoiditis, treat for 6 to 8 weeks (IV + oral).

Rhinosinusitis / sinusitis

Rhinosinusitis refers to inflammation of the nasal mucosa (rhinitis) and the paranasal sinuses (sinusitis), although the term sinusitis is commonly used to describe this condition. Rhinitis can occur in isolation and is usually caused by an allergy.

Acute rhinosinusitis is usually a self-limiting viral infection, often called 'the common cold'. Secondary acute bacterial rhinosinusitis may follow viral upper respiratory tract infections, but this occurs in less than 2% of patients. It is important to differentiate between viral and bacterial causes of acute rhinosinusitis – yellow/green-coloured nasal discharge alone is not a sign of bacterial infection and is **not** an indication for antibiotic therapy.

Symptomatic therapy, including analgesics, saline nasal spray or drops and topical or oral decongestants (available over-the-counter from private pharmacies), can be helpful.

The usual pathogens in bacterial sinusitis are *Streptococcus pneumoniae* and *Haemophilus influenzae*. Most cases do not require antibiotics and recover with supportive care alone within 10 days. Symptoms may include persistent nasal discharge (> 10 days), nasal obstruction, maxillary toothache, unilateral facial pain, headache and fever.

Clinical features of bacterial infection extending beyond the paranasal sinuses and nasal cavity into adjacent spaces (e.g. meninges, ocular space, periorbital space) include acute-onset confusion or impaired consciousness, diplopia or impaired vision, neck stiffness, severe headache, photophobia, proptosis, periorbital oedema or cellulitis, signs of sepsis or septic shock. If any of these features are present, hospitalisation for intravenous antibiotics and urgent surgical referral are required.

Acute rhinosinusitis refers to rhinosinusitis that lasts less than 4 weeks. If symptoms persist for longer than 12 weeks, the condition is termed chronic rhinosinusitis.

Acute bacterial sinusitis

Acute bacterial sinusitis is usually a self-limiting condition and **antibiotics make little difference to the course of the illness.**

Consider antibiotics in patients with high fever for more than 3 days or severe symptoms for more than 5 days, including purulent nasal discharge, sinus tenderness or maxillary toothache.

Avoid routine antibiotic use.

If antibiotics are indicated (see comments), use:

amoxicillin *500 mg (child: 25 mg/kg up to 500 mg) orally, 8-hourly.*

For patients with hypersensitivity to penicillins, use:

doxycycline *100 mg (child: 2 mg/kg up to 100 mg) orally, 12-hourly.*[4]

If symptoms do not improve in 5 days or if symptoms worsen, or if the patient has been treated with amoxicillin within the last month, change to:

amoxicillin+clavulanate *500+125 mg (child: 22.5+3.2 mg/kg up to 500+125 mg) orally, 8-hourly.*

If symptoms worsen after initial improvement or there are clinical features of bacterial infection extending beyond the paranasal sinuses and nasal cavity, the patient requires referral to an ENT specialist for review and consideration of nasal endoscopy or surgical intervention. Seek ENT review and change to:

amoxicillin+clavulanate *IV*

adult: 1+0.2 g, 6-hourly

child younger than 3 months and less than 4 kg: 25+5 mg/kg, 12-hourly

child younger than 3 months and 4 kg or more: 25+5 mg/kg, 8-hourly

child 3 months or older: 25+5 mg/kg up to 1+0.2 g, 6-hourly.

cont...

4 Unlike older tetracyclines, doxycycline has not been associated with tooth discolouration, enamel hypoplasia or bone deposition with short-term use (< 21 days), even in children younger than 8 years, so is increasingly used in this age group. However, use is limited by the lack of a suitable paediatric formulation.

Alternatively, if a parenteral formulation of amoxicillin+clavulanate is not available, as a two-drug regimen, use:

ceftriaxone *2 g (child: 50 mg/kg up to 2 g) IV, 12-hourly*

PLUS

metronidazole *500 mg (child: 12.5 mg/kg up to 500 mg) IV, 12-hourly.*

Duration (uncomplicated infection): Treat for 7 days

For complicated infection, i.e. the infection has spread beyond the paranasal sinuses and nasal cavity into adjacent spaces, seek appropriate advice for ongoing management and duration of antibiotic therapy.

Sore throat (pharyngitis and tonsillitis)

Sore throat is often referred to as pharyngitis (inflammation of the pharynx) or tonsillitis (inflammation of the palatine tonsils), but it can be a symptom of many other conditions.

Viruses are the most common cause of acute pharyngitis and tonsillitis; these infections are self-limiting, and symptoms usually resolve within 7 days. Oesophageal candidiasis often presents with pain on swallowing, see **oesophageal candidiasis** (page 137) in 'Gastrointestinal infections.'

Provide paracetamol or nonsteroidal anti-inflammatory drugs (NSAIDs) to relieve pain and fever. Medicated or non-medicated lozenges can also be recommended to relieve throat pain in adults and adolescents.

Bacterial infection is a less common cause of sore throat; *Streptococcus pyogenes* (group A streptococcus) is the most frequently implicated bacterial pathogen and is more common in children than in adults.

While streptococcal pharyngitis and tonsillitis are usually self-limiting with symptoms lasting 7 days, some patient groups are at higher risk of developing acute rheumatic fever and other non-suppurative complications such as post-streptococcal glomerulonephritis, particularly following recurrent streptococcal throat infections. These are common in Papua New Guinea. Suppurative complications include peritonsillar abscess and retropharyngeal abscesses.

Streptococcal pharyngitis and tonsillitis are difficult to diagnose based on clinical features alone. The clinical features traditionally associated with streptococcal infection are abrupt onset of symptoms, fever (above 38°C), tender cervical lymphadenopathy, tonsillar exudate, and the **absence** of cough, rhinorrhoea or nasal congestion.

Consider Epstein-Barr virus infection in patients (particularly adolescents and young adults) with severe sore throat, fever, nausea, lymphadenopathy, splenomegaly, hepatomegaly, rash and fatigue.

Management of pharyngitis and tonsilitis

Presumed streptococcal pharyngitis or tonsillitis in a child or adolescent who presents with sore throat with an abrupt onset of symptoms, fever (above 38 °C), tender cervical lymphadenopathy, tonsillar exudate, and the **absence** of cough, rhinorrhoea or nasal congestion.

Use:

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

OR (including for patients with penicillin hypersensitivity)

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

It is important to complete the antibiotic course even after recovery to prevent acute rheumatic fever. For patients with poor compliance to oral therapy, use:

benzathine benzylpenicillin *1.2 million units (child < 20 kg: 600 000 units) IM, as a single dose.*

For patients who are not improving on standard therapy, consider alternative diagnoses, e.g. peritonsillar abscess, and treat accordingly.

Peritonsillar abscess

Peritonsillar abscess (or quinsy) presents with trismus (the inability to open the jaw), severe unilateral throat pain, high fever and a change in voice (e.g. muffled voice). Pooling of saliva or drooling may be present. Most abscesses are polymicrobial; pathogens include *Streptococcus pyogenes* (group A streptococcus) and *Fusobacterium* species.

Monitor patients for signs of airway obstruction – an early sign is the inability of a patient to stick their tongue out of their mouth.

Treatment of peritonsillar abscess (quinsy)

Refer to an ENT specialist for consideration of drainage if there is odynophagia (painful swallowing) and/or dysphagia.

Adequate drainage is essential, usually requiring aspiration in hospital.

Send aspirated fluid for culture.

For patients whose abscess is drained or if there is no accumulation of pus, use:

benzylpenicillin *1.2 g (child: 50 mg/kg up to 1.2 g) IV, 6-hourly.*

For patients whose abscess is not drained, use:

benzylpenicillin *1.2 g (child 50 mg/kg up to 1.2 g) IV, 6-hourly*

PLUS

metronidazole *500 mg (child: 12.5 mg/kg up to 500 mg) IV, 12-hourly.*

Alternatively, as a single-drug regimen, use:

amoxicillin+clavulanate *IV*

adult: 1+0.2 g, 6-hourly

child younger than 3 months and less than 4 kg: 25+5 mg/kg, 12-hourly

child younger than 3 months and 4 kg or more: 25+5 mg/kg, 8-hourly

child 3 months or older: 25+5 mg/kg up to 1+0.2 g, 6-hourly.

Alternatively, including for patients with hypersensitivity to penicillins, use:

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

Switch to oral antibiotics once the patient improves, according to the results of culture and susceptibility testing. If a pathogen is not identified, use:

amoxicillin+clavulanate *500+125 mg (child: 22.5+3.2 mg/kg up to 500+125 mg) orally, 8-hourly.*

For patients with hypersensitivity to penicillins, use:

clindamycin *450 mg (child: 10 mg/kg up to 450 mg) orally, 8-hourly.*

Duration

Switch to oral antibiotics 1 to 2 days after abscess drainage and the patient has improved. Treat for a total of 10 days (IV + oral).

Retropharyngeal and parapharyngeal abscesses

Retropharyngeal and parapharyngeal abscesses are uncommon, but potentially life-threatening conditions. They are most often seen in children under 5 years of age as a complication of infection but can also result from local trauma from a procedure or ingestion of a foreign body, in both children and adults.

They are often associated with sore throat and/or trismus (the inability to open the jaw). Other presenting features include fever, odynophagia (pain on swallowing), dysphagia, neck swelling and tenderness, neck stiffness or torticollis (abnormal head or neck position) and retropharyngeal bulge.

Urgently refer all cases to an ENT specialist.

Send a pus sample, taken during drainage, for Gram stain and culture.

For suspected retropharyngeal/parapharyngeal abscess not responding to therapy, consider other infections such as *Cryptococcus*, *Histoplasma* or TB; see **cervical lymphadenitis** (page 315) in 'Soft tissue infections.'

Management of retropharyngeal/parapharyngeal abscess

Refer to ENT for consideration of imaging and ongoing management.

Initial management of retropharyngeal abscess involves:

- urgent transfer to hospital with airway management
- referral to an otolaryngologist for early surgical drainage
- intravenous antibiotic therapy.

Use:

amoxicillin+clavulanate *IV*

adult: 1+0.2 g 6-hourly

child younger than 3 months and less than 4 kg: 25+5 mg/kg 12-hourly

child younger than 3 months and 4 kg or more: 25+5 mg/kg 8-hourly

child 3 months or older: 25+5 mg/kg up to 1+0.2 g 6-hourly.

Alternatively, including in patients with **immediate nonsevere** or **delayed nonsevere** hypersensitivity to penicillins, use:

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

PLUS

metronidazole *500 mg (child: 12.5 mg/kg up to 500 mg) IV, 12-hourly.*

cont...

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

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

PLUS

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

Switch to oral therapy once improved, use:

amoxicillin+clavulanate *500+125 mg (child: 22.5+3.2 mg/kg up to 500+125 mg) orally, 8-hourly.*

For patients with hypersensitivity to penicillins, use:

trimethoprim+sulfamethoxazole *160+800 mg (child 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.*

Duration: If drainage is complete, treat for a total of 10 days (IV + oral). A longer duration of treatment is often required for an undrained or incompletely drained abscess.

Epiglottitis

Epiglottitis is a life-threatening infection caused by infection of the epiglottis and surrounding structures. Pathogens include *Haemophilus influenzae* and *Streptococcus pyogenes*. *Staphylococcus aureus* (including methicillin-resistant *S. aureus* [MRSA]) is a potential, but less common cause.

Symptoms include sudden onset of respiratory distress, stridor, toxic appearance, high fever, odynophagia (pain on swallowing) or dysphagia, and cervical lymphadenopathy.

Acute epiglottitis/supraglottitis

Refer all patients to an ENT specialist and/or anaesthetist for airway management.

For patients with sepsis or septic shock, see ‘Sepsis and bloodstream infections,’ page 245.

All patients require urgent hospitalisation, with intensive monitoring for airway obstruction.

Consider using:

dexamethasone 10 mg (child: 0.15 mg/kg up to 10 mg) oral/IV/IM, as a single dose; repeat after 24 hours if required.

Consider adding nebulised adrenaline for upper airway obstruction:

adrenaline 0.1% (1:1000, 1 mg/mL) solution 5 mL by inhalation via nebuliser, repeated after 30 minutes if no improvement.

Collect blood specimens for culture prior to commencing antibiotics.

If the patient has sepsis or septic shock, start antibiotic therapy within 1 hour of presentation.

In children, minimise distress, unnecessary examination and invasive procedures until advanced airway management is available. Use:

ceftriaxone *1 g (child: 50 mg/kg up to 1 g) IV, daily (or 12-hourly if patient requires ICU)*

PLUS

flucloxacillin *2 g (child: 50 mg/kg up to 2 g) orally, 6-hourly.*

For severe infections, or if the patient does not respond to initial therapy, for additional cover against MRSA, **add**:

chloramphenicol *1 g (child: 25 mg/kg up to 1 g) IV, 6-hourly.*

Switch to oral antibiotics once the patient improves, according to the results of culture and susceptibility testing. If microbiological results are not available, use:

amoxicillin+clavulanate *500+125 mg (child: 22.5+3.2 mg/kg up to 500+125 mg) orally, 8-hourly.*

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

cefuroxime *500 mg (child: 15 mg/kg up to 500 mg) orally, 12-hourly.*

For patients with **immediate severe** or **delayed severe** hypersensitivity to penicillins or, if neither of the above regimens are available, use:

chloramphenicol *500 mg (child: 10 mg/kg up to 500 mg) orally, 6-hourly.*

Duration: Treat for a total of 7 to 10 days (IV + oral).

Salivary gland infections

Swelling of a parotid, submandibular or sublingual salivary gland may indicate salivary gland infection; however, a noninfective cause of swelling (e.g. salivary gland obstruction) is more likely.

Infective causes include viral infections (e.g. mumps, coxsackievirus infection, Epstein-Barr virus [EBV] infection), chronic infections (e.g. TB) as well as acute bacterial infections caused by caused by *Staphylococcus aureus*, streptococci or mixed anaerobes.

Acute suppurative sialadenitis (including parotitis) is usually caused by *Staphylococcus aureus*. The glands are enlarged, often hot and tense, and pus may be expressed from the gland duct. The patient is usually systemically unwell, dehydrated and has difficulty swallowing.

Management of salivary gland infections

Management of acute suppurative sialadenitis includes urgent referral to hospital for surgical review and rehydration.

Send blood and pus samples for culture and susceptibility testing. If *S. aureus* is identified, treat as ***S. aureus* bacteraemia**, see page 253 in 'Sepsis and bloodstream infections.'

If the results of culture and susceptibility testing indicate a polymicrobial bacteraemia, seek appropriate advice.

Initiate empirical antibiotic therapy for acute suppurative sialadenitis in conjunction with local intervention or drainage; use:

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

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

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

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

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

For patients who do not improve after 48 to 72 hours of flucloxacillin or cefazolin, switch to clindamycin as for patients with severe hypersensitivity to penicillins as this will also cover MRSA.

cont...

Switch to oral continuation therapy once the patient can swallow and based on the results of culture and susceptibility testing. If results are not available, use:

flucloxacillin *500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly.*

Alternatively, including for patients with **immediate nonsevere** or **delayed nonsevere** hypersensitivity to penicillins, use:

cefalexin *500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly.*

For patients with **immediate severe** 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*

OR

clindamycin *450 mg (child: 10 mg/kg up to 450 mg) orally, 8-hourly.*

Duration: Treat for a total of 10 days (IV + oral).

Key additional references

Leach AJ, Morris P, Coates HLC, et al. Otitis media guidelines for Australian Aboriginal and Torres Strait Islander children: summary of recommendations. Med J Aust 2021; 214 (5): 228-233

National institute for health and care excellence. Sinusitis (acute): antimicrobial prescribing, NICE guideline [NG79]. UK; 2017.

National institute for health and care excellence. Sore throat (acute): antimicrobial prescribing, NICE guideline [NG84]. UK; 2018.

Pocket book of hospital care for children: guidelines for the management of common childhood illnesses – 2nd ed. Geneva: World Health Organization; 2013.

Rosenfeld R, Schwartz S, Cannon C, Roland P, Simon G, Kumar K, et al. Clinical practice guideline: acute otitis externa. Otolaryngol Head Neck Surg 2014; 150(Suppl 1): S1-24. Doi: 10.1177/0194599813517083.

Eye infections

This topic includes advice on the management of the following conditions in adults and children 3 months and older:

- **blepharitis**, page 123
- **stye**, page 124
- **endophthalmitis**, page 125
- **conjunctivitis** including bacterial, chlamydial and gonococcal conjunctivitis, page 127
- **periorbital** (preseptal) **and orbital cellulitis**, page 130
- **infectious keratitis** including bacterial corneal ulcer, dendritic corneal ulcer caused by herpes simplex virus and fungal corneal ulcer, page 131
- **eye injuries** including corneal abrasion, non-penetrating eye injuries and penetrating eye injuries, page 133
- **dacryocystitis** (acute and chronic), page 134
- **ocular tuberculosis**, page 135.

The following topics are not included in this section:

- **conjunctivitis in neonates** including gonococcal ophthalmia neonatorum (page 212) in 'Infections in neonates and young infants.'

Blepharitis

Blepharitis is an inflammation of the eyelid margins. Anterior blepharitis refers to inflammation mainly centred around eyelashes and follicles, while posterior blepharitis involves the meibomian glands.

While the pathophysiology is not fully understood, it involves staphylococcal enzymes and toxins, and immune-mediated damage. Blepharitis is often associated with other conditions such as seborrhoeic dermatitis, acne, rosacea and dry eyes. While it can be categorised into anterior or posterior blepharitis, there is considerable overlap of symptoms, and they often co-exist.

Ophthalmological review is needed to differentiate anterior versus posterior blepharitis.

Management of anterior blepharitis

Eyelid hygiene is the mainstay of therapy. Eyelid hygiene involves:

- daily warm compresses applied to the eyelids (with eyes closed) for 2 to 5 minutes to soften the crusts, followed by
- gentle scrubbing of the eyelid margin with either sodium bicarbonate solution (1 teaspoon of sodium bicarbonate in 500 mL freshly boiled and cooled water) or baby shampoo solution (5 drops in 100 mL freshly boiled and cooled water).

If symptoms of anterior blepharitis are not controlled despite adequate eyelid hygiene, consider adding:

chloramphenicol *1% ointment topically, once daily at night for up to 1 week.*

OR

tetracycline *1% ointment topically, once daily at night for up to 1 week.*

Management of posterior blepharitis

Use eyelid hygiene, as outlined for anterior blepharitis.

If symptoms of posterior blepharitis are not controlled despite adequate eyelid hygiene, consider antibiotic therapy. Systemic antibiotics are used mainly for their anti-inflammatory effects.

Use:

doxycycline *100 mg (child: 2 mg/kg up to 100 mg) orally, daily for 3 to 8 weeks.*[5]

OR

azithromycin *500 mg (child: 10 mg/kg up to 500 mg) orally, once daily for 3 days at 1-week intervals for 3 cycles.*

Stye (external hordeolum)

A stye is an abscess of a small sebaceous gland associated with the eyelash; it is usually caused by a staphylococci.

Most styes do not require any therapy aside from warm compresses.

Removal of the eyelash often aids resolution.

If the lesion does not reduce in size in 1 to 2 weeks refer to ophthalmology for consideration of incision and drainage. Refer patients with recurrent styes.

5 Unlike older tetracyclines, doxycycline has not been associated with tooth discolouration, enamel hypoplasia or bone deposition with short-term use (< 21 days), even in children younger than 8 years, so is increasingly used in this age group. However, use is limited by the lack of a suitable paediatric formulation.

Management of styes

Styes will often disappear on their own. Treat with warm compresses (a clean, warm washcloth held against the closed eyelid) for 2 to 5 minutes, up to 20 times per day. Most will expand in size and then spontaneously rupture.

There is little evidence that treating with topical antibiotics improves outcomes; only consider this in patients with frequent styes who do not achieve adequate improvement with warm compresses and removal of eyelid margin debris. Consider:

chloramphenicol *1% ointment topically, 3 or 4 times a day*

OR

tetracycline *1% ointment topically, 3 times a day.*

Endophthalmitis

Urgent ophthalmology review is required. Delayed treatment may result in loss of vision or loss of eye.

Endophthalmitis is an inflammatory condition of the intraocular cavity, usually caused by infection. Presentation is usually acute with impaired vision, eyelid oedema, a congested eye, redness, and pain. It can also occur as a serious complication following cataract surgery, penetrating eye injury or as a result of metastatic bacterial infection.

Endogenous endophthalmitis results from micro-organism seeding from a bloodstream infection. If this is suspected, take two sets of blood specimens for culture and susceptibility testing prior to commencing antibiotic therapy, and consider the possibility of endocarditis as the source of infection. Identify and treat the primary underlying infection with systemic antibiotics in addition to intravitreal antibiotics. If the source of infection is unclear, use ciprofloxacin and vancomycin (see next section).

If an organism is identified from blood cultures, see management advice in **directed therapy for bloodstream infections**, page 245 in 'Sepsis and bloodstream infections.'

Do not use topical antibiotics if an open-globe injury is suspected as preservatives in these products are toxic to the endothelium/intraocular contents.

Management of endophthalmitis

All cases of endophthalmitis require **urgent** same-day management by an ophthalmologist with intravitreal antibiotic injections.

If there is a delay in accessing ophthalmology, use:

ciprofloxacin *750 mg (child: 20 mg/kg up to 750 mg) orally, 12-hourly until intravitreal antibiotics are available*

PLUS

vancomycin *slow IV infusion until intravitreal antibiotics are available,* ***consider a loading dose in critically ill adults and children****. See 'Appendix 2: Vancomycin dosing' (page 390) for information on loading dose, dosing frequency and infusion time*

adult ≥ 40 years: 15 mg/kg, see Table 18 for dosing frequency (page 390)

adult < 40 years 20 mg/kg, see Table 17 for dosing frequency (page 389)

child 3 months and older: 15 mg/kg, 6-hourly.

Intravitreal treatment can only be given by an ophthalmologist. Use:

vancomycin ***1 mg in 0.1 mL*** *by* ***intravitreal*** *injection*

PLUS

ceftazidime ***2 mg in 0.1 mL*** *by* ***intravitreal*** *injection.*

If fungal infection is **not** suspected, consider adding:

dexamethasone 0.4 mg (400 mcg) in 0.1 mL by intravitreal injection.

If a fungal infection is suspected in a vegetative open-globe injury, do **not** use steroids initially and **add:**

fluconazole 400 mg orally or IV, once daily

PLUS

amphotericin B ***5 micrograms in 0.1 mL*** *by* ***intravitreal*** *injection, as a single dose.*

Intravitreal steroids can be considered after 7 days of treatment.

Ongoing management of endophthalmitis should be under the care of an ophthalmologist and based on clinical response and source of infection.

Conjunctivitis

Conjunctivitis is inflammation of the conjunctiva. There are numerous causes, including viral and bacterial infections, and allergy. Symptoms and signs can help to differentiate between the aetiologies and avoid unnecessary use of antibiotics.

Conjunctivitis in the neonatal period requires urgent treatment. See **neonatal conjunctivitis** (page 212) in 'Infections in neonates and young infants.'

Immediately refer to an ophthalmologist if corneal opacity develops.

Table 7: Comparative features of allergic, viral and bacterial conjunctivitis

	Allergic	**Viral**	**Bacterial [Note 1]**
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 (e.g. 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 (e.g. to nasolacrimal duct obstruction). Pathogens include *Staphylococcus aureus*, *Streptococcus pneumonia*, *Haemophilus 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.
Antibiotic therapy	Not required	Not required	Consider (see recommendations)
Note 1: Excluding chlamydial conjunctivitis and gonococcal conjunctivitis.			

Bacterial conjunctivitis

Management of bacterial conjunctivitis (excluding chlamydial and gonococcal conjunctivitis)

Presents as irritated red eyes with purulent discharge stuck to the eyelid. Symptoms usually begin unilaterally.

Antibiotics are often **not** required. Many cases of bacterial conjunctivitis resolve within 7 days without treatment.

If symptoms are severe or not resolving, use:

chloramphenicol *1% ointment massaged into lid margin, 3 or 4 times a day for up to 7 days.*

OR

chloramphenicol *0.5% eye drops, 1 drop into the affected eye, 1- to 2-hourly for the first 24 hours, then 4 times a day for up to 7 days*

OR

tetracycline *1% ointment to the affected eye, 3 times a day for up to 7 days.*

If failing to respond to antibiotic therapy, significant pain, loss of vision or photophobia, refer immediately to ophthalmologist.

Note that chloramphenicol can cause contact hypersensitivity reactions that can be severe.

Chlamydial and gonococcal conjunctivitis

Trachoma (chlamydial conjunctivitis)

Trachoma is a form of chronic conjunctivitis caused by *Chlamydia trachomatis* and is the leading cause of preventable infectious blindness in the world.

In 2015, Papua New Guinea's National Prevention of Blindness Committee found endemic trachoma in some areas. However, unlike trachoma-endemic countries in Africa, there appears to be little blindness from trachoma. This means that mass drug administration to eliminate trachoma is not required in Papua New Guinea. However, antibiotic treatment is required for individuals with trachoma folliculitis.

In areas where trachoma is prevalent, treatment of all household contacts is recommended.

Ensure people in all communities understand the importance of face washing to stop eye-seeking flies that spread infection.

Environmental improvement, particularly improving access to water and sanitation, is an important part of eliminating trachoma.

Treatment of active trachoma

Use:

azithromycin *1 g (child > 6 months: 20 mg/kg up to 1 g) orally, as a single dose.*

Alternatively, including in infants less than 6 months old, use:

azithromycin *20 mg/kg orally, daily* ***for 3 days***

OR

tetracycline *1% ointment to both eyes, twice daily, for at least 6 weeks. Repeat after an interval of 6 months for another 6 weeks, if necessary.*

Gonococcal conjunctivitis

For gonococcal conjunctivitis in neonates 1 month or younger, see page 212 in 'Infections in neonates and young infants.'

Conjunctivitis caused by *Neisseria gonorrhoea* usually presents with an acute onset of copious, purulent discharge.

If gonococcal conjunctivitis is suspected clinically, take conjunctival swabs for microbiological testing, then start empirical antimicrobial therapy immediately.

Gonococcal conjunctivitis is an ophthalmic emergency – seek advice from an ophthalmologist urgently.

Evaluate the patient for other sites of infection, as well as other sexually transmissible infections, see 'Genital and sexually transmissible infections' (page 159) for further information.

Management of gonococcal conjunctivitis

Gonococcal conjunctivitis requires systemic treatment; topical antimicrobial therapy is not adequate.

For adults and children older than 1 month, use:

ceftriaxone *1 g (child: 50 mg/kg up to 1 g) IM or IV, as a single dose*

PLUS

azithromycin *1 g (child: 20 mg/kg up to 1 g) orally, as a single dose.*

Periorbital (preseptal) and orbital cellulitis

Periorbital (preseptal) cellulitis is an infection of the eyelid and surrounding skin. Orbital (postseptal) cellulitis is an infection within the orbit, the deeper tissues behind the septum, which can lead to serious complications, including loss of vision.

It can be difficult to distinguish the two conditions, both of which may present with swelling, redness, tenderness, or pain around one eye. Periorbital cellulitis can also progress to become orbital cellulitis.

Treat any patient with periorbital or orbital cellulitis as for orbital cellulitis and seek ophthalmologist advice.

Management of orbital cellulitis

Use:

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

PLUS

metronidazole *500 mg IV, 12-hourly*

PLUS either

gentamicin *IV, see 'Appendix 1: Gentamicin dosing' (page 381) for information on dosing frequency, maximum dose and maximum number of doses*

adults: 5 mg/kg (7 mg/kg in critical illness), see Table 14 for dosing frequency (page 384)

children 3 months and older: 7 mg/kg up to 560 mg, once daily

OR

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

If flucloxacillin is not available, or in patients with hypersensitivity to penicillins, use:

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

PLUS

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

When improving, change to:

amoxicillin+clavulanate *500+125 mg (child: 25+5 mg/kg up to 500+125 mg) orally, 8-hourly.*

cont...

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.*

Duration: Treat for a total of 14 days (IV + oral).

Infectious keratitis

Infectious keratitis is a sight-threatening condition involving infection of the cornea. Causes include bacteria such as *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus pneumoniae* and *Pseudomonas aeruginosa*, and viruses such as herpes simplex virus (HSV). Keratitis caused by fungi, mycobacteria or *Acanthamoeba* is rarer and more difficult to treat.

Urgent consultation with an ophthalmologist is essential in all cases.

Fluorescein staining is helpful to differentiate causes of infectious keratitis:

- a well-circumscribed lesion suggests a bacterial corneal ulcer
- a branching pattern (dendritic appearance) suggests a dendritic ulcer caused by HSV
- feathery edges of the ulcer suggest a fungal corneal ulcer.

Corneal scraping for culture of the specimen should be performed by ophthalmologist for suspected bacterial or fungal corneal ulcers.

If fluorescein staining is unavailable, admit the patient and treat as a bacterial corneal ulcer, and seek advice from an ophthalmologist or ophthalmology nurse, if available.

Bacterial corneal ulcer

Symptoms include pain and worsening photophobia. A small white spot is often evident on the cornea.

Topic therapy is more effective than oral or IV treatment. Use:

chloramphenicol *1% ointment or 0.5% solution 1 drop into the affected eye, every hour initially*

Alternatively, use:

ciprofloxacin *0.3% eye drops 1 drop into the affected eye, every hour initially.*

cont...

Strict hourly dosing (including overnight) for the first 48 hours improves outcomes. Treatment may need to be supplemented with subconjunctival injection by an ophthalmologist if there is pus present in the anterior chamber.

Frequency should be decreased according to clinical response under supervision of an ophthalmologist.

Duration: Treat for 14 days, based on clinical response. A longer duration may be required.

Dendritic corneal ulceration caused by herpes simplex virus

As this is a viral infection, antibacterial agents have no place in treatment of this condition.

Treat confirmed dendritic ulcer with:

aciclovir 3% eye ointment topically into the affected eye, 5 times daily.

If the eye ointment is not available, there is no response to topical therapy, or if there is corneal involvement, use oral antiviral therapy:

aciclovir 400 mg orally, 5 times daily.

Duration

For topical aciclovir, treat for 14 days, or for at least 3 days after healing, whichever is shorter.

For oral aciclovir, treat for 7 to 10 days.

Fungal corneal ulcer

Suspect if there is a history of trauma, especially caused by contact with wood, tree branches or vegetative matter (including soil).

In Papua New Guinea, the most common organisms are filamentous fungi, like *Fusarium* species and *Aspergillus* species with a strong relationship to trauma (unlike other settings where Candida infections are more common in contact lens wearers).

Use:

natamycin 5% eye drops, 1 drop into the affected eye, every 1 to 2 hours for 3 to 4 days, then reduce to 6 to 8 times per day (approximately 3-hourly to 4-hourly).

Duration: Treat for 2 to 3 weeks or until resolution of infection.

Eye injuries

Corneal abrasion without infection

Infection is suggested by corneal opacification around the injury, redness and discharge. If present, treat as corneal ulcer.

Use:

chloramphenicol *1% ointment massaged into lid margin 3 or 4 times a day for 3 days*

OR

chloramphenicol *0.5% solution, 1 drop into the affected eye, 4 times daily for 3 days.*

Non-penetrating eye injuries

Provide first aid, e.g. wash eyes with clean water.

Consider the patient's proximity to a health facility. For patients with limited access to a health facility or eye care centre, careful assessment for signs of infection is required.

If there are signs of infection (e.g. sticky discharge) in any patient, treat as for bacterial conjunctivitis.

Penetrating eye injuries/open-globe injuries

Immediately refer to **ophthalmologist**

Apply an eye shield.

Give tetanus prophylaxis if indicated, see Table 13: Guide to tetanus prophylaxis in wound management, page 378 in 'Prevention of infection for medical conditions.'

Give:

ciprofloxacin *750 mg (child: 20mg/kg up to 750 mg) orally, 12-hourly for 5 to 7 days*

For contaminated wounds, consider continuing treatment with gentamicin eye drops following 3 days of parenteral gentamicin.

Dacryocystitis

Dacryocystitis is an infection of nasolacrimal sac.

Acute dacryocystitis

Characterised by pain, redness and swelling. Acute dacryocystitis is usually caused by *S. aureus*, *S. pyogenes* (group A streptococcus) or Gram-negative bacteria. Swab discharge for Gram stain and culture.

Use:

flucloxacillin *500 mg (child 12.5 mg/kg up to 500 mg) orally, 6-hourly for 7 days.*

Flucloxacillin targets important Gram-positive causes of dacryocystitis. Alternatively, cefalexin can be used as it has activity against both Gram-positive and some Gram-negative organisms. Use:

cefalexin *500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly.*

Alternatively, including for patients with hypersensitivity to penicillins, use:

trimethoprim+sulfamethoxazole *320+1600 mg (child: 8+40 mg/kg up to 320+1600 mg) orally, 12-hourly for 7 days*

OR

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

Refer to ophthalmology for dacryocystorhinostomy (DCR) surgery.

Chronic dacryocystitis

Presents as a unilateral watery eye (occasionally bilateral) with conjunctivitis-like symptoms for months to years.

There is no role for antibiotics, but surgical management is usually required.

Refer to ophthalmologist for dacryocystorhinostomy.

Ocular tuberculosis (TB)

Ocular TB (primary active infection) can affect any part of the eye (intraocular, superficial or surrounding the eye), with or without systemic involvement.

Secondary ocular TB occurs through haematogenous seeding and is sometimes an initial presentation of extrapulmonary dissemination of infection.

Posterior uveitis is the most common presentation of intraocular TB.

Fundoscopic patterns include:

- solitary tubercule
- miliary choroidal tubercules
- tuberculoma (single lesion which may mimic a tumour).

Refer patients to an ophthalmologist for confirmation and, if confirmed, treat as extrapulmonary TB. See *Papua New Guinea National Tuberculosis Management Protocol* for management recommendations.

Key additional references

Ko R, Macleod C, Pahau D, Sokana O, Keys D, Burnett A, Willis R, Wabulembo G, Garap J, Solomon AW. Population-Based Trachoma Mapping in Six Evaluation Units of Papua New Guinea. Ophthalmic Epidemiol. 2016;23(sup1):22-31. doi: 10.1080/09286586.2016.1235715. Epub 2016 Nov 28. PMID: 27893297; PMCID: PMC5706965.

Macleod CK, Butcher R, Javati S, Gwyn S, Jonduo M, Abdad MY, Roberts CH, Keys D, Koim SP, Ko R, Garap J, Pahau D, Houinei W, Martin DL, Pomat WS, Solomon AW. Trachoma, Anti-Pgp3 Serology, and Ocular Chlamydia trachomatis Infection in Papua New Guinea. Clin Infect Dis. 2021 Feb 1;72(3):423-430. doi: 10.1093/cid/ciaa042. PMID: 31965155; PMCID: PMC7850549.

Gastrointestinal tract infections

This topic includes advice on the management of the following conditions in adults and children 3 months and older:

- **oral and oesophageal Candida infections** including oral candidiasis, angular cheilitis (angular stomatitis) and oesophageal candidiasis, page 137
- **diarrhoeal diseases** including acute infectious diarrhoea (acute gastroenteritis), severe dysentery, giardiasis, strongyloidiasis, persistent diarrhoea in children 5 years or younger; antibiotic-associated diarrhoea, and cholera, page 140
- **typhoid** (enteric fever) in adults and children, page 148
- ***Helicobacter pylori* infection**, page 151
- **pigbel** (enteritis necroticans), page 152
- **gastrointestinal helminth infections** including hookworm, roundworm, whipworm and threadworm/pinworm, page 153
- **viral hepatitis** (chronic hepatitis B and chronic hepatitis C), page 155.

The following topics are not included in this section:

- **appendicitis, diverticulitis, peritonitis, cholecystitis and cholangitis, liver abscess** and **acute pancreatitis**, see 'Intraabdominal infections' (page 179)
- **oral candidiasis** (thrush) in neonates, see (page 210) in 'Infections in neonates and infants younger than 3 months.'

Oral and oesophageal *Candida* infections

Candida species are a commensal organism of the oral cavity. Oral candidiasis is an opportunistic infection that is uncommon in healthy individuals. Common risk factors for oral candidiasis include:

- local risk factors: dentures, salivary gland hypofunction, corticosteroid inhalers, poor oral hygiene, smoking
- systemic risk factors: immune compromise (e.g. poorly controlled diabetes, HIV), and drugs (e.g. systemic corticosteroids, antibiotics) or poor oral hygiene.

Oral candidiasis

A fungal infection of the buccal mucosa caused by *Candida* species. White plaques are seen on the tongue, cheeks, or roof of the mouth.

Management of oral candidiasis (thrush)

Evaluate patients with intractable candidiasis for systemic disease (e.g. diabetes, human immunodeficiency virus (HIV) infection).

Use:

nystatin oral suspension 100 000 units/mL, 1 mL orally, 6-hourly after food. Place under the tongue or in the buccal cavity, then swallow. Continue for 7 to 14 days or until several days after symptoms have resolved.

Advise patients that it is best to use nystatin oral liquid after (rather than before) a meal or drink.

If nystatin oral suspension is not available, consider using aqueous gentian violet (refer to product information or seek appropriate dosing advice for the product available).

In immunocompromised patients, severe infection or for those with no improvement after topical treatment, use:

fluconazole 200 mg (child: 6 mg/kg up to 200 mg) orally, on day 1 then 100 mg (child: 3 mg/kg up to 100 mg) to 200 mg, orally, daily for a further 6 days.

Angular cheilitis (angular stomatitis)

Image: 'angular cheilitis in skin of colour' from DermNet New Zealand Trust, licenced under CC BY-NC-ND 3.0 NZ DEED

Angular cheilitis, also known as angular stomatitis, is painful erythema and fissuring of the corners of the mouth usually caused by a mixed infection of *Candida*, *Staphylococcus aureus* and *Streptococcus* species, and is often associated with intraoral candidiasis.

Angular cheilitis can occur on one or both sides of the mouth.

In addition to the risk factors for oral candidiasis (see page 137), predisposing factors include:

- deep skin folds around the mouth (associated with worn down teeth, ill-fitting dentures or not wearing dentures)
- iron, folate or vitamin B deficiency
- Crohn disease
- granulomatous disease
- atopic and seborrhoeic dermatitis.

Management of angular cheilitis

Address predisposing factors and, if relevant, arrange dental review to assess dental or denture-related causes. Also consider whether a lip lesion is more indicative of herpes simplex infection (recurrent cold sores or crops of small vesicles over lip and perioral region).

For angular cheilitis, use:

miconazole 2% cream topically to the angles of the mouth, twice daily.

A mild topical corticosteroid can be added to treat the associated inflammatory dermatitis, use:

hydrocortisone 1% cream topically to the angles of the mouth, twice daily until inflammation subsides.

Treat oral candidiasis, if present, with topical antifungal therapy for oral candidiasis.

Duration

Continue topical antifungal treatment for 14 days after symptoms resolve.

Combination products containing a topical corticosteroid and antifungal are available but should only be used until inflammation subsides. Treatment should be completed with a topical antifungal alone, for 14 days after symptoms resolve.

Oesophageal candidiasis

Oesophageal candidiasis is most commonly seen in the setting of immunocompromise.

Test all patients for HIV.

In children, suspect oesophageal candidiasis if the child has difficulty or pain while vomiting or swallowing, is reluctant to take food, is salivating excessively or cries during feeding. The condition may occur with or without evidence of oral thrush;

treatment with fluconazole may be trialled, even if oral thrush is not found. Exclude other causes of painful swallowing (such as cytomegalovirus, herpes simplex, lymphoma and, rarely, Kaposi sarcoma), if necessary, by referral to a larger hospital where appropriate testing is possible.

Management of oesophageal candidiasis

In patients with severe disease and no known immunocompromise, evaluate patients for systemic disease (e.g. diabetes, HIV infection).

For symptomatic or immunocompromised patients, use:

fluconazole 200 mg (child: 6 mg/kg up to 200 mg) orally for the first dose, followed by 100 mg (child: 3 mg/kg up to 100 mg) orally, daily[6].

If the patient is unable to tolerate oral therapy, give this regimen intravenously.

Nystatin oral suspension can be used to treat oesophageal candidiasis (use a 5 mL dose), but it is less effective than oral fluconazole.

In patients who do not respond to initial therapy or who are at risk of disseminated candidiasis (e.g. leucopenia) 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.

For patients with confirmed or suspected infection with azole-resistant *Candida* species, seek advice from a clinical microbiologist or infectious disease physician.

Duration

Treat for 14 to 21 days. For refractory infection, extend treatment to 28 days.

Diarrhoeal diseases

Diarrhoea is an increased frequency of liquid or semiliquid stools. In some cases of acute gastrointestinal infections (especially norovirus), upper gastrointestinal symptoms such as nausea and vomiting are prominent.

Antibiotic therapy is **only** indicated when bacterial infection is suspected, such as with high fever, tachycardia, leucocytosis, marked abdominal tenderness, severe abdominal pain or blood in the stool. If this occurs, treat as severe dysentery.

Consider symptoms/signs suggestive of cholera, e.g. profuse 'rice-water' stools, severe dehydration, occurrence of a cluster of cases (see **cholera**, page 146 in this topic).

6 For patients who have trouble swallowing, provide advice on preparing the capsules as a suspension: open the capsule and add the contents to a small cup, add 10 mL of water and mix well. Take the mixture immediately. Rinse the cup with a further 10 mL of water, and drink, to ensure the entire dose is taken.

In acute diarrhoea, collection of stool for cultures should be reserved for grossly bloody stool, severe dehydration, signs of sepsis, symptoms lasting more than 3 to 7 days, immunocompromise and suspected nosocomial infections.

Blood specimens for culture should be obtained from infants under 3 months, people of any age with signs of sepsis or when enteric fever is suspected, people with systemic manifestations of infection and people who are immunocompromised.

In hospitalised adults and children 2 years or older with onset of diarrhoea > 72 hours after admission, test for *Clostridioides (Clostridium) difficile* (if possible); see **antibiotic-associated diarrhoea** on page 147 in this topic.

Pathogenic gastrointestinal protozoa can cause chronic infectious diarrhoea. Rapid antigen tests are more useful for diagnosis of *Giardia* and *Entamoeba* infection than stool microscopy. These tests were not available in Papua New Guinea at the time of writing, however, sending stool samples to a microbiology laboratory for smear examination for ova and parasites is encouraged for patients with abdominal symptoms (e.g. abdominal pain, diarrhoea) for more than 2 weeks.

For children with diarrhoea, admit the following to hospital:

- young infants (< 2 months)
- severely ill children who look lethargic, have abdominal distension and tenderness, or convulsions
- children with another condition requiring hospital treatment.

Empirical treatment of acute infectious diarrhoea

Acute infectious diarrhoea (acute gastroenteritis)

There are many bacterial, viral and toxin-mediated causes. Most cases are self-limiting and resolve without specific treatment, but may persist for 7 to 10 days.

The major concern with diarrhoea is a rapid loss of fluid and risk of dehydration. **Oral and/or intravenous rehydration is usually all that is required.**

In children younger than 5 years, zinc supplementation has been shown to reduce the severity and duration of diarrhoea. Use:

zinc sulfate:

child less than 6 months: 10 mg orally, daily for 10 to 14 days

child 6 months or older: 20 mg orally, daily for 10 to 14 days.

There is no role for routine antibiotic therapy for patients with watery diarrhoea unless cholera is suspected or known (see **cholera**, page 146 in this topic).

cont...

Consider antidiarrhoeal drugs if available (e.g. loperamide) in adults with persisting watery diarrhoea.

Never use antidiarrhoeal drugs to treat acute diarrhoea in infants and children.

For diarrhoea in malnourished children, see *Severe Acute Malnutrition: A Guideline to the Treatment Protocol* and *Standard Treatment for Common Illnesses of Children in Papua New Guinea* for additional advice on management, including supplementation.

Management of severe dysentery

Small-volume loose stools containing blood and mucous associated with severe abdominal pain prior to bowel opening (tenesmus) and is usually associated with systemic symptoms. It is commonly caused by *Shigella, Salmonella (*non-typhoidal species) or *Campylobacter.* Treatment is especially required in infants under 12 months because of the risk of bacteraemia and other systemic manifestations.

If enteric fever is suspected or confirmed, see **typhoid** (enteric fever) on page 148 in this topic. If intestinal amoebiasis is suspected, see page 145 in this topic.

Rehydration (and electrolyte replacement) is the most important component of treatment. The presence of seizures should prompt consideration of hypoglycaemia, hyponatraemia and hypernatraemia.

Give zinc supplements for children with watery diarrhoea (dosing as for acute infectious diarrhoea above).

For adults and children, use:

ceftriaxone *2 g (child: 50 mg/kg up to 2 g) IV, daily for 3 days*

OR

ciprofloxacin *500 mg (child: 12.5 mg/kg up to 500 mg) orally, 12-hourly for 3 days*

Alternatively, if neither of the above agents are available, use:

azithromycin *1 g (child: 10 mg/kg up to 500 mg) orally, daily for 3 days.*

If none of these agents are available, refer the patient to a facility where they are available.

If there is a lack of treatment response within 48 hours, treat presumptively as amoebiasis (see **intestinal amoebiasis**, page 145 in this topic).

Persistent diarrhoea in children 5 years or younger

Persistent diarrhoea is diarrhoea continuing for more than 14 days. It is associated with a high mortality, especially if associated with dehydration and malnutrition.

Diarrhoea may be due to an intestinal or non-intestinal infection (pneumonia, sepsis, urinary tract infections, oral thrush, otitis media) which requires appropriate treatment.

Admit the child to a hospital or health centre.

Persistent diarrhoea can be further classified as:

- nonsevere persistent diarrhoea (no signs of dehydration or malnutrition)
- severe persistent diarrhoea (with signs of dehydration).

Persistent diarrhoea may be a presenting symptom of HIV infection. All children with persistent diarrhoea should have provider-initiated counselling and testing for HIV infection.

Stools commonly remain loose for 1 to 2 weeks after an episode of acute gastroenteritis.

Transient lactose intolerance may occur after gastroenteritis, particularly in infants and young children. Frothy, watery, explosive stools (which may cause perianal excoriation) shortly after drinking milk may indicate lactose intolerance.

Check for lactose intolerance in infants, this usually presents with is significant skin breakdown around the anus. If seen:

- reduce the amount and frequency of breastfeeds for 2 days
- keep mother's breasts expressed
- give lactose-free milk at least 6 times daily, if available
- if lactose-free milk is not available, give oral rehydration solution or other clear fluids (e.g. rice-water, coconut water), and give extra food.

In all children, look for signs of malnutrition and treat if present – see *Severe Acute Malnutrition: A Guideline to the Treatment Protocol.*

Check for signs of dehydration and treat as appropriate. Encourage carer to increase fluids (including breast milk) and food.

Management of persistent diarrhoea in children 5 years or younger

Test for malaria (if RDT are not available, use microscopy), and treat if present. If neither RDT nor microscopy are available, very sick and febrile children may require presumptive treatment for severe malaria, see *National Malaria Treatment Protocol.*

If there is blood in stools, treat as for severe dysentery (see previous section).

Give zinc to all children:

zinc sulfate orally

child less than 6 months: 10 mg orally, daily for 10 to 14 days

child 6 months or older: 20 mg orally, daily for 10 to 14 days.

Send a stool sample for testing and treat according to results. If testing is unavailable or the results are inconclusive, treat presumptively for giardiasis. Use:

tinidazole 50 mg/kg up to 2 g orally, as a single dose.

Repeat the dose if the child vomits within 30 minutes of taking the dose. Extend tinidazole treatment to 3 days in any of the following circumstances:

- microscopic examination of fresh faeces reveals trophozoites of *Entamoeba histolytica* ingesting red blood cells
- trophozoites or cysts of giardia are seen in the faeces
- 2 different antibiotics that are usually effective for *Shigella* locally have been given without clinical improvement
- if stool examination is not possible, when diarrhoea persists for more than 1 month.

If the child is malnourished, treat presumptively for strongyloidiasis.

Specific causes of diarrhoeal diseases

Giardiasis

Often characterised by yellow diarrhoea, excess gas, abdominal cramps, and/or nausea.

Tinidazole is the preferred agent, use:

tinidazole 2 g (child: 50 mg/kg up to 2 g) orally, as a single dose.

Alternatively, use:

***metronidazole** 400 mg (child: 10 mg/kg up to 400 mg) orally, 8-hourly for 5 days.*

For refractory giardiasis, after excluding reinfection, use combination treatment with albendazole. **Add** to either of the above regimens:

albendazole daily for 5 days

adult or child 2 years or older and 10 kg or over: 400 mg orally

child 2 years or older and under 10 kg: 200 mg orally.

Intestinal amoebiasis

Invasion of the intestinal lining by *Entamoeba histolytica* trophozoites causes amoebic bloody diarrhoea or colitis. Severe colitis may be complicated by perforation.

For diagnosed or suspected intestinal amoebiasis, use:

tinidazole 2 g (child: 50 mg/kg up to 2 g) orally, daily for 3 days (up to 5 days for severe disease).

Alternatively, use:

metronidazole *600 mg (child: 10 mg/kg up to 600 mg) orally,* **8-hourly** *for 7 days.*

Response to treatment is typically seen within 48 hours.

For severe amoebic colitis (e.g. frequent blood-stained stools, perforation, peritonitis or toxic megacolon), use:

metronidazole *800 mg (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.*

While luminal ameobicides (e.g. paromomycin, diloxanide) are often recommended to eliminate cysts following treatment to reduce the risk of relapse, they do not prevent later re-infection. These agents are not available on the PNG Medical & Dental Catalogue.

Strongyloidiasis

Uncomplicated disease is frequently asymptomatic or may involve gastrointestinal symptoms including abdominal pain or diarrhoea. Pulmonary symptoms can occur during the pulmonary migration phase. Dermatological manifestations include urticarial rashes, pruritus and larva currens.

Chronic infection in childhood is associated with stunted growth.

Diagnosis of strongyloidiasis depends on microscopic identification of larvae in the stool, or in sputum in disseminated infection. The diagnosis may be supported by the presence of eosinophilia in the blood.

Management of strongyloidiasis

For patients with disseminated strongyloidiasis, seek advice from an infectious diseases physician or clinical microbiologist.

cont...

For an immunocompetent patient (adult or child), use:

ivermectin 200 micrograms/kg (rounded up to the nearest 1.5 mg) orally with fatty food, for 2 days.[7]

Ivermectin is the drug of choice to treat strongyloidiasis. Albendazole is less effective but is an alternative if ivermectin is unavailable or contraindicated. Use:

albendazole 400 mg (child ≤10 kg: 200 mg) orally with fatty food, 12-hourly 7 days.

For immunocompromised patients with uncomplicated disease, use:

ivermectin 200 micrograms/kg orally with fatty food, on days 1, 2, 15 and 16.

Disseminated strongyloidiasis occurs when patients with chronic strongyloidiasis become immunocompromised. This can be rapidly fatal. Reduce immunocompromise if possible, and seek appropriate advice.

Cholera

Cholera is a life-threatening diarrhoeal disease caused by infection of the intestine with the bacterium *Vibrio cholerae*. Approximately 20% of cases develop severe watery diarrhoea with vomiting. If these patients are not promptly and adequately treated, the loss of such large amounts of fluid and salts can lead to severe dehydration and death within hours.

Cholera is a notifiable disease.

Urgently notify the Provincial Disease Control Officer if you suspect a case of cholera.

Management of cholera

Rehydration (and replacement of electrolytes) is the most important aspect of cholera treatment.

Provide oral or intravenous (Hartmann solution or normal saline) fluids, depending on the severity of dehydration. Use oral rehydration solution during and after IV therapy.

Take stool samples before starting antibiotic treatment, then use:

azithromycin *1 g (child: 20 mg/kg up to 1 g) orally, as a single dose.*

cont...

7 Ivermectin is not currently licensed for use in children weighing less than 15 kg because of a lack of safety data. However, limited data suggest that oral ivermectin in children weighing less than 15 kg is well tolerated with no serious or long-term adverse effects. Ivermectin should not be used in pregnancy.

Regularly monitor the following:

- state of consciousness
- pulse
- signs of dehydration
- number and appearance of stools
- respiratory rhythm
- urine output (present or not)
- temperature: hypothermia is common with cholera; if the temperature is high there may be an additional condition, e.g. malaria.

Antibiotic-associated diarrhoea

Most cases of antibiotic-associated diarrhoea (AAD) are a direct side effect of the antibiotic medication. A small proportion is caused by superinfection with *Clostridioides difficile* (formerly known as *Clostridium difficile)*.

Frequent small-volume stools (with or without mucous, with or without blood) are characteristic of colitis. Colitis due to *C. difficile* is associated with stool that has a sickly-sweet smell. Severe cases develop abdominal pain and rebound tenderness, leucocytosis, and/or sepsis.

C. difficile is usually a hospital-acquired infection. For inpatients who have been exposed to antibiotics who develop diarrhoea more than 4 to 5 days after admission, treat presumptively as *C. difficile* infection.

Abdominal X-ray or CT may indicate colonic enlargement with mural thickening and/or ileus. Seek surgical advice.

Management of antibiotic-associated diarrhoea

Send stool for *C. difficile* testing, if available.

Cease other antibiotics if possible. Rehydration is an important addition to antibiotics when treating AAD.

If *C. difficile* is confirmed or strongly suspected, use:

metronidazole *400 mg (child: 10 mg/kg up to 400 mg) orally,* ***8-hourly*** *for 10 days.*

Response to treatment is typically within 48 hours. If response to treatment is poor or slow, seek appropriate advice.

cont...

Surgical management may be required in severe cases (e.g. colectomy for toxic megacolon).

For recurrent or refractory disease, add:

vancomycin *125 mg (child: 10 mg/kg up to 125 mg)* ***orally****, 6-hourly for 10 days.*

The injectable formulation of vancomycin can be given orally for this indication: dissolve 500 mg of vancomycin powder in 10 mL of water and measure the appropriate dose (e.g. 125 mg = 2.5 mL). Giving vancomycin intravenously is **not** effective due to inadequate penetration of the drug into the lumen of the colon.

For complicated cases (e.g. hypotension or shock, ileus, megacolon) in addition to oral vancomycin, use:

metronidazole *500 mg (child: 12.5 mg/kg up to 500 mg) IV,* ***8-hourly*** *for 10 days.*

Typhoid (enteric fever)

Typhoid is caused by ingestion of contaminated water or transmitted by poor hygiene practices during food handling.

Typhoid may be suspected in the presence of fever > 38 °C for > 3 days, particularly in regions where typhoid is prevalent. In addition to fever, typhoid can be associated with a dry cough, bowel changes (constipation in adults, diarrhoea in children), abdominal tenderness and/or distension, headache, confusion, malaise, cough or rash.

Obtain blood for culture to diagnose typhoid, ideally prior to commencing antibiotics. Also send stool samples for culture.

The Widal test is no longer considered useful as a positive result may just represent past exposure.

In coastal areas of Papua New Guinea, the differential diagnoses include dengue.

Although there is increasing resistance to ciprofloxacin internationally, *Salmonella typhi* and *Salmonella paratyphi* isolates in Papua New Guinea remain susceptible.

Treatment for typhoid and paratyphoid fever should continue for at least 48 hours after fever resolution, but total treatment duration (IV + oral) depends on the patient's age and the antibiotic agents used.

Typhoid in adults

Management of proven or suspected typhoid in adults (mild to moderate)

In addition to antibiotic therapy, patients with gastrointestinal symptoms may require supportive management. Rehydration is the mainstay of therapy.

Use:

ciprofloxacin *500 mg orally, 12-hourly for 5 to 7 days*

OR

azithromycin *1 g orally, daily for 5 days.*

Management of proven or suspected typhoid in adults (severe)

Use:

ceftriaxone *2 g IV, daily.*

Switch to oral antibiotics when clinically improved, although not necessarily until fever resolves as this may persist for several days despite clinical improvement.

Select an oral regimen according to the results of susceptibility testing. If the results of susceptibility testing are not available, use either azithromycin or ciprofloxacin as for mild to moderate disease to complete the course. If neither is available, use:

amoxicillin *2 g IV, 8-hourly; when clinically improved, switch to amoxicillin 1 g orally, 8-hourly to complete 10 to 14 days (IV + oral)*

OR

chloramphenicol *1 g IM or IV, 6-hourly; when clinically improved, switch to chloramphenicol 500 mg orally, 6-hourly to complete at least 2 weeks (3 weeks if possible) (IV + oral).*

Typhoid in children

Admit the child to a hospital or health centre. If the location is a health centre, start treatment and transfer urgently to a hospital if the child:

- has a distended, tender abdomen
- has rectal bleeding or melaena (black, sticky stools)
- has severe abdominal pain
- is unconscious or confused.

Rehydration is the mainstay of therapy. If the child is vomiting or has a distended, tender abdomen, give maintenance IV fluids. If the child is not vomiting and the abdomen is soft, give milk (infants) and other oral fluids (all children).

If dehydrated, rehydrate with either an oral rehydration solution or with IV fluids (normal saline, Hartmann solution, or half-strength Darrow's solution).

Following treatment, children need extra nutrition to build themselves back to normal. Give extra food and 1 mL multiple vitamin liquid daily.

Management of typhoid in children - proven or suspected

Note that even with the correct treatment, the child may take 1 to 2 weeks to get better. The fever may remain for up to 1 week.

In addition to antibiotic therapy, patients with gastrointestinal symptoms may require supportive management.

For mild to moderate disease in children older than 1 year, use:

ciprofloxacin *12.5 mg/kg up to 500 mg orally, 12-hourly for 5 to 7 days*

OR

azithromycin *20 mg/kg up to 1 g orally, daily for 5 days.*

For severe disease and for all children aged 1 year or younger, use:

ceftriaxone *80 mg/kg up to 2 g IV, daily*

OR

ciprofloxacin *10 mg/kg up to 400 mg IV, 12-hourly for 7 days in children aged 3 to 12 months, or 10 days in children younger than 3 months.*

For children aged 1 year or younger, use IV for the entire course of treatment.

For children older than 1 year, switch to oral antibiotics when clinically improved, although not necessarily until fever has resolved as this may persist for several days despite clinical improvement. Select an oral regimen according to the results of susceptibility testing. If the results of susceptibility testing are not available, use either azithromycin or ciprofloxacin as for mild to moderate disease to complete the course.

If other agents are not available, use:

amoxicillin *50 mg/kg up to 2 g IV, 8-hourly; when clinically improved, switch to amoxicillin 30 mg/kg up to 1 g orally, 8-hourly to complete 10 to 14 days (IV + oral)*

OR

cont...

chloramphenicol *25 mg/kg up to 1 g IV, 6-hourly; when clinically improved switch to chloramphenicol 10 mg/kg up to 500 mg orally, 6-hourly to complete at least 2 weeks; 3 weeks if possible (IV + oral).*

Helicobacter pylori

Patients infected with *H. pylori* have a 10 to 20% lifetime risk of developing peptic ulcers and a 1 to 2% risk of developing stomach cancer. *H. pylori* infection is also a common cause of gastritis.

It is not often diagnosed in children.

Always ask a patient with suspected *H. pylori* infection about exposure to other agents that may be associated with gastritis and/or ulcers (e.g. alcohol and NSAIDs).

Management of *Helicobacter pylori* infection

Antibiotic treatment for *Helicobacter pylori*

Treat all patients with a duodenal ulcer, proven *H. pylori* peptic ulcers or with mucosa-associated lymphoid tissue (MALT) lymphoma.

Optimum therapy, if available:

omeprazole 20 mg orally, 12-hourly

PLUS

amoxicillin *1 g orally, 12-hourly*

PLUS

clarithromycin *500 mg orally, 12-hourly.*

If clarithromycin is unavailable, substitute with:

azithromycin *500 mg orally, daily for the first 3 days of the treatment course.*

Alternatively, if neither clarithromycin nor azithromycin are available, use:

omeprazole 20 mg orally, 12-hourly

PLUS

amoxicillin *1 g orally, 12-hourly*

PLUS

metronidazole *500 mg orally, 12-hourly.*

cont...

If omeprazole is not available, an H2-receptor antagonist (e.g. ranitidine) can be used in any of the above regimens, but they are less effective.

Duration of treatment

Treat for 7 days. If symptoms are not resolving or in patients who have previously been treated, treat for 14 days.

Maintenance acid suppression therapy

Maintenance acid suppression therapy is usually unnecessary for *H. pylori*–associated ulcers after successful eradication. However, if *H. pylori* eradication is not successful or practicable, or if a nonsteroidal anti-inflammatory drug (NSAID) is required, the risk of ulcer recurrence is markedly reduced by treatment with a proton pump inhibitor (PPI) at the standard dose. For all complicated ulcers, large gastric ulcers, ulcers occurring in high risk patients or NSAID-induced ulcers, ongoing PPI therapy for approximately 8 weeks is appropriate. This maximises the likelihood of ulcer healing, particularly in patients who remain infected after eradication therapy. Some patients (especially those who had an ulcer associated with *H. pylori* infection and NSAID use) may need long-term secondary prophylaxis with PPIs to prevent relapse.

Pigbel (enteritis necroticans)

Pigbel, or enteritis necroticans, is caused by *Clostridium perfringens*.

Patients experience severe abdominal pain starting up to 5 days after eating a protein meal (often pig meat).

Presentation includes abdominal swelling, black-flecked or coffee ground vomitus, and/or mild diarrhoea with blood (but sometimes constipation).

Anti-helminthic therapy is included in the empirical treatment regimen, as patients also often have an underlying helminth infection.

Severe cases should be sent to hospital immediately for urgent surgical review.

Management of pigbel (enteritis necroticans)

Give IV fluids to all patients with suspected pigbel. Do not give the patient anything to eat or drink.

Antibiotic therapy for pigbel (enteritis necroticans)

For nonsevere pigbel, use:

benzylpenicillin *1.2 g (child: 50 mg/kg up to 1.2 g) IV, 6-hourly*

PLUS

albendazole orally, as a single dose

adult, child > 10 kg: 400 mg

child > 6 months and < 10 kg: 200 mg

PLUS, if the patient is malnourished, give:

tinidazole 2 g (child: 50mg/kg up to 2 g) orally, as a single dose.

For severe infections, start antibiotics as for **Peritonitis due to perforated bowel, intraperitoneal abscess** (see page 181 in 'Intraabdominal infections') within 1 hour of presentation to a healthcare facility, and seek urgent surgical review.

Ongoing management

If the symptoms worsen or if there is no improvement within 2 days, begin treatment with IV chloramphenicol and send to hospital.

If the patient improves (reduced abdominal swelling and pain, no vomiting, feels hungry and has bowel motions):

- after 24 hours of improvement, stop IV fluids, remove the nasogastric tube, and give oral rehydration solution
- after another 24 hours of improvement, give full strength milk (for infants) over the next 24 hours, then give soft food, gradually introducing solid food.

Gastrointestinal helminth infestations

Send a stool sample for microscopy to aid identification of helminths.

Management of gastrointestinal helminth infestations

Hookworm (*Ancylostoma duodenale* or *Necator americanus*)

Use:

albendazole 400 mg (child 10 kg or less: 200 mg) orally, a single dose.

Alternatively, including for pregnant patients, use:

pyrantel (adult and child) 10 mg/kg up to 1 g orally, daily for 3 days.

Roundworm (*Ascaris lumbricoides*)

Use:

albendazole 400 mg (child 10 kg or less: 200 mg) orally, as a single dose.

Alternatively, including for pregnant patients, use:

pyrantel (adult and child) 10 mg/kg up to 1 g orally, as a single dose (repeat after 7 days if heavy infection).

Whipworm (*Trichuris trichiura*)

Use:

albendazole 400 mg (child 10 kg or less: 200 mg) orally, daily for 3 days.

The treatment of choice is albendazole (or mebendazole, which is not on the Medical and Dental Catalogue in Papua New Guinea). However, while treatment reduces worm burden, it is often not curative. Reinfection is also common.

Worm burden correlates with associated morbidity, such as anaemia, gastrointestinal disturbance, stunted growth and, rarely, rectal prolapse.

For severe or recurrent infections, use:

albendazole 400 mg orally, daily for 3 days

PLUS

ivermectin 600 mcg/kg (rounded up to the nearest 1.5 mg) orally, daily with fatty food, for 3 days.[8]

Threadworm/pinworm (*Enterobius vermicularis*)

Use:

albendazole 400 mg (child 10 kg or less: 200 mg) orally, as a single dose.

Alternatively, including for pregnant patients, use:

pyrantel (adult and child) 10 mg/kg up to 1 g orally, as a single dose.

Due to the frequency of reinfection and autoinfection, consider repeating the dose after 2 weeks.

Treat current household members and carers at the same time to reduce the risk of reinfection.

8 Ivermectin is not currently licensed for use in children weighing less than 15 kg because of a lack of safety data. However, limited data suggest that oral ivermectin in children weighing less than 15 kg is well tolerated with no serious or long-term adverse effects. Ivermectin should not be used in pregnancy.

Viral hepatitis

The goals of antiviral treatment are:

- to prevent cirrhosis, liver failure and hepatocellular carcinoma (HCC)
- to prevent transmission of hepatitis B (HBV) and C (HCV).

Chronic hepatitis B

Also see the *Pacific Islands and Territories Hepatitis B Treatment and Care Guidelines*, available from path-png.org/clinical-guidelines/.

The indications for antiviral treatment include patients who are hepatitis B surface antigen (HBsAg) positive patients and have **any** of the following features:

- cirrhosis, irrespective of alanine aminotransferase (ALT) or viral load
- persistently raised ALT (> 20 IU/L in females, > 30 IU/L males) **and** positive HBV DNA > 2000 IU/mL (if available; if HBV DNA is unavailable, treat based on ALT level alone)
- are a first-degree relative of a patient with HCC
- extrahepatic manifestations such as glomerulonephritis or vasculitis.

Screen all patients for HIV infection prior to treatment. The treatment recommendation in these guidelines are for HIV-negative patients.

Refer to *Pacific Islands and Territories Hepatitis B Treatment and Care Guidelines* for important considerations concerning:

- decompensated cirrhosis
- pregnancy and prevention of mother-to-child transmission
- care of neonates
- immunocompromised patients
- healthcare staff
- HBV/hepatitis D virus (HDV)/HCV /HIV coinfection
- acute hepatitis B
- metabolic syndrome/alcohol excess.

Priority groups for hepatitis HBsAg screening using WHO prequalified rapid diagnostic tests (RDT), include those:

- with liver disease
- with HCV, HIV or tuberculosis
- undergoing antenatal screening
- who are STI clinic clients
- who are health care workers
- receiving immunosuppressive therapy.

A hepatitis B vaccination course is strongly recommended for HBsAg negative patients who have not had prior vaccination, and their partners and household members.

Chronic hepatitis B is a dynamic disease. All HBsAg positive patients should be considered as potential candidates for antiviral therapy and regular (i.e. annual) monitoring. History, physical examination, baseline bloods (AST, ALT, creatinine and full blood count) and ultrasound should be completed.

Monitor HBsAg positive cirrhotic patients 3-monthly for the first 6 months, thereafter 6-monthly with ALT and creatinine. There is no role for routine viral load testing. Lifelong treatment is recommended; treatment must **not** stop for any reasons. Counsel on the risk of treatment interruption – life-threatening liver decompensation may occur due to reactivation of the virus.

Monitor HBsAg positive non-cirrhotic patients 6-monthly with ALT and creatinine for 12 months, and annually thereafter. Selected patients are able to cease treatment after 5 years, see *Pacific Islands and Territories Hepatitis B Treatment and Care Guidelines*.

Antiviral therapy for chronic hepatitis B

For adults and children > 12 years in whom antiviral therapy is indicated, use:

tenofovir disoproxil fumarate (TDF) 300 mg orally, daily.

For patients with renal impairment (i.e. Cr > 190 in males or Cr > 135 in females), use (if available):

tenofovir alafenamide (TAF) 25 mg orally, daily

Tenofovir alafenamide does not require dose adjustment in mild to moderate renal impairment. See 'Appendix 5: Renal impairment and antimicrobial dosing,' page 403 for dose adjustment of tenofovir alafenamide in severe renal impairment or dosing for tenofovir disoproxil fumarate in renal impairment.

Monitoring for HCC (6-monthly liver ultrasound +/- serum alpha-fetoprotein if available) recommended for patients with known cirrhosis, regardless of age OR other risk factors, including family history of HCC OR age (40 years and older).

Chronic hepatitis C

Priority groups for hepatitis C antibody screening include:

- blood donors
- patients with chronic liver disease
- patient withs hepatitis B and/or HIV
- healthcare workers
- injecting drug users.

A positive HCV antibody result requires confirmation with HCV polymerase chain reaction (PCR) assay to provide evidence of current infection.

Offer treatment to **all** patients with confirmed infection, defined by the presence of HCV RNA in the blood using PCR.

Key steps in pretreatment assessment include:

- ascertaining whether the patient has had any prior treatment with direct-acting antivirals
- assessing for the presence of cirrhosis or decompensated liver disease
- checking for hepatitis B or HIV coinfection
- reviewing medications for potential drug interactions (see www.hep-druginteractions.org/prescribing_resources/hep-summaries-hcv).

Post treatment, perform liver function tests and HCV PCR 12 weeks after last dose as proof of cure. Long-term follow up is required in some patients (cirrhosis, abnormal liver biochemistry, ongoing risk factors for hepatitis C infection, chronic liver disease) – refer to the WHO *Updated recommendations on treatment of adolescents and children with chronic HCV infection, and HCV simplified service delivery and diagnostics.*

Antiviral therapy for chronic hepatitis C

Defer treatment in children until after the age of 12 years.

It is essential to carefully explain the treatment to the patient and interact with them weekly to encourage compliance. Document all patient interactions.

For adults and children > 12 years, use:

sofosbuvir 400 mg + daclatasvir 60 mg orally, daily for 12 weeks.

Extend the treatment duration to 24 weeks in patients with compensated cirrhosis.

Key additional references

Hepatitis C. Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM) website: Management and Treatment of Hepatitis C. Available from: https://www.ashm.org.au/hcv/.

Hepatitis C Virus Infection Consensus Statement Working Group. Australian recommendations for the management of hepatitis C virus infection: a consensus statement (2022). Melbourne: Gastroenterological Society of Australia, 2022.

Pacific Islands and Territories Hepatitis B Treatment and Care Guidelines. 2024. Available from: https://path-png.org/clinical-guidelines/

Clinical practice guidelines panel, European Association for the Study of the Liver. EASL 2017 Clinical practice guidelines on the management of hepatitis B virus infection. J Hepatol 2017; 67:370-398

Dong J, Yu XF, Zou J. Azithromycin-containing versus standard triple therapy for Helicobacter pylori eradication: a meta-analysis. World J Gastroenterol. 2009 Dec 28;15(48):6102-10. doi: 10.3748/wjg.15.6102. PMID: 20027685; PMCID: PMC2797669.

El Raziky, M., Hamdy, S., Hamada, Y. et al. Efficacy and safety of sofosbuvir and daclatasvir in patients with chronic hepatitis C virus induced cirrhosis with Child-Pugh class B. Egypt Liver Journal 12, 11 (2022). https://doi.org/10.1186/s43066-022-00174-3

Guidelines for the care and treatment of persons diagnosed with chronic hepatitis C virus infection. Geneva: World Health Organization; 2018. Licence: CC BY-NC-SA 3.0 IGO

Pappas P, Kauffman C, Andes D, Clancy C, Marr K, Ostrosky-Zeichner L, et al. Clinical Practice Guidelines for the management of candidiasis: 2016 update by the Infectious Diseases Society of America. Clin Infect Dis 2016; 62(4):e1-e50. https://doi.org/10.1093/cid/civ933

Shah S, Iyer P, Moss S. AGA Clinical practice update on the management of refractory Helicobacter pylori infection: expert review. Gastroenterology 2021; 160(5):1831-1841. Doi: 10.1053/j.gastro.2020.11.059

Terrault N, Lok A, McMahon B, Chang K-M, Hwang J, Jonas M et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. Hepatology 2018; 67 (4):1560-1599

Updated recommendations on treatment of adolescents and children with chronic HCV infection, and HCV simplified service delivery and diagnostics. Geneva: World Health Organization; 2022. Licence: CC BY-NC-SA 3.0 IGO.

Genital and sexually transmissible infections

This topic includes advice on the management of the following conditions in adults:

- **pelvic inflammatory disease**, page 160
- **postprocedural pelvic infection**, page 162
- **vulvovaginitis**, page 164
- **Bartholin's abscess**, page 166
- **infective proctitis**, page 167
- **genital herpes**, page 168
- **chancroid**, page 169
- **lymphogranuloma venereum**, page 170
- **granuloma inguinale** (donovanosis), page 170
- **syphilis** (primary, secondary and tertiary), page 171
- **genital warts**, page 173
- **acute epididymitis and epididymo-orchitis**, page 174
- **urethritis and cervicitis**, page 175
- **post–sexual assault care**, page 176

The following topics are not included in this section:

- see 'Infections in neonates and infants younger than 3 months' for advice on the management of **gonococcal ophthalmia neonatorum** (page 212), **herpes simplex virus prophylaxis and treatment** (page 215)

Overview

There are over 30 known bacterial, viral and parasitic pathogens that are commonly spread by sexual contact. Sexually transmissible infections (STIs) are some of the most common conditions in the world. Published estimates suggest that the prevalence of human immunodeficiency virus (HIV) in adults in Papua New Guinea is among the highest in the Asia–Pacific region, as well as prevalence rates of curable STIs (such as chlamydia, gonorrhoea, trichomoniasis and syphilis) that exceed those of other high-prevalence regions.

STIs cause acute urogenital conditions such as urethritis, cervicitis, vaginitis and genital ulceration; these in turn increase the risk of acquiring further STIs, including HIV. Early recognition and prompt diagnosis of STIs is particularly important in reducing HIV transmission.

Possible severe complications and long-term sequelae associated with STIs include pelvic inflammatory disease (PID), chronic pelvic pain, ectopic pregnancy and infertility. Patients with these conditions may experience debilitating stigma from families and communities.

Approaches to reduce the period of infectiousness include laboratory-based diagnosis, contact tracing, antibiotic treatment and easy access to these services. Since adequate laboratory services are not available in most health facilities in Papua New Guinea, presumptive treatment is recommended for those presenting with symptoms consistent with STIs in order to prevent complications and transmission.

The emergence of antibiotic-resistant strains of sexually transmissible agents, high incidence and prevalence of STIs and the prevalence of fatal pregnancy-related sepsis in Papua New Guinea emphasises the necessity for antibiotic guidelines on STIs and perinatal infections.

Pelvic inflammatory disease and postprocedural pelvic infection

Pelvic inflammatory disease (PID)

PID is an infection of the female upper genital tract that includes any combination of endometritis, salpingitis, tubo-ovarian abscess and peritonitis. Women with PID often have nonspecific symptoms such as cervicitis or are asymptomatic, resulting in delay in making the diagnosis and receiving treatment and thus allowing time for the sequelae to develop. Cervicitis is characterised by a mucopurulent cervical discharge and contact bleeding (e.g. postcoital bleeding) from a friable cervix and can progress to PID if untreated. While PID is polymicrobial, a significant proportion of women with clinical PID initially had *Chlamydia trachomatis* or *Neisseria gonorrhoea* infection.

The presentation of PID involves fever and lower abdominal pain that usually follows menses either for the first time (if acute) or over a period of time (if chronic). Difficulty in getting pregnant and deep dyspareunia are common complaints, while lower abdominal and pelvic tenderness are usually present on examination. The treatment of PID depends on the severity of the disease at presentation.

For treatment of cervicitis, see page 175.

Nonsevere (mild or moderate) PID

PID is considered nonsevere if the patient does not have severe pain, fever (38 °C or higher), systemic features (e.g. tachycardia, vomiting), sepsis or septic shock, or suspected tubo-ovarian abscess.

As a two-drug regimen, use:

azithromycin *1 g orally, as a single dose*

PLUS either

metronidazole *400 mg orally, 12-hourly for 14 days*

OR

tinidazole 1 g orally 12-hourly for 3 days.

If azithromycin is not available, substitute with:

doxycycline *100 mg orally, 12-hourly for 14 days.*[9]

Severe PID

PID is considered severe if the patient has severe pain, fever (38 °C or higher), systemic features (e.g. tachycardia, vomiting), sepsis or septic shock, or suspected tubo-ovarian abscess.

Start treatment with a two-drug regimen, using:

ceftriaxone *2 g IV, daily*

OR

chloramphenicol *1 g IV, 6-hourly*

PLUS either

metronidazole *500 mg IV or rectally, 12-hourly; switch to oral formulation when appropriate to complete 14 days*

OR

tinidazole 1 g orally, 12-hourly for 5 days.

Once the patient is clinically stable, give:

azithromycin *1 g orally, as a single dose.*

Presumptively, treat current sexual partners with:

azithromycin *1 g orally, as a single dose.*

PLUS

tinidazole 2 g orally, as a single dose.

cont...

9 Azithromycin is preferred in this regimen as it is intended to provide activity against both *Chlamydia* and *Gonorrhoea*. From the available susceptibility data in Papua New Guinea, there are high rates of gonococcal resistance to doxycycline.

If azithromycin is not available for either treatment or for presumptive regimens, substitute with:

doxycycline *100 mg orally, 12-hourly for 14 days.*[10]

Postprocedural or surgical pelvic infection

Infections following pelvic procedures and surgery are common in obstetrics and gynaecology, causing significant morbidity and mortality.

These infections include abdominal wound infection, pelvic cellulitis and abscess, puerperal and postprocedural endometritis, and septic pelvic thrombophlebitis.

Postprocedural or surgical pelvic infections can be mild or severe. Severe cases present with lower abdominal pain, fever (≥38°C), tachycardia, nausea and vomiting, sepsis, septic shock or pelvic abscess.

Nonsevere postprocedural infection

Postprocedural pelvic infection is considered nonsevere if the patient does not have severe pain, fever (38°C or higher), systemic features (e.g. tachycardia, vomiting), sepsis or septic shock, or suspected tubo-ovarian abscess.

Use:

amoxicillin *500 mg orally, 8-hourly for 14 days*

PLUS

metronidazole *400 mg orally, 12-hourly for 14 days.*

In patients with hypersensitivity to penicillins, use:

trimethoprim+sulfamethoxazole *160+800 mg orally, 12-hourly for 14 days*

PLUS

metronidazole *400 mg orally, 12-hourly for 14 days.*

Consider escalating to the IV antibiotic regimen for severe postprocedural infection if there is no improvement with oral treatment after 48 to 72 hours.

10 Azithromycin is preferred in this regimen as it is intended to provide activity against both *Chlamydia* and *Gonorrhoea*. From the available susceptibility data in Papua New Guinea, there are high rates of gonococcal resistance to doxycycline.

Severe postprocedural infection

Postprocedural pelvic infection is considered severe if the patient has severe pain, fever (38°C or higher), systemic features (e.g. tachycardia, vomiting), sepsis or septic shock, or suspected tubo-ovarian abscess.

Use:

gentamicin *IV, 5 mg/kg (7 mg/kg in critical illness), see Table 14 (page 384) for dosing frequency for information on dosing frequency, maximum dose and maximum number of doses*

PLUS

amoxicillin *2 g IV, 6-hourly*

PLUS

metronidazole *500 mg IV, 12-hourly.*

Alternatively, in patients with **immediate nonsevere** or **delayed nonsevere** hypersensitivity to penicillins, use:

ceftriaxone *2 g IV, daily*

PLUS

metronidazole *500 mg IV, 12-hourly.*

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

gentamicin *IV, 5 mg/kg (7 mg/kg in critical illness), see Table 14 (page 384) for dosing frequency for information on dosing frequency, maximum dose and maximum number of doses*

PLUS

clindamycin *600 mg IV, 8-hourly.*

Switch to oral therapy once the patient is clinically stable. Use an oral regimen as for nonsevere postprocedural infection.

Duration: total treatment duration (intravenous + oral) of at least 14 days.

Vulvovaginitis

Inflammation of the vagina and vulva (vulvovaginitis) is a very common gynaecological complaint. Patients present with abnormal vaginal discharge (in amount, colour or smell), vulvovaginal discomfort (irritation, itching or burning), or both. The most common causes of vulvovaginitis are candidiasis, bacterial vaginosis and trichomoniasis, which account for over 90% of infectious vaginitis. Trichomoniasis is the only sexually transmissible cause.

Management of vulvovaginitis

Bacterial vaginosis

Bacterial vaginosis (BV) is the most common cause of vaginitis (40 to 50%) among women in their reproductive years.

Symptoms include a malodorous, thin white or greyish vaginal discharge.

BV is a polymicrobial dysbiosis characterised by a change from a *Lactobacillus* dominant state to one with high diversity and quantities of anaerobic bacteria including *Gardnerella vaginalis*, *Mobiluncus* species, *Mycoplasma hominis* and *Peptostreptococcus* species.

Use:

metronidazole *2 g orally, as a single dose*

OR

tinidazole 2 g orally, as a single dose

OR

metronidazole *400 mg orally, 12-hourly for 7 days.*

Single-dose regimens have better adherence, but the cure rate is lower. Use the longer metronidazole regimen for recurrent infections.

Candida vulvovaginitis

The second most common cause of vaginal infection. Approximately 75% of women will have at least one episode in their reproductive life. *Candida albicans* is identified in 90% of cases. Candidal vulvovaginitis presents as genital or vulval pruritus or discomfort, sometimes with pain or terminal dysuria. It is often accompanied by a variable discharge ranging from curd-like to watery. An odour is significantly absent.

Examination reveals copious to minimal discharge, white plaque on vaginal walls and severe vulvovaginal erythema.

For treatment of nonsevere candidal vulvovaginitis, use:

clotrimazole 1% vaginal cream 1 applicatorful intravaginally, once daily at bedtime for 6 nights

OR

clotrimazole 500 mg pessary intravaginally, at bedtime once only.

For severe candidal vulvovaginitis (e.g. extensive vulval erythema, oedema, excoriation and fissuring on external examination), use:

clotrimazole 500 mg pessary intravaginally, at bedtime on day 1 and day 4.

OR

fluconazole 150 mg orally, on day 1 and day 4.

Trichomoniasis

Trichomoniasis is caused by the protozoa, *Trichomonas vaginalis*, which attaches to the vaginal walls and causes an intense inflammatory response, genital tract symptoms and reproductive sequelae.

Female patients complain of copious green or yellow discharge, vaginal/vulval itch, urinary tract infection symptoms, painful intercourse or pelvic pain. Examination findings include vulvovaginal erythema and frothy yellow or green vaginal discharge. Petechial haemorrhages on vaginal walls and cervix (strawberry cervix) may be present with high density of organism.

Male patients are usually asymptomatic but may present with urethral discharge, testicular discomfort, dysuria and frequency of urine or cloudy urine.

Use:

tinidazole 2 g orally, as a single dose

OR

***metronidazole** 400 mg orally, 12-hourly for 7 days.*

Approximately 50 to 75% of people infected with *T. vaginalis* are asymptomatic, so contact tracing and presumptive treatment of sexual partners is recommended.

Bartholin's abscess

Bartholin's abscess is a very painful condition arising from infection, swelling and collection of pus in one of the two Bartholin glands located on either side of the vaginal opening.

Bartholin gland infections are caused by aerobic and anaerobic pathogens from the perineum. While cultures are mostly polymicrobial, Gram-negative bacteria including *Escherichia coli* and anaerobes are commonly isolated, and occasionally *Neisseria gonorrhoeae* or *Chlamydia trachomatis* are present.

The management of Bartholin's abscess includes analgesics to control pain, antibiotics to control the infection and drainage of the pus.

Treatment of Bartholin's abscess

Use:

amoxicillin *500 mg orally, 8-hourly for 7 days*

PLUS

azithromycin *1 g orally, as a single dose*

PLUS either

metronidazole *400 mg orally, 12-hourly for 5 days*

OR

tinidazole 500 mg orally, 12-hourly for 3 days.

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

ceftriaxone *500 mg IV, as a single dose*

PLUS

metronidazole *400 mg orally, 12-hourly for 5 days.*

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

clindamycin *450 mg orally, 6-hourly*

PLUS

azithromycin *1 g orally, as a single dose.*

Infective proctitis

Proctitis is the inflammation of the rectum which is commonly associated with inflammatory bowel disease. However, there has been a notable increase in the incidence of infectious proctitis caused by STIs, especially among individuals who practise receptive anal exposures (oral-anal, digital-anal or genital-anal). Infectious proctitis is associated with anorectal pain, tenesmus or rectal discharge which may be purulent, bloody or contain mucous. The most frequently reported pathogens include *Neisseria gonorrhoeae*, *Chlamydia trachomatis* (including *Lymphogranuloma venereum* (LGV) serovars), *Treponema pallidum* and herpes simplex.

All patients with proctitis should be tested for HIV and syphilis.

Treatment of infectious proctitis

Treatment is initiated either empirically or after establishing the diagnosis.

Use:

ceftriaxone *500 mg IV, as a single dose*

PLUS

doxycycline *100 mg orally, 12-hourly for 10 days.*

Prescribe an extended course of presumptive treatment for LGV in individuals with bloody discharge and perianal or mucosal ulcers, use:

doxycycline *100 mg, 12-hourly for 3 weeks.*

If there is inadequate clinical response to initial therapy, consider herpes simplex virus and treat accordingly – see **genital herpes**, page 168 in this topic.

STIs causing genital ulcer disease (GUD)

Anogenital ulcers can be caused by sexually transmissible infections (STIs) or other conditions. In well-resourced settings, laboratory tests (e.g. nucleic acid amplification testing [NAAT], such as polymerase chain reaction [PCR], and serology) are used to diagnose infectious causes. However, as these are not available in Papua New Guinea, the diagnosis is made clinically.

The commonly occurring STIs that cause genital ulcer disease are:

- chancroid (*Haemophilus ducreyi*)
- lymphogranuloma venereum (LGV) / chancre (*Chlamydia trachomatis* L1, L2, L3)
- donovanosis / granuloma inguinale (*Klebsiella granulomatis)*
- genital herpes (herpes simplex virus)
- syphilis *(Treponema pallidum)* – see **syphilis**, page 171 in this topic.

Genital herpes

Genital herpes is a lifelong viral infection caused by herpes simplex virus (HSV)-1 and HSV-2. Since most individuals infected with HSV present with non-classical symptoms or are asymptomatic, the majority remain undiagnosed while shedding the virus.

The first clinical episode of genital herpes presents as clusters of painful blisters on the genitalia and perineum that erode to erythematous ulcers. They can also occur on other areas of the body, such as along the sacral dermatomes. Other clinical symptoms include lymphadenopathy, fever, malaise and myalgia.

Almost everyone who has a first clinical episode of genital herpes will have subsequent recurrent episodes. Those who had mild first episodes can experience prolonged and severe recurrent episodes, so treatment is recommended for everyone.

For patients who experience frequent recurrences (4 to 6 times a year or more), suppressive therapy, which reduces recurrences by 70 to 80%, is recommended. Disease progression can be reassessed every 3 months within the first year to determine whether treatment should be continued or not. Long-term safety and efficacy have been reported, and HSV antiviral resistance is uncommon.

Intravenous aciclovir treatment is recommended for patients with severe HSV infection requiring hospital admission. Such patients can present with pneumonia, hepatitis, meningitis or encephalitis, see **encephalitis**, page 88 in ‘Central nervous system infections.’

Treatment of genital herpes

First clinical episode of genital herpes Including people living with HIV (PLWHIV) and immunocompromised individuals.
Use: *aciclovir 400 mg orally, 8-hourly for 10 days. If clinical response is rapid, stop therapy after 5 days.*

Recurrent episodes (episodic treatment) In adults including PLWHIV.
Start antivirals at the onset of prodromal symptoms or lesions. Advise patients to self-initiate treatment at the first hint of symptoms: *aciclovir 800 mg orally, 8-hourly for 2 days.*

Suppressive treatment for recurrent episodes

Use:

aciclovir 400 mg orally, 12-hourly, continuously.

Review after 3 months.

Treatment of severe HSV infection

Use:

aciclovir 5 to 10 mg/kg IV, 8-hourly.

Continue intravenous therapy until clinical improvement, then switch to:

aciclovir 400 mg orally, 8-hourly.

Duration: complete 10 to 14 days of total treatment (IV + oral).

Recurrent genital herpes during pregnancy

Consult an obstetrician in the management of cases of genital herpes in pregnancy.

Suppressive therapy (see introduction on previous page) for women with recurrent genital herpes during late pregnancy reduces the chance of recurrence of herpes simplex virus at delivery and increases the likelihood of a vaginal delivery.

After 36 weeks' gestation, it is reasonable to increase the dosing frequency of suppressive treatment; use:

aciclovir 400 mg orally, 8-hourly.

Continue until delivery.

Suppressive therapy may not always protect against HSV transmission to neonates – see **herpes simplex prophylaxis and treatment**, page 215 in 'Infections in neonates and young infants.'

Chancroid

Chancroid is caused by *Haemophilus ducreyi*. It initially appears as a small bump or blister on the foreskin, shaft or head of the penis or on the labia before the ulcer develops. The ulcer is painful with soft and sharp borders and yellowish-grey base. Half of all patients present with enlarged inguinal lymph nodes that can develop into abscesses. In advanced cases, genital scarring and rectal or urogenital fistulas can develop despite successful treatment; early presentation, diagnosis and treatment are important in averting serious long-term sequelae.

Treatment of chancroid

Use:

azithromycin *1 g orally, as a single dose*

OR

ceftriaxone *500 mg IM (in 2 mL of 1% lidocaine), or 500 mg IV, as a single dose*

OR

ciprofloxacin *500 mg orally, 12-hourly for 3 days*

OR

erythromycin *500 mg orally, 8-hourly for 7 days.*

Lymphogranuloma venereum (LGV)

LGV is caused by *Chlamydia trachomatis* serovars L1, L2 and L3. Unlike serovars A-K that are mild and often asymptomatic, LGV causes intense and invasive inflammation. Clinical presentations include genital ulcers, tender inguinal lymph nodes that can burst into discharging sinuses, and rectal discharge and pain when the rectum and lower gastrointestinal tract are involved (proctocolitis).

Treatment of LGV

Use:

doxycycline *100 mg orally, 12-hourly for 3 weeks*

Doxycycline is the preferred treatment, but alternative regimens include:

azithromycin *1 g orally, once a* ***week*** *for 3 weeks.*

OR

erythromycin *500 mg orally, 6-hourly for 3 weeks.*

Granuloma inguinale (donovanosis)

Granuloma inguinale (donovanosis) is caused by the intracellular bacterium *Klebsiella granulomatis* (previously known as *Calymmatobacterium granulomatis*).

It begins as painless nodules in the genital, inguinal or perineal areas that break down to form raised, beefy, red ulcers that can easily bleed due to their high vascularity. The lymph nodes are usually not involved. The infection may cause ulceration of the cervix that may resemble carcinoma.

Treatment of granuloma inguinale (donovanosis)

Use:

azithromycin *500 mg orally, daily for 7 days*

OR

azithromycin ***1 g*** *orally, once* ***weekly*** *for at least 4 weeks*

OR

doxycycline *100 mg orally, 12-hourly for at least 4 weeks.*

Doxycycline is contraindicated for the treatment of pregnant people; if azithromycin is not available or not suitable, use:

erythromycin *500 mg orally, 6-hourly.*

Duration: Treat for at least 3 weeks and until all lesions have completed healed.

Response to treatment is usually slow. Cancer should be ruled out if there is no response to treatment.

Syphilis

Syphilis is a systemic STI that is caused by *Treponema pallidum*. It is categorised in stages based on clinical presentation during the natural progression of the disease.

Classification of syphilis

Primary syphilis

Initially, syphilis presents as a self-limiting painless ulcer or chancre with indurated edges and clean base at the site of infection, which is usually the penis, labia or cervix.

Secondary syphilis

Clinical presentations include acute illness with rash, condyloma lata (painless clusters of raised plaques that occur within the skin folds of the anogenital area, axilla or under the breasts) and enlarged lymph nodes.

Tertiary syphilis

The manifestations include gummatous lesions, cardiovascular and late central nervous system (CNS) involvement such as tabes dorsalis and general paresis (neurosyphilis).

Syphilis cases that do not manifest clinically but are detected by serological tests are referred to as latent syphilis. Neurosyphilis can present at any stage of the disease.

Serological tests, Venereal Disease Research Laboratory (VDRL) or the Determine Syphilis TP Rapid test should be employed to support a suspected diagnosis of syphilis. Screen patients with suspected syphilis for other STIs, including HIV.

The recommended antibiotic regimen in the treatment of syphilis aims not only to treat the clinical manifestations, but also to prevent potential short- and long-term complications, and to prevent onward transmission.

Penicillin is the drug of choice for treating patients in all stages of syphilis.

Carefully assess any patient reporting hypersensitivity to penicillins.

Treatment of syphilis

Treatment of syphilis for all stages (excluding syphilis in pregnancy and tertiary / neurosyphilis)

See separate management recommendations for syphilis in pregnancy and tertiary/ neurosyphilis.

Use:

benzathine benzylpenicillin *2.4 million units IM, weekly for 3 consecutive weeks.*

The interval between doses for benzathine benzylpenicillin should not exceed 14 days.

Alternatively, for patients with confirmed hypersensitivity to penicillins, use:

doxycycline *100 mg orally, 12-hourly for 14 days.*

Treatment of tertiary syphilis / neurosyphilis

Tertiary syphilis refers to syphilis of longer than 2 years' duration, or of unknown duration, with cardiovascular, CNS or skin and bone (gummatous syphilis) involvement. Expert advice is essential.

Use:

benzylpenicillin *1.8 g IV, 4-hourly for 15 days.*

Management of syphilis in pregnancy

Syphilis is one of the commonest causes of avoidable stillbirths in Papua New Guinea. Screen all pregnant people for syphilis at the first antenatal clinic visit.

Treat the partners of pregnant people who test positive simultaneously.

Penicillin is the only known effective antimicrobial for treating fetal infection and preventing congenital syphilis. Assess patients reporting hypersensitivity to penicillins for immune-mediated hypersensitivity.

Macrolides do not reliably cross the placenta, and erythromycin and azithromycin therapy has failed to prevent congenital syphilis. Doxycycline is not recommended during pregnancy as it can affect tooth and bone development in the baby.

For patients with immediate hypersensitivity to penicillins, desensitisation should be performed – seek expert advice.

Use:

benzathine benzylpenicillin *2.4 million units IM, weekly for 3 consecutive weeks.*

The interval between doses for benzathine benzylpenicillin should not exceed 14 days.

Genital warts

Anogenital warts (condyloma acuminatum) are a common STIs caused by certain types of human papillomavirus (HPV) infection. They spread by skin-to-skin contact, usually during sex. Warts may occur separately or in clusters around anogenital skin or mouth. There is usually little discomfort, although they are occasionally painful and/or pruritic, but often psychological distress is significant.

Atypical lesions, lesions with variable pigmentation or raised plaque-like lesions should be biopsied to exclude pre-cancerous change especially in patients who are immunocompromised or have HIV.

Treatment is cosmetic, rather than curative, and topical therapy is preferred. Clinician initiated cryotherapy or, rarely, cautery or excision under local anaesthetic, are alternative options.

It is important to determine the HIV status of patients because there may be very little response to treatment for patients with HIV infection that are not on antiretroviral therapy, and because excision may lead to sepsis in immunocompromised people living with HIV.

Warts can grow rapidly in pregnancy. While cryotherapy can be used, there is often a poor response. Pregnant people can undergo a normal vaginal delivery as the risk of transmission to the baby is extremely low and lesions often resolve spontaneously postnatally when immune function returns to normal following delivery.

Treatment of genital warts

Treatment with topical preparations is recommended only if there are less than 10 lesions

Use:

podophyllotoxin 0.5% paint topically, twice daily for 3 days followed by a 4-day break; repeat weekly for 4 to 6 cycles until warts resolve.

Do not use podophyllin in pregnant patients.

Acute epididymitis and epididymo-orchitis

Acute epididymitis is the painful swelling and inflammation of the epididymis.

The involvement of the testis (epididymo-orchitis) results in painful swelling of the testis. Always exclude testicular torsion, as it is a surgical emergency.

People with symptoms lasting longer than 6 weeks should be investigated for infectious granulomatous conditions. *Mycobacterium tuberculosis* (TB) is a common cause of chronic cases of scrotal discomfort or pain, swelling and epididymitis that lasts for longer than 6 weeks.

Treatment of acute epididymitis and epididymo-orchitis

Acute epididymo-orchitis – sexually acquired

The commonest causes of acute epididymitis in sexually active men are STIs such as *Chlamydia trachomatis, Neisseria gonorrhoeae* and *Mycoplasma genitalium*, or enteric organisms (for men involved in insertive anal sex).

Sexually active men should be empirically treated for chlamydia and gonorrhoea. Use:

azithromycin *1 g orally, as a single dose*

PLUS

ceftriaxone *500 mg IM, as a single dose.*

cont...

In healthcare facilities where ceftriaxone is unavailable, give:

azithromycin *1 g orally, as a single dose.*

PLUS either

amoxicillin+clavulanate ***1000+250 mg*** *(2 x 500+125 mg tablets) orally, 8-hourly for 7 days*

OR

ciprofloxacin *500 mg orally, 12-hourly for 10 days.*

Recent partner(s) should be treated with:

azithromycin *1 g orally, as a single dose.*

For all the above regimens, if azithromycin is not available, use:

doxycycline *100 mg orally, 12-hourly for 10 days.*

Acute epididymitis – non-sexually acquired

Acute epididymitis can be caused by enteric organisms and can occur in men who have undergone prostate biopsy, vasectomy and other invasive urinary tract procedures.

Use:

trimethoprim+sulfamethoxazole *160+800 mg orally, 12-hourly for 10 days*

OR

ciprofloxacin *500 mg orally, 12-hourly for 10 days.*

In addition to antimicrobial treatment, recommend bed rest, scrotal elevation and nonsteroidal anti-inflammatory drugs until fever, pain and swelling subsides

Urethritis and cervicitis

Inflammation of the urethra can be caused by either infectious or noninfectious conditions. The symptoms of urethritis include urethral discomfort, dysuria, urethral itchiness and urethral mucoid, mucopurulent or purulent discharge.

Cervicitis is characterised by a mucopurulent cervical discharge and contact bleeding (e.g. postcoital bleeding) from a friable cervix and can progress to PID if untreated.

While *Neisseria gonorrhoeae* and *Chlamydia trachomatis* are well recognised infectious causes of urethritis and cervicitis, *Mycoplasma genitalium* and *Trichomonas vaginalis* are also possible causes.

Treatment of urethritis and cervicitis (sexually acquired)

As part of a three- or four-drug regimen, use one of the following options:

ceftriaxone *500 mg IM, as a single dose*

OR

cefixime *800 mg orally, as a single dose*

OR

***amoxicillin* 3 g** *orally, as a single dose PLUS probenecid 1 g orally, as a single dose*

PLUS one of the following:

azithromycin *1 g orally, as a single dose*

OR

doxycycline *100 mg orally, 12-hourly for 7 days*

OR

erythromycin *500 mg orally, 6-hourly for 7 days*

PLUS one of the following:

metronidazole *2 g orally, as a single dose*

OR

tinidazole 2 g orally, as a single dose.

Post–sexual assault care

Assess the need for immediate care e.g. first aid or injuries that need attention.

Investigations for STIs, pregnancy and forensic purposes should be performed on a case-by-case basis and should follow established local protocols. Any examination of survivors of sexual assault should be conducted by an experienced clinician to avoid causing further trauma during consultation and examination. The management of people who have been sexually assaulted should include accurately documenting findings, collecting specimens for diagnostic and forensic purposes, preventing potential pregnancy, preventing STIs, and addressing physical and psychological trauma.

Providing prophylaxis against STIs (gonorrhoea, chlamydia and trichomoniasis) is an integral part of the care of people who have been sexually assaulted. Also offer baseline and follow up screening for HIV, hepatitis B, syphilis and pregnancy.

Prophylaxis post–sexual assault

Provide emergency contraception (if a pregnancy test is negative) and prophylaxis for gonorrhoea, chlamydia, *Trichomonas* and HIV (if HIV negative), see *Papua New Guinea National Guidelines for HIV Care and Treatment* for an appropriate regimen; start postexposure prophylaxis as soon as possible, preferably within 72 hours of exposure.

Test for syphilis and treat if positive, see page 171 in this topic.

Provide postexposure hepatitis B vaccination if patient has not been previously vaccinated.

For prophylaxis for gonorrhoea, chlamydia and trichomoniasis, as a three- (or four)-drug regimen, use:

azithromycin *1 g orally, as a single dose*

PLUS one of the following

cefixime *800 mg orally, as a single dose*

OR

amoxicillin ***3 g*** *orally, as a single dose PLUS probenecid 1 g orally as a single dose*

PLUS one of the following

metronidazole *2 g orally, as a single dose*

OR

tinidazole 2 g orally, as a single dose.

Key additional references

Bachmann LH, Kirkcaldy RD, Geisler WM, et al.; the MAGNUM Laboratory Working Group. Prevalence of Mycoplasma genitalium infection, antimicrobial resistance mutations and symptom resolution following treatment of urethritis. Clin Infect Dis 2020;71:e624–32.

Catchpole M. Sexually Transmitted Infections: Control strategies. BMJ 2001; 322: 1135-6.

Faro C, Faro S. Postoperative pelvic infections. Infect Dis Clin North Am. 2008 Dec;22(4):653-663.

Guidelines for the management of symptomatic sexually transmitted infections. Geneva: World Health Organization; 2021.

Larsen JW, Hager WD, Livengood CH, Hoyme U. Guidelines for the diagnosis, treatment and prevention of postoperative infections. Infect Dis Obstet Gynecol. 2003;11(1):65-70.

Mola, G. Manual of standard managements in Obstetrics and Gynaecology for doctors, HEOs and nurses in Papua New Guinea.7th Edition 2016.

Rane VS, Fairley CK, Weerakoon A, et al. Characteristics of acute nongonococcal urethritis in men differ by sexual preference. J Clin Microbiol 2014;52:2971–6.

Rietmeijer CA, Mungati M, Machiha A, et al. The etiology of male urethral discharge in Zimbabwe: results from the Zimbabwe STI Etiology Study. Sex Transm Dis 2018;45:56–60.

Rowley J, Hoorn SV, Korenromp E, et al. Chlamydia, Gonorrhoea, Trichomoniasis and Syphilis: Global prevalence and incidence, 2016. Bull World Health Organ 2019;97: 548-562P.

Toliman, P, Ford, R. L, Mition, Y. Koata, A. Toto, B. Nightinggale, C. Valley, A. Whileys, J. Wapling, G. Law, G. Greenhill, A. R. Antimicrobial resistance in Neisseria gonorrhoeae from the highlands of Papua New Guinea. Papua New Guinea Institute of Medical Research.

Toliman, P. Mition, Y. Toto, B. Koata, A. Wapling, J. Ford, R. Greenhill, A. Gonococcal Antimicrobial Susceptibility Survey, Goroka, Eastern Highlands Province. Papua New Guinea Institute of Medical Research.

Vallely LM, Toliman P, Ryan C, et al. Prevalence and risk factors of Chlamydia trachomatis, Neisseria gonorrhoeae, Trichomonas vaginalis and other sexually transmissible infections among women attending antenatal clinics in three provinces in Papua New Guinea: a cross-sectional survey. 2016 Oct;13(5):420-427.

van der Veer C, van Rooijen MS, Himschoot M, de Vries HJ, Bruisten SM. Trichomonas vaginalis and Mycoplasma genitalium: age-specific prevalence and disease burden in men attending a sexually transmitted infections clinic in Amsterdam, the Netherlands. Sex Transm Infect 2016;92:83–5.

WHO Guidelines for the treatment of Treponema pallidum (syphilis). Geneva: World Health Organization; 2016.

Willie B, Sweeney EL, Badman SG, Chatfield M, Vallely AJ, Kelly-Hanku A, Whiley DM. The Prevalence of Antimicrobial Resistant Neisseria gonorrhoeae in Papua New Guinea: A Systematic Review and Meta-Analysis. Int J Environ Res Public Health. 2022 Jan 28;19(3):1520.

Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines, 2021. MMWR Recomm Rep, 2021; 70 (4):124-5

Intraabdominal infections

This topic includes advice on the management of the following conditions in adults and children older than 3 months:

- **uncomplicated appendicitis**, page 180
- **uncomplicated diverticulitis**, page 180
- **peritonitis due to perforated bowel, intraperitoneal abscess, complicated appendicitis and complicated (severe) diverticulitis**, page 181
- **cholecystitis and cholangitis**, page 183
- **liver abscess**, page 185
  - empirical therapy, page 186
  - amoebic liver abscess, page 186
  - bacterial liver abscess, page 186
- **acute pancreatitis**, page 187.

The following topic is not included in this section:

- **necrotising enterocolitis** (NEC) (page 208) in 'Infections in neonates and young infants.'

For the treatment of intraabdominal infections, gentamicin (in combination with amoxicillin or ampicillin) is preferred to broad-spectrum penicillins or cephalosporins for empirical therapy because it is active against a greater percentage of *Enterobacterales*[11], and is more rapidly bactericidal. Gentamicin is also less likely to contribute to the development of post antibiotic, hospital-associated diarrhoea/colitis due to *Clostridioides difficile* infection (formerly known as *Clostridium difficile* infection) and the selection of antibiotic-resistant organisms. Reduced renal function is not a contraindication to gentamicin. A single dose of an aminoglycoside can be used in patients with chronically impaired kidney function, with rapidly deteriorating kidney function unrelated to sepsis, or who are frail and elderly (e.g. 80 years or older). See 'Appendix 2: Gentamicin dosing,' page 381 for further dosing advice.

11 *Enterobacterales* are a large family of bacteria, including many of the more familiar pathogens such as *Salmonella* species, *Shigella* species and *Escherichia coli.*

Appendicitis

Treatment of appendicitis (uncomplicated/no perforation)

For **complicated appendicitis**, treat as for peritonitis due to perforated bowel, peritonitis – see next section in this topic.

Surgical drainage and appendicectomy are the mainstays of treatment for appendicitis; evidence does not support the routine treatment of appendicitis with antibiotic therapy alone. Randomised controlled trials have shown treatment failure rates for antibiotics alone (i.e. readmission, complications and need for repeat surgery) in the first year were 15 to 30% and up to 40% at 5 years. Treatment failure rates for appendicectomy were less than 2%.

Use:

amoxicillin *500 mg (child: 15 mg/kg up to 500 mg) orally, 8-hourly*

PLUS

metronidazole *400 mg (child: 10 mg/kg up to 400 mg) orally, 12-hourly.*

Alternatively, as a single agent, use:

amoxicillin+clavulanate *500+125 mg (child: 25+5 mg/kg) orally, 8-hourly.*

Alternatively, in 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*

PLUS

metronidazole *400 mg (child: 10 mg/kg up to 400 mg) orally, 12-hourly.*

Cease treatment immediately after appendicectomy.

Diverticulitis

Treatment of uncomplicated (mild) diverticulitis

For **complicated diverticulitis**, treat as for peritonitis due to perforated bowel – see next section in this topic.

Diverticulitis occurs when a colonic diverticulum becomes inflamed. Diverticulitis usually presents with abdominal pain in the left lower quadrant and fever, often with an altered bowel habit.

The majority of diverticulitis episodes are uncomplicated (nonsevere).

Patients with uncomplicated diverticulitis may not require antibiotic therapy.

Antibiotic therapy is appropriate for patients with any of the following:

- immune compromise
- right-sided diverticulitis
- failure to improve after 72 hours of conservative management (i.e. no antibiotic therapy).

Use:

amoxicillin *500 mg orally, 8-hourly for 5 days*

PLUS

metronidazole *400 mg orally, 12-hourly for 5 days.*

Alternatively, as a single agent, use:

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

In patients with hypersensitivity to penicillins, use:

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

PLUS

metronidazole*400 mg orally, 12-hourly for 5 days.*

Complicated (severe) diverticulitis refers to diverticulitis with a positive blood culture result, perforation, peritonitis, sepsis or septic shock, or an abscess larger than 5 cm in diameter – see next section for management.

Peritonitis due to perforated bowel, intraperitoneal abscess

Treatment of peritonitis, intraperitoneal abscess

Also use this treatment regimen for **complicated appendicitis** and **complicated (severe) diverticulitis**.

Patients who are unstable or septic require emergency surgery.

Refer all patients to the surgical team – effective and early source control is the most important aspect of management.

Take blood specimens for culture prior to commencing antibiotics. Send tissue specimens for culture from the operating theatre.

If the patient is septic, start antibiotics within 1 hour of presentation, use:

gentamicin *IV, see 'Appendix 1: Gentamicin dosing' (page 381) for information on dosing frequency, maximum dose and maximum number of doses*

adults: 5 mg/kg (7 mg/kg in critical illness), see Table 14 for dosing frequency (page 384)

children 3 months and older: 7 mg/kg up to 560 mg, once daily

PLUS

amoxicillin *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 the IV regimen is needed for longer than 72 hours or if gentamicin is contraindicated, as a three-drug regimen, use:

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

PLUS

amoxicillin *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.*

In patients with hypersensitivity to penicillins, use gentamicin plus metronidazole as a two-drug regimen.

Switch to oral antibiotics when patient has clinically improved. If the results of susceptibility testing are unavailable, use:

amoxicillin *500 mg (child: 15 mg/kg up to 500 mg) orally, 8-hourly*

PLUS

metronidazole *400 mg (child: 10 mg/kg up to 400 mg) orally, 12-hourly.*

Alternatively, as a single agent, use:

amoxicillin+clavulanate *500+125 mg (child: 25+5 mg/kg up to 500+125 mg) orally, 8-hourly.*

cont...

Alternatively, for patients with hypersensitivity to penicillins, use:

trimethoprim+sulfamethoxazole *160+800 mg (child 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.*

For patients who do not improve on empirical antibiotic therapy after 72 hours, despite adequate source control, consider escalating to:

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

Antifungal therapy is not usually required. However, consider empirical antifungal therapy (usually with fluconazole) in patients who are not improving with empirical antibacterial therapy and have high risk presentations (e.g. necrotising pancreatitis, upper gastrointestinal perforation, recurrent bowel leak). Antifungal therapy is also required if yeasts are identified in samples from deep surgical sites – seek expert advice.

Duration

Treat for a total of 5 days after surgical control of infection.

For patients who remain critically unwell requiring intensive care support after surgical control of the source of infection, a total duration of up to 8 days (IV + oral) may be used. For patients who do not improve after 8 days of antibiotic therapy, consider causes of treatment failure, including residual undrained intraabdominal collections or abscesses. Patients with residual undrained intraabdominal collections or abscesses often require a longer duration of therapy (up to 4 to 6 weeks depending on clinical and radiological progress). Seek specialist advice for patients with undrained residual intraabdominal collections or abscesses.

Cholecystitis, cholangitis

In cholecystitis, cholecystectomy should be considered early in initial presentation. Severe suppurative cholecystitis or cholangitis requires surgery and biliary decompression within 24 hours.

Treatment of cholecystitis and cholangitis

Refer all patients to the surgical team.

If patient is septic give antibiotics within 1 hour of presentation.

For directed management of identified pathogens, see page 253 in ‘Sepsis and bloodstream infections.’

Take blood for culture prior to commencing antibiotics and send tissue (preferred) or pus taken in the operating theatre for microscopy and culture. Treat with:

gentamicin *IV, see 'Appendix 1: Gentamicin dosing' (page 381) for information on dosing frequency, maximum dose and maximum number of doses*

adults: 5 mg/kg (7 mg/kg in critical illness), see Table 14 for dosing frequency (page 384)

children 3 months and older: 7 mg/kg up to 560 mg, once daily

PLUS

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

If the IV regimen is needed for longer than 72 hours or if gentamicin is contraindicated, cease gentamicin and switch to the ceftriaxone-containing regimen below. As a single agent, use:

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

In late presenting or severely septic patients, **add** to either of the above regimens:

metronidazole *500 mg (child: 12.5 mg/kg up to 500 mg) IV, 12-hourly.*

In patients with hypersensitivity to penicillins, use gentamicin plus metronidazole.

When clinically well, switch to oral therapy. If the results of susceptibility testing are unavailable, use:

amoxicillin *500 mg (child: 15 mg/kg up to 500 mg) orally, 8-hourly*

PLUS

metronidazole *400 mg (child: 10 mg/kg up to 400 mg) orally, 12-hourly.*

Alternatively, as a single agent, use:

amoxicillin+clavulanate *500+125 mg (child: 25+5 mg/kg up to 500+125 mg) orally, 8-hourly.*

Alternatively, 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*

PLUS for patients with chronic biliary obstruction or acalculous cholecystitis:

metronidazole *400 mg (child: 10 mg/kg up to 400 mg) orally, 12-hourly.*

Duration of therapy

Cholangitis with biliary drainage

Stop antibiotics 5 days after drainage and monitor patient for signs of recurrent infection.

Cholangitis **without** biliary drainage

Treat for a total of 7-10 days (IV plus oral).

Calculous cholecystitis with cholecystectomy

Stop antibiotics immediately after cholecystectomy.

Acalculous cholecystitis with cholecystectomy

Continue treatment for a further 5 days after cholecystectomy (IV plus oral).

Cholecystitis **without** cholecystectomy

Treat for a total of 7 to 10 days (IV plus oral).

Liver abscess

A liver abscess is a collection of pus inside the liver. Symptoms and signs include fever, lethargy, right upper quadrant discomfort, anorexia, a large and tender liver, and pleural effusion. Normal liver function tests do not exclude the diagnosis. Liver abscesses are usually bacterial (pyogenic) or amoebic. In Papua New Guinea, an isolated liver abscess is more likely to be an amoebic, rather than bacterial, abscess.

Where possible, blood should be collected for culture and susceptibility testing in all patients with liver abscess prior to commencing antibiotics. If an abscess is drained, send pus for microscopy and culture. Ultrasound or CT is required for diagnosis.

Hydatid disease not been described in Papua New Guinea, but that does not exclude its presence. If hydatid disease is suspected, send samples for histological confirmation.

Treatment of liver abscess

Empirical therapy for liver abscess

Use:

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

PLUS

metronidazole *750 mg (child: 15 mg/kg up to 750 mg) IV,* ***8-hourly***

OR

metronidazole *800 mg (child: 15 mg/kg up to 800 mg) orally,* ***8-hourly***.

If not responding to antibiotics, or if abscess > 5 cm, seek surgical opinion regarding drainage.

Treatment of proven amoebic liver abscess

Surgical drainage of large abscesses may be required.

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.

While luminal amoebicides (e.g. paromomycin, diloxanide) are often recommended to eliminate cysts following treatment to reduce risk of relapse, they do not prevent later reinfection. These agents are not available on the PNG Medical & Dental Catalogue.

Treatment of bacterial liver abscess

Drainage is the mainstay of therapy for the treatment of bacterial liver abscess. For antibiotic treatment, use:

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

PLUS

metronidazole *800 mg (child: 15 mg/kg up to 800 mg) orally,* ***8-hourly***

OR

metronidazole *750 mg (child: 15 mg/kg up to 750 mg) IV,* ***8-hourly***.

cont...

If the response to initial drainage is good, switch to directed oral therapy after 2 weeks. If the results of culture and susceptibility testing are not available, a reasonable oral option is:

amoxicillin+clavulanate *500+125 mg (child: 25+5 mg/kg up to 500+125 mg) orally, 8-hourly.*

Alternatively, in patients with hypersensitivity to penicillins, use:

trimethoprim+sulfamethoxazole *160+800 mg (child: 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****.*

If drainage was incomplete, 4 to 6 weeks of intravenous antibiotic therapy may be required.

Duration

The total duration of therapy is usually 4 to 6 weeks (IV + oral).

Acute pancreatitis

Causes of acute pancreatitis include biliary obstruction with stones, prolonged excessive alcohol consumption, exposure to certain therapeutic drugs, or, on occasion, viral infections.

Antibiotic therapy is not recommended for the management of acute pancreatitis except to treat infected pancreatic necrosis or pancreatic abscess.

Patients with severe acute pancreatitis (organ failure that persists for more than 48 hours) can intermittently appear septic during a prolonged hospitalisation; however, this may not necessarily indicate infection. In practice, infection can be difficult to differentiate from severe systemic inflammatory response syndrome.

Patients with acute pancreatitis may go on to develop pancreatic fluid collections. Two-thirds of pancreatic fluid collections are sterile and will resolve with conservative management. Following onset of pancreatitis, infected pancreatic fluid collections are very rare in the first week, and peak in weeks 2 and 3. Antibiotics are indicated when infection is proven, and also when infected necrosis is suspected clinically or radiologically— based on observations, biochemistry (C-reactive protein, albumin) or imaging (gas in necrosum).

Management of acute pancreatitis includes fluid administration and analgesia. For patients with alcohol-associated pancreatitis, advise the patient to stop drinking alcohol.

Treatment of infected pancreatic necrosis and pancreatic abscess

Management of an infected pancreatic fluid collection involves endoscopic drainage, percutaneous aspiration or surgery, and antibiotic therapy.

For empirical therapy of infected pancreatic necrosis or pancreatic abscess, use:

ceftriaxone *2 g (child: 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*

If Gram-positive cocci are identified on Gram stain, **add**:

vancomycin *slow IV infusion,* ***consider a loading dose in critically ill adults and children****. See 'Appendix 2: Vancomycin dosing' (page 386) for information on loading dose, dosing frequency and infusion time*

adult ≥ 40 years: 15 mg/kg, see Table 18 for dosing frequency (page 390)

adult < 40 years 20 mg/kg, see Table 17 for dosing frequency (page 389)

child 3 months and older: 15 mg/kg, 6-hourly.

For patients who do not improve on empirical regimen above after 48 to 72 hours, switch to piperacillin+tazobactam as a single agent:

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

Duration

The optimal duration of therapy is uncertain. If adequate surgical control of the source of infection has been achieved, stop antibiotic therapy after 5 to 7 days and observe for clinical deterioration.

For cases that do not resolve within 7 to 10 days, consider secondary infection with *Candida* species or multidrug-resistant organisms such as vancomycin-resistant enterococci or multidrug-resistant Enterobacterales.

Key additional references

Alto WA, Nettleton LB. Hydatid disease: the threat within Papua New Guinea. P N G Med J. 1989 Jun;32(2):139-42. PMID: 2683476.

Maternal infections associated with pregnancy

This topic includes advice on the management of the following conditions in women during pregnancy, childbirth and the postnatal period:

- **urinary tract infections in pregnancy** including asymptomatic bacteriuria, acute cystitis and pyelonephritis, page 189
- **prelabour rupture of membranes** including preterm prelabour rupture of membranes (PPROM) and prelabour rupture of membranes at term, page 191
- **chorioamnionitis**, page 193
- **postpartum endometritis**, page 195
- **presumptive treatment following fetal death in utero or retained placenta**, page 197.

Other related guidelines:

- *Manual of Standard Managements in Obstetrics and Gynaecology for Doctors, HEOs and Nurses in Papua New Guinea.*

Urinary tract infection in pregnancy

The physiological changes in pregnancy predispose to urinary tract infection (UTI). These conditions are classified as asymptomatic bacteriuria, cystitis and pyelonephritis. Cystitis (lower urinary tract infection) is usually diagnosed clinically based on symptoms such as lower abdominal or suprapubic pain, dysuria and frequency of urine without fever. Pyelonephritis presents acutely with fever, costovertebral angle tenderness and pyuria. Pyelonephritis is one of the leading causes of sepsis in pregnancy, complicating about 2% of all pregnancies. The majority (70 to 80%) of cases are caused by *Escherichia coli* while the rest are due to *Klebsiella, Proteus* and *Enterobacter* species.

Pyelonephritis has also been associated with an increased risk of preterm birth, both spontaneous and iatrogenic.

Avoid trimethoprim+sulfamethoxazole (cotrimoxazole) in the first trimester, as its use has been associated with congenital abnormalities (e.g. cardiovascular defects, neural tube defects and orofacial clefts). There is also a theoretical concern that sulfamethoxazole use near term can increase the risk of adverse neonatal outcomes such as jaundice, neonatal kernicterus and haemolytic anaemia.

Asymptomatic bacteriuria in pregnancy

Asymptomatic bacteriuria refers to the presence of uropathogenic bacteria (e.g. *E. coli*) in the urine, in the absence of any symptoms of a UTI.

Screening for asymptomatic bacteriuria during pregnancy is accepted practice in many countries to identify women at increased risk for pyelonephritis later in pregnancy. However, the evidence to support screening is from older and less methodologically robust studies and recent evidence indicates that pregnant women with pyelonephritis who are managed in a timely and appropriate manner are not at increased risk of preterm delivery (the previous rationale for screening).

In these guidelines, screening for asymptomatic bacteriuria in pregnancy is **not** recommended; incidentally detected asymptomatic bacteriuria in pregnancy should also **not** prompt antibiotic treatment.

Acute cystitis and pyelonephritis in pregnancy

Acute cystitis in pregnancy

Use:

cefalexin *500 mg orally, 12-hourly for 7 days*

OR

nitrofurantoin *100 mg orally, 6-hourly for 5 days.*

Avoid nitrofurantoin from week 36 of pregnancy due to an increased risk of neonatal jaundice and haemolytic anaemia.

Acute pyelonephritis in pregnancy

For empirical treatment, use:

gentamicin *IV, 5 mg/kg (7 mg/kg in critical illness), see Table 14 (page 384) for dosing frequency for information on dosing frequency, maximum dose and maximum number of doses*

PLUS

amoxicillin *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, use (as monotherapy):

ceftriaxone *1 g IV, daily.*

cont...

Modify empirical therapy based on the results of culture and susceptibility testing. If susceptibility results are not available by 72 hours and empirical IV therapy is still required, stop the gentamicin-containing regimen and use ceftriaxone.

Switch to oral therapy once the patient is clinically stable (i.e. afebrile, pulse of less than 90 beats per minute). Oral therapy should be based on the results of culture and susceptibility testing. If susceptibility is confirmed, suitable regimens include:

cefalexin *500 mg orally, 6-hourly*

OR

amoxicillin+clavulanate *500+125 mg orally, 8-hourly.*

If culture and susceptibility results are not available, use amoxicillin+clavulanate except in women who also have preterm rupture of membranes (due to an increased risk of neonatal necrotising enterocolitis) or in patients with penicillin hypersensitivity. If neither oral alternative is suitable, seek advice from an obstetrician.

Duration: 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.

Prelabour rupture of membranes

For patients with prelabour rupture of membranes who have a suspected or confirmed intra-amniotic infection (chorioamnionitis), i.e. fever (38°C or more) with other clinical manifestations such as uterine tenderness and purulent amniotic fluid), treat as for chorioamnionitis, see page 193 in this topic.

Preterm prelabour rupture of membranes (PPROM)

PPROM (i.e. membrane rupture before 37 weeks' gestation and before the onset of uterine contractions) is the commonest cause of preterm birth.

Antibiotic prophylaxis for PPROM is significantly associated with reduction in neonatal morbidity, including chorioamnionitis and a reduction in the number of babies born within 48 hours of membrane rupture.

The optimal antibiotic regimen for prophylaxis for PPROM is uncertain[12]. A suitable regimen is:

amoxicillin *2 g IV, 6-hourly for 48 hours, followed by amoxicillin 250 mg orally, 8-hourly for a total of 7 days (IV + oral) or until delivery (whichever is sooner)*

PLUS

erythromycin *250 mg orally, 6-hourly for 7 days or until delivery (whichever is sooner).*

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

By consensus, the preterm viability gestational age in Papua New Guinea is 28 weeks to 36 weeks + 6 days. Any antibiotics prescribed for women with PPROM at any gestational age less than 28 weeks should be only for maternal benefit.

Prolonged prelabour rupture of membranes at term (≥37 weeks)

If chorioamnionitis is diagnosed or suspected, expedite delivery and administer broad-spectrum antibiotics as for chorioamnionitis (see next page).

If the membranes have ruptured for ≥18 hours (prolonged rupture of membranes), commence antibiotic prophylaxis for GBS and induce labour. Use:

benzylpenicillin *3 g IV for the first dose, then 1.8 g IV, 4-hourly until delivery.*

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

cefazolin *2 g IV, 8-hourly until delivery.*

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

clindamycin *600 mg IV, 8-hourly until delivery.*

OR

vancomycin *slow IV infusion until delivery,* ***consider a loading dose in critically ill adults and children****. See 'Appendix 2: Vancomycin dosing' (page 386) for information on loading dose, dosing frequency and infusion time*

adult ≥ 40 years: 15 mg/kg, see Table 18 for dosing frequency (page 390)

adult < 40 years 20 mg/kg, see Table 17 for dosing frequency (page 389).

12 Although some international centres use oral erythromycin as monotherapy, based on a large RCT, the methodology of the study has been criticised; the reduction in neonatal morbidity found with monotherapy may have been due to chance.

Chorioamnionitis

Chorioamnionitis (also known as intra-amniotic infection) is an infection involving the amniotic fluid (liquor), fetal membranes and placenta. It is commonly polymicrobial due to ascending bacteria through the birth canal after rupture of membranes. It is a prominent risk factor for neonatal and maternal sepsis, and presents with fever, uterine tenderness and purulent amniotic fluid.

Women with intra-amniotic infection often present with nonspecific signs of infection. The key criterion is maternal fever after the onset of labour or rupture of membranes without another identifiable source. Suspect intra-amniotic infection in a pregnant woman with fever (38 °C or more) with or without any of the following features:

- uterine tenderness
- purulent amniotic fluid (or clear but offensive amniotic fluid)
- maternal tachycardia >100bpm
- fetal tachycardia >160bpm for ≥10 minutes
- maternal leucocytosis >15

Labour should be induced immediately as soon as the diagnosis of chorioamnionitis is made, regardless of the gestational age.

Ureaplasma species are the most common microorganisms isolated from the amniotic fluid of patients with clinical chorioamnionitis. Note that antibiotics studied in clinical trials do not provide coverage against *Ureaplasma* and *Mycoplasma* species.

Neonates born to mothers with intra-amniotic infection are at increased risk of complications including pneumonia, meningitis and early-onset sepsis. Neonates at risk may require presumptive antibiotic therapy, see **prevention of neonatal sepsis**, page 206 in 'Infections in neonates and young infants.' For a neonate with signs of sepsis, see **sepsis, septic shock and meningitis**, page 199 in 'Infections in neonates and young infants.'

Treatment of chorioamnionitis

Empirical treatment of chorioamnionitis

Induce labour and use:

gentamicin *IV, 5 mg/kg (7 mg/kg in critical illness), see Table 14 (page 384) for dosing frequency for information on dosing frequency, maximum dose and maximum number of doses*

PLUS

amoxicillin *2 g IV, 6-hourly*

PLUS

metronidazole *500 mg IV, 12-hourly.*

If the patient is not improving on initial treatment, switch to:

ceftriaxone *1 g IV, daily*

PLUS

clindamycin *600 mg IV, 8-hourly.*

For patients with hypersensitivity to penicillins, use:

gentamicin *IV, 5 mg/kg (7 mg/kg in critical illness), see Table 14 (page 384) for dosing frequency for information on dosing frequency, maximum dose and maximum number of doses*

PLUS

clindamycin *600 mg IV, 8-hourly.*

Duration

The optimal duration of antibiotic therapy is uncertain; however, delivery is required for resolution of infection.

If there are no features of sepsis following delivery:

- following vaginal delivery, stop antibiotic therapy.
- following caesarean section, give one further dose of each antibiotic started preoperatively.

For patients with ongoing features of sepsis:

- continue treatment until 48 hours after features (e.g. uterine tenderness, offensive lochia and maternal fever) have resolved.

Postpartum endometritis

Postpartum endometritis is an infection of the pregnancy endometrium following delivery which can result in potentially lethal complications such as secondary postpartum haemorrhage, pelvic abscess and septic shock. Always ensuring that the uterine cavity is totally empty following delivery, and immediately commencing antibiotic therapy if infection occurs, are paramount to reducing maternal morbidity and mortality.

Postpartum endometritis can be mild or severe depending on the spread of the infection in the uterus and into the pelvis. Patients present with fever, tachycardia, lower abdominal pain, a tender uterus and offensive vaginal discharge (lochia).

Treatment of postpartum endometritis

Nonsevere postpartum endometritis

Postpartum endometritis is considered nonsevere if the infection is localised and the patient does not have fever or other systemic features.

Use:

amoxicillin *500 mg orally, 8-hourly for 7 days*

PLUS either

metronidazole *400 mg orally, 12-hourly for 7 days*

OR

tinidazole 500 mg orally, 12-hourly for 7 days.

In patients with hypersensitivity to penicillins, replace amoxicillin with:

trimethoprim+sulfamethoxazole *160+800 mg orally, 12-hourly for 7 days.*

Severe postpartum endometritis (puerperal sepsis)

Postpartum endometritis is considered severe if the infection is associated with systemic features, sepsis or septic shock.

Start antibiotic therapy **within 1 hour** of presentation to medical care (or, for ward-based patients, within 1 hour of development of sepsis or septic shock), immediately after taking appropriate specimens for culture.

Use (as a three-drug regimen):

gentamicin *IV, 5 mg/kg (7 mg/kg in critical illness), see Table 14 (page 384) for dosing frequency for information on dosing frequency, maximum dose and maximum number of doses*

PLUS

cont...

amoxicillin *2 g IV, 6-hourly*

PLUS

metronidazole *500 mg IV, 12-hourly.*

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

gentamicin *IV, 5 mg/kg (7 mg/kg in critical illness), see Table 14 (page 384) for dosing frequency for information on dosing frequency, maximum dose and maximum number of doses*

PLUS

cefazolin *2 g IV, 8-hourly*

PLUS

metronidazole *500 mg IV, 12-hourly.*

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

gentamicin *IV, 5 mg/kg (7 mg/kg in critical illness), see Table 14 (page 384) for dosing frequency for information on dosing frequency, maximum dose and maximum number of doses*

PLUS

clindamycin *600 mg IV, 8-hourly.*

If none of the above options are available, as a single agent, use:

chloramphenicol *1 g IV, 6-hourly.*

Duration

For uncomplicated infections, continue intravenous antibiotic therapy for at least 24 to 48 hours after the resolution of leucocytosis and clinical signs and symptoms (i.e. fever, uterine tenderness, purulent vaginal discharge), and then stop antibiotic therapy. Oral antibiotic therapy is not required.

For complicated infection (e.g. abscess, bacteraemia), a longer course of IV therapy may be required followed by a switch to oral therapy once the patient is clinically stable. Select oral antibiotics based on the results of culture and susceptibility testing, if available. If unavailable, use an oral regimen as for nonsevere postpartum endometritis.

Presumptive treatment following fetal death in utero or retained placenta

Provide presumptive treatment for endometritis for the high-risk events/procedures including intrauterine destructive delivery of a fetal death in utero (FDIU), manual removal of a retained placenta and internal podalic version of a FDIU.

Presumptive treatment following fetal death in utero or retained placenta

Use:

gentamicin *IV, 5 mg/kg (7 mg/kg in critical illness), see Table 14 (page 384) for dosing frequency for information on dosing frequency, maximum dose and maximum number of doses*

PLUS

amoxicillin *2 g IV, 6-hourly*

PLUS

metronidazole *500 mg IV, 12-hourly.*

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

gentamicin *IV, 5 mg/kg (7 mg/kg in critical illness), see Table 14 (page 384) for dosing frequency for information on dosing frequency, maximum dose and maximum number of doses*

PLUS

cefazolin *2 g IV, 8-hourly*

PLUS

metronidazole *500 mg IV, 12-hourly.*

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

gentamicin *IV, 5 mg/kg (7 mg/kg in critical illness), see Table 14 (page 384) for dosing frequency for information on dosing frequency, maximum dose and maximum number of doses*

PLUS

clindamycin *600 mg IV, 8-hourly.*

cont...

If none of the above options are available, as a single agent, use:

chloramphenicol *1 g IV, 6-hourly.*

When clinically improved, switch to:

amoxicillin *500 mg orally, 8-hourly*

PLUS

metronidazole *400 mg orally, 12-hourly*

OR

tinidazole 500 mg orally, 12-hourly.

Alternatively, for patients with hypersensitivity to penicillins or if the above regimens are unavailable, as a single agent, use:

chloramphenicol *500 mg orally, 6-hourly.*

Duration: complete a total duration of 7 days (IV + oral).

Key additional references

Ely JW, Rijhsinghani A, Bowdler NC, Dawson JD. The association between manual removal of the placenta and postpartum endometritis following vaginal delivery. Obstet Gynecol 1995;86: 1002-6.

Kazemier BM, Koningstein FN, Schneeberger C, Ott A, Bossuyt PM, de Miranda E, Vogelvang TE, Verhoeven CJ, Langenveld J, Woiski M, Oudijk MA, van der Ven JE, Vlegels MT, Kuiper PN, Feiertag N, Pajkrt E, de Groot CJ, Mol BW, Geerlings SE. Maternal and neonatal consequences of treated and untreated asymptomatic bacteriuria in pregnancy: a prospective cohort study with an embedded randomised controlled trial. Lancet Infect Dis. 2015 Nov;15(11):1324-33.

Kenyon S, Boulvain M, Neilson JP. Antibiotics for preterm rupture of membranes. Cochrane Database Syst Rev. 2013 Dec 2;(12):CD001058.

Kenyon SL, Taylor DJ, Tarnow-Mordi W, Group OC. Broad-spectrum antibiotics for preterm, prelabour rupture of fetal membranes: the ORACLE I randomised trial. ORACLE Collaborative Group. Lancet 2001;357(9261):979-88.

Mercer BM, Miodovnik M, Thurnau GR, et al. Antibiotic Therapy for Reduction of Infant Morbidity After Preterm Premature Rupture of the Membranes: A Randomized Controlled Trial. *JAMA.* 1997;278(12):989–995.

Morgan J, Roberts S. Maternal sepsis. Obstet Gynecol Clin North Am. 2013 Mar;40(1):69-87.

Smail FM, Vazquez JC. Antibiotics for asymptomatic bacteriuria in pregnancy. Cochrane Database Syst Rev 2019; (8): CD 000490.

Infections in neonates and young infants

This topic includes advice on the management of the following conditions in neonates and infants younger than 3 months of age:

- **sepsis, septic shock and meningitis**, page 199
  - early-onset sepsis (with and without meningitis), page 202
  - late-onset sepsis (with and without meningitis), page 203
  - directed therapy for meningitis, page 206
- **prevention of neonatal sepsis**, page 206
- **septic arthritis**, page 207
- **necrotising enterocolitis**, page 208
- **oral candidiasis** (thrush), page 210
- **skin pustules** in neonates, page 210
- **mastitis and breast abscess** in neonates, page 211
- **conjunctivitis** in neonates, page 212
- **management of neonates born to mothers with specific infections**, page 213: gonorrhoea, chlamydia and syphilis (page 214), herpes simplex virus (page 215), varicella-zoster virus (page 216) and hepatitis B (page 217)
- other conditions: **tetanus in neonates** (prophylaxis), **neonatal/congenital tuberculosis, malaria** in neonates, page 218.

The following topic is not included in this section:

- **bronchiolitis** (page 243) in 'Respiratory tract infections.'

In these guidelines, the following definitions are used:

- term neonates: gestational age 37 weeks or older
- preterm neonates: gestational age younger than 37 weeks.

Sepsis, septic shock and meningitis in neonates and young infants

Overview

Neonatal sepsis has a high risk of morbidity and mortality. Prompt recognition and treatment of these syndromes is vital because appropriate resuscitation and organ support, together with rapid initiation of antibiotic therapy, reduces mortality.

The clinical features of sepsis or septic shock in neonates may be nonspecific. As infection is the most likely cause of an unwell neonate or young infant, it is usually appropriate to start antibiotics after taking blood and other relevant specimens for culture. Antibiotic therapy is then modified or stopped based on clinical progress, microbiology and other laboratory investigations.

Empirical antibiotic regimens vary depending on the age of the infant and whether meningitis is suspected or confirmed.

Meningitis

Meningitis must be considered in neonates and young infants being treated for sepsis or septic shock as symptoms and clinical signs in young infants may be subtle and nonspecific. Possible symptoms include fever, temperature instability, poor feeding, hyper- or hypotonia, lethargy, irritability, vomiting or a bulging fontanelle. Neck stiffness may not be present.

The most likely pathogens are *Streptococcus agalactiae* (group B streptococcus [GBS]), enteric Gram-negative bacilli or, rarely, and generally only in children up to 1 month of age, *Listeria monocytogenes*.

Treat as for sepsis or septic shock, using the regimens for infants with clinically/CSF confirmed meningitis. Dexamethasone is not indicated in neonates (up to 3 months of age) because there is insufficient evidence to support its use.

Herpes simplex virus infection as a potential cause of neonatal sepsis

Herpes simplex virus (HSV) is an important cause of neonatal illness. Consider HSV in neonates born to mothers with active genital HSV infection at delivery or with any of the features listed in Box 2 below.

Box 2: Symptoms or signs of herpes simplex virus (HSV) disease in neonates

- vesicular or atypical pustular or bullous lesions, especially on the presenting part (note: may be absent)
- seizures
- unexplained sepsis with negative blood cultures not responding to antibiotics
- elevated liver function tests
- disseminated intravascular coagulopathy (DIC)
- respiratory distress (after day 1 of life)
- corneal ulcer or keratitis.

Source: Palasanthiran P, Starr M, Jones C, Giles M, editors. Management of perinatal infections. Sydney: Australasian Society for Infectious Diseases; 2022.

Management of sepsis, septic shock and meningitis

Collect blood samples, as well as appropriate samples from sites considered to be a potential source of infection; specimen collection should not be a delay to administering intravenous fluid and antibiotics. There should be a high suspicion of meningitis and a lumbar puncture is usually required – where possible, seek advice from a senior clinician before performing a lumbar puncture.

Start therapy (resuscitation and antibiotics) within 1 hour of presentation to a health facility.

Treatment can be given intravenously or through intraosseous access. If intravenous or intraosseous access cannot be rapidly established (e.g. within 15 minutes), the initial dose of antimicrobial therapy can be administered **intramuscularly** for the following antimicrobials: benzylpenicillin, cefotaxime, ceftriaxone and gentamicin. Aciclovir and vancomycin are **not** suitable for intramuscular administration.

Empirical regimens for sepsis, septic shock and meningitis

Empirical antibiotic regimens for neonates and infants younger than 3 months with sepsis or septic shock vary depending on:

- the age of the infant or neonate
- whether or not meningitis is suspected or confirmed (usually by lumbar puncture)
- whether or not encephalitis is suspected.

Empirical regimens are intended for initial therapy only – modify as soon as additional information is available (e.g. source of infection; results of Gram stain and/or CSF examination, culture and susceptibility testing).

Early-onset sepsis or septic shock in neonates

These recommendations apply to neonates with sepsis or septic shock occurring **within 72 hours of birth**.

The causative organisms are most commonly acquired from mothers (e.g. GBS, *Escherichia coli*, HSV, *L. monocytogenes*).

Treatment for early-onset sepsis Select the antimicrobial regimen based on whether or not meningitis is suspected or confirmed. For information on duration of therapy, see **duration of treatment early- and late-onset sepsis or septic shock with or without meningitis**, page 205 in this topic.	
Neonates with early-onset sepsis or septic shock **without** meningitis	Use (doses for up to 7 days of life): ***gentamicin*** *5 mg/kg IV* *gestational age < 30 weeks: 48-hourly* *gestational age 30 to 34 weeks: 36-hourly* *gestational age ≥ 35 weeks: 24-hourly* *PLUS* ***benzylpenicillin*** *60 mg/kg IV, 12-hourly.*
Neonates with early-onset sepsis or septic shock **with** meningitis (clinically suspected or confirmed by lumbar puncture),	Use (doses for up to 7 days of life): ***cefotaxime*** *50 mg/kg IV* *preterm neonates: 12-hourly* *0 to 7 days of life: 8-hourly* *PLUS* ***benzylpenicillin*** *90 mg/kg IV* *preterm neonates 0 to7 days of life: 12-hourly* *preterm neonates from 8 days of life: 8-hourly* *term neonates from first day of life: 8-hourly.* Alternatively, if cefotaxime is not available, use: ***ceftriaxone*** *50 mg/kg IV, 12-hourly.*
Neonates at risk of HSV infection	For neonates born to a mother with active genital HSV infection at delivery or with any of the features listed in Box 2 (page 200) **add** aciclovir to any of the above regimens. Use: *aciclovir 20 mg/kg IV, 8-hourly* ***for 21 days***.

Late-onset sepsis or septic shock in neonates

These recommendations apply to neonates with sepsis or septic shock occurring **more than** 72 hours after birth.

The causative organisms may be acquired from mother or from the caregiving environment, and include GBS *E. coli* and other Gram-negative bacteria, HSV, *Staphylococcus aureus*, coagulase-negative staphylococci and *L. monocytogenes*).

Treatment for late-onset sepsis

Select the antimicrobial regimen based on whether or not meningitis is suspected or confirmed.

For information on duration of therapy, see **Duration of treatment early- and late-onset sepsis or septic shock with or without meningitis**, page 205 in this topic.

Neonates with late-onset sepsis or septic shock **without** meningitis	Use: ***gentamicin*** *5 mg/kg IV* *gestational age < 30 weeks* *0 to 14 days of life: 48-hourly* *15 or more days of life: 36-hourly* *gestational age 30 to 34 weeks* *0 to 10 days of life: 36-hourly* *11 or more days of life: 24-hourly* *gestational age ≥ 35 weeks: 24-hourly* *PLUS* ***flucloxacillin*** *50 mg/kg IV* *0 to 7 days of life: 12-hourly* *8 to 28 days of life: 8-hourly* *from 29 days of life: 6-hourly.*

Neonates with late-onset sepsis or septic shock **with** meningitis (clinically suspected or confirmed by lumbar puncture)	Use: ***cefotaxime*** *50 mg/kg IV* *preterm neonates: 12-hourly* *0 to 7 days of life: 8-hourly* *8 to 28 days of life: 6-hourly* *from 29 days of life: 4 to 6-hourly* *PLUS EITHER* ***benzylpenicillin*** *90 mg/kg IV* *preterm neonates 0 to7 days of life: 12-hourly* *preterm neonates from 8 days of life: 8-hourly* *term neonates from first day of life: 8-hourly.* OR ***amoxicillin*** *100 mg/kg IV* *0 to 7 days of life: 12-hourly* *8 to 28 days of life: 8-hourly* *from 29 days of life: 6-hourly.* Alternatively, if cefotaxime is not available, use: ***ceftriaxone*** *50 mg/kg IV, 12-hourly.*
For infants who are deteriorating or not improving after 48 to 72 hours of treatment (despite adequate source control) or for infants initially presenting with severe sepsis, provide cover for potential MRSA	**Add** vancomycin to any of the above regimens. Use: ***vancomycin*** *IV, calculate dose using the* **Vancomycin intermittent dosing calculator for infants aged 0-90 days***: www.kidscalc.org/van-dose-calc/* *if unable to use the calculator, see Table 19 (page 391) in 'Appendix 2: Vancomycin dosing' for further advice.*
For infants born to a mother with active genital HSV infection at delivery or with signs or symptoms of HSV disease (see Box 2, page 200 in this topic)	**Add** aciclovir to either of the above regimens, use: *aciclovir 20 mg/kg IV, 8-hourly* ***for 21 days****.*

Duration of treatment (early- and late-onset sepsis or septic shock with or without meningitis)

The duration of antibiotic treatment depends upon the clinical condition of the infant and the results of culture and susceptibility testing.

Sepsis without meningitis

Where the likelihood of infection is low, i.e. well infants with negative infective indices, stop antibiotics if the results of culture are negative after 48 hours.

If sepsis or septic shock is strongly suspected, despite negative blood culture at 48 hours, take repeat bloods for culture and continue antibiotics for at least 5 days or for 48 hours after indices are normal.

For **proven Gram-negative bacteraemia** with clear cerebrospinal fluid (CSF), treat for 10 days. Modify antibiotic therapy based on the results of culture and sensitivity testing.

For **proven GBS bacteraemia** with clear CSF, 10 days of antibiotic therapy should be sufficient.

Meningitis

Direct therapy based on the results of culture and sensitivity testing (see the next section for regimens).

If unable to perform a lumbar puncture and/or obtain the results of culture and susceptibility testing, stop treatment after 14 days if the infant is clinically well.

Suspected HSV disease

The duration of treatment is guided by expert advice; it depends on the clinical presentation and investigation results. For infants with disseminated disease or encephalitis, the treatment duration is at least 21 days of intravenous therapy. For infants with disease affecting the skin, eyes and mouth, see HSV prophylaxis/ treatment, page 215 in this topic.

Directed therapy for meningitis (organism and susceptibility known)

Group B streptococcus (GBS)

Use:

benzylpenicillin *90 mg/kg IV,* ***for 14 to 21 days***

preterm neonates 0 to7 days of life: 12-hourly
preterm neonates from 8 days of life: 8-hourly
term neonates from first day of life: 8-hourly.

Listeria

Use:

benzylpenicillin *90 mg/kg IV,* ***for 21 days***

preterm neonates 0 to7 days of life: 12-hourly
preterm neonates from 8 days of life: 8-hourly
term neonates from first day of life: 8-hourly

OR

amoxicillin *100 mg/kg IV,* ***for 21 days***

0 to 7 days of life: 12-hourly
8 to 28 days of life: 8-hourly
from 29 days of life: 6-hourly.

Prevention of neonatal sepsis

Early infections (those presenting in the first 3 days after birth) are often associated with obstetric risk factors for infection.

As symptoms of neonatal sepsis may be nonspecific, give antibiotics to well infants who are born to mothers with any of the following obstetric risk factors for infection to prevent complications of early-onset neonatal sepsis:

- babies born before arrival (BBA)
- rupture of membranes > 12 hours
- purulent amniotic fluid (liquor)
- maternal chorioamnionitis, fever or sepsis
- maternal history of a previous neonatal death from sepsis.

Prophylactic antibiotics for a neonate with obstetric risk factors for infection

If fever or other systemic symptoms are present, take blood specimens for culture (and perform lumbar puncture if indicated) and **treat as sepsis**.

Take specimens for culture before starting antibiotics, then use:

gentamicin *5 mg/kg IV*

gestational age < 30 weeks

0 to 14 days of life: 48-hourly

15 or more days of life: 36-hourly

gestational age 30 to 34 weeks

0 to 10 days of life: 36-hourly

11 or more days of life: 24-hourly

gestational age ≥ 35 weeks: 24-hourly

PLUS

amoxicillin *50 mg/kg IV*

0 to 7 days of life: 12-hourly

8 to 28 days of life: 8-hourly

from 29 days of life: 4 to 6-hourly.

Duration: Treat for 2 to 5 days.

Septic arthritis

Septic arthritis in neonates is an emergency and requires urgent drainage.

The presentation of septic arthritis in neonates may be similar to undifferentiated sepsis. Likely pathogens in neonates are GBS, *Hemophilus influenzae, Staphylococcus aureus* and Gram-negative enteric bacilli such as *Escherichia coli*.

Management of septic arthritis

Use:

cefotaxime *50 mg/kg IV*

preterm neonates: 12-hourly

term neonates 0 to 7 days of life: 8-hourly

cont...

term neonates 8 to 28 days of life: 6-hourly

term neonates from 29 days of life: 4- to 6-hourly

PLUS

flucloxacillin *50 mg/kg IV*

0 to 7 days of life: 12-hourly

8 to 28 days of life: 8-hourly

from 29 days of life: 6-hourly.

If methicillin-resistant S. *aureus* (MRSA) is identified, switch to IV vancomycin as a single agent:

vancomycin *IV, calculate dose using the* **Vancomycin intermittent dosing calculator for infants aged 0-90 days***: www.kidscalc.org/van-dose-calc/*

if unable to use the calculator, see Table 19 (page 391) in 'Appendix 2: Vancomycin dosing' for further advice.

Duration

Treat acute infections for 3 weeks with IV antibiotics. A longer duration is required for chronic infections, seek appropriate advice.

Necrotising enterocolitis

Necrotising enterocolitis (NEC) is an infection that occurs when sections of neonatal bowel die. It is the most common gastrointestinal emergency in neonates and is associated with high rates of mortality.

The most important risk factors are prematurity and low birthweight, although it may also occur in term neonates. Other risk factors include enteral feeding (although cases may occur in infants who have never been enterally fed) and it is more likely in low birthweight formula-fed infants.

Clinical signs and symptoms of NEC are highly variable but include abdominal distention or tenderness, feed intolerance (evidenced by vomit containing bile or bile-stained fluid in the nasogastric tube) or bloody stools. General signs of systemic illness include apnoea, drowsiness or unconsciousness, fever or hypothermia. There is often an abnormal white cell count and thrombocytopaenia.

Bowel rest and antibiotics are important components of treatment of this condition. Antibiotics target enteric organisms including Gram-positive, Gram-negative and anaerobic pathogens.

Early or suspected NEC is difficult to diagnose. If in doubt, treat early and conservatively (nil by mouth and broad-spectrum antibiotics).

Management of NEC

Stop enteral feeds and use a nasogastric tube for free drainage.

Send blood for culture before starting antibiotics, then use:

gentamicin *5 mg/kg IV*

gestational age < 30 weeks

0 to 14 days of life: 48-hourly

15 or more days of life: 36-hourly

gestational age 30 to 34 weeks

0 to 10 days of life: 36-hourly

11 or more days of life: 24-hourly

gestational age ≥ 35 weeks: 24-hourly

PLUS

amoxicillin *50 mg/kg IV*

0 to 7 days of life: 12-hourly

8 to 28 days of life: 8-hourly

from 29 days of life: 4 to 6-hourly

PLUS

metronidazole *7.5 mg/kg IV*

0 to 28 days of life: 12-hourly

from 29 days of life: 8-hourly.

For infants who are not improving after 48 to 72 hours of treatment and if results of culture and susceptibility testing are unavailable, ensure blood cultures are taken and (while awaiting results), use:

meropenem *40 mg/kg IV, 8-hourly*

PLUS

vancomycin *IV, calculate dose using the* **Vancomycin intermittent dosing calculator for infants aged 0-90 days***: www.kidscalc.org/van-dose-calc/*

if unable to use the calculator, see Table 19 (page 391) in Appendix 2: Vancomycin dosing for further advice.

Duration: Treat for 7 to 10 days

Oral candidiasis (thrush)

Treatment of oral candidiasis (thrush)

Use:

nystatin liquid 100 000 units/mL 1 mL applied topically to the inside of the infant's mouth, ***4*** *times daily for 7 to 10 days.*

If not improving, switch to:

fluconazole 3 mg/kg orally, daily until symptoms have resolved (usually 7 days).

If the mother is breastfeeding, treat the mother's breasts with:

miconazole 2% cream topically twice per day; continue for 2 weeks after symptoms resolution.

Oral candidiasis (thrush) prophylaxis

Give prophylaxis to neonates with any of the following:

- < 32 weeks corrected gestational age
- receiving antibiotics for > 7 days
- on continuous positive airway pressure (CPAP).

Use:

nystatin liquid 100 000 units/mL 1 mL applied topically to the inside of the infant's mouth, ***3*** *times daily.*

Continue until tolerating full enteral feeds and (if on antibiotics) for 48 hours after stopping antibiotics.

Skin pustules in neonates and young infants

Consider noninfective causes such as miliaria and erythema toxicum neonatorum, which do **not** require antibiotic treatment.

Skin infections in neonates are usually caused by *Staphylococcus aureus*. However, consider HSV infection in neonates with vesicular, atypical pustular or bullous lesions or any other features in (see Box 2, page 200 in this topic).

If fever or other systemic symptoms are present, take blood for culture and susceptibility testing (and lumbar puncture if indicated), and treat as early- or late-onset sepsis as appropriate; see page 199 in this topic.

Management of skin pustules (without systemic symptoms)

Take pus swabs for culture.

Wash the infant's skin with soap and water, dry skin and clean it with an antiseptic solution. Rupture and drainage of pustules is not usually required.

Use:

flucloxacillin *25 mg/kg orally or IV, for 5 to 7 days*

0 to 7 days of life: 12-hourly

8 to 28 days of life: 6-hourly

from 29 days of life: 4-hourly.

If methicillin-resistant *S. aureus* is identified in cultures, switch to IV vancomycin as a single agent. Use:

vancomycin *IV, calculate dose using the* **Vancomycin intermittent dosing calculator for infants aged 0-90 days***: www.kidscalc.org/van-dose-calc/*

if unable to use the calculator, see Table 19 (page 391) in Appendix 2: Vancomycin dosing for further advice.

If herpes simplex is suspected (see Box 2, page 200 in this topic), **add** to the above:

aciclovir 20 mg/kg IV, 8-hourly for 14 days.

Mastitis and breast abscess

Mastitis and breast abscess in neonates and young infants may present as redness and swelling. Surgical drainage is needed for an abscess.

For lactational mastitis in mothers, see **lactational mastitis**, page 313 in 'Soft tissue infections.'

Management of mastitis and breast abscess

Use:

flucloxacillin *50 mg/kg IV*

0 to 7 days of life: 12-hourly

8 to 28 days of life: 8-hourly

from 29 days of life: 6-hourly.

cont...

If there is no improvement after 48 to 72 hours of treatment, **add** vancomycin to cover potential methicillin-resistant *Staphylococcus aureus* (MRSA). Use:

> ***vancomycin*** *IV, calculate dose using the* **Vancomycin intermittent dosing calculator for infants aged 0 to 90 days***: www.kidscalc.org/van-dose-calc/*
>
> *if unable to use the calculator, see Table 19 (page 391) in Appendix 2: Vancomycin dosing for further advice.*

If MRSA is identified in cultures, switch to IV vancomycin as a single agent.

Duration

Stop antibiotics when clinically improved. The usual duration of treatment is 5 to 7 days; however, if systemic symptoms resolve rapidly following drainage, a shorter course may be sufficient.

Conjunctivitis in neonates

Neonatal conjunctivitis or ophthalmia neonatorum refers to conjunctivitis occurring within the first 28 days of life. It may have a bacterial, viral or chemical cause. Chemical conjunctivitis typically results from the use of topical prophylactic agents shortly after birth; redness and discharge are usually mild and resolve without treatment. Neonatal eye discharge can also be associated with a blocked tear duct.

Infectious conjunctivitis can lead to permanent blindness and disseminated infection which may be life-threatening.

Organisms associated with infectious neonatal conjunctivitis are commonly transferred to the baby during delivery. They include bacteria e.g. *Chlamydia trachomatis* and *Neisseria gonorrhoeae* and viruses e.g. HSV. Gonococcal conjunctivitis in neonates usually presents in the first 2 weeks of life with sudden, severe, grossly purulent conjunctivitis. It can rapidly lead to perforation of the globe and blindness. Gonococcal ophthalmia neonatorum is preventable with the use of prophylactic antibiotics for infants born to mothers with confirmed gonococcal infection – see next section.

Management of gonococcal conjunctivitis in neonates (gonococcal ophthalmia neonatorum)

Urgent review by an ophthalmologist is required.

Send a swab for culture.

Irrigate the eye with saline several times daily until purulence subsides.

Topical antibiotics alone are insufficient. For systemic treatment, use (as a two-drug regimen):

cefotaxime *100 mg/kg IM or IV, as a single dose*

OR

ceftriaxone *50 mg/kg IM or IV, as a single dose*

PLUS (with either of the above)

azithromycin *20 mg/kg orally, daily for 3 days.*

Exclude disseminated gonococcal infection by careful physical examination. Disseminated disease may present as sepsis, arthritis, meningitis or skin abscesses.

If disseminated disease is suspected, send blood for culture, and cerebrospinal fluid and/or synovial fluid specimens if clinically indicated.

If there is evidence of disseminated gonococcal disease, give:

cefotaxime *50 mg/kg IV, for 10 days*

preterm neonates: 12-hourly

0 to 7 days of life: 8-hourly

8 to 28 days of life: 6-hourly

from 29 days of life: 4 to 6-hourly.

If cefotaxime is not available, use:

ceftriaxone *50 mg/kg IV, daily for 10 days.*

The infant's mother and their sexual contacts should also be treated; see 'Genital and sexually transmissible infections,' page 159.

Management of neonates born to mothers with specific infections

Prophylaxis or treatment is indicated for neonates born to mothers with specific infections. For infants born to mothers with HIV, see *National Guidelines for HIV Care and Treatment.*

Neonatal gonorrhoea prophylaxis

If the mother is successfully treated prior to delivery, no prophylaxis is required for the neonate. If the mother has not been treated, the risk of vertical transmission is 30 to 40%.

A single dose of ceftriaxone provides effective prophylaxis for the neonate. Give:

ceftriaxone *50 mg/kg IV/IM, as a single dose.*

Treat the mother of the infected neonate and their sexual contacts – see 'Genital and sexually transmissible infections,' page 159.

Monitor for active infection, and if this occurs treat as for gonococcal ophthalmia neonatorum.

Neonatal chlamydia prophylaxis

If the mother has an active chlamydial infection that has not been treated, the risk of the neonate developing chlamydial conjunctivitis is 20 to 50%, and the risk of chlamydial pneumonia is 5 to 10%.

Prophylactic antibiotics are not effective at preventing chlamydial conjunctivitis or pneumonia in neonates.

Treat the mother of the infected neonate and their sexual contacts – see 'Genital and sexually transmissible infections,' page 159.

Families should be advised to monitor infants for signs of conjunctivitis or pneumonia and, if signs occur, present for treatment early.

Neonatal syphilis prophylaxis/treatment

Infants born to mothers with syphilis should be assessed for clinical evidence of congenital syphilis. The risk of transmission from mothers with early syphilis is 40 to 90% and with late syphilis is < 10%. Symptoms and signs of congenital syphilis may include growth restriction, respiratory distress, rash (palms/soles), mucosal lesions, anaemia, jaundice, hepatosplenomegaly, nasal discharge, bony tenderness or periostitis on X-ray.

Send a serum specimen for nontreponemal testing (Venereal Disease Research Laboratory [VDRL], rapid plasma reagin [RPR] test). If the baby's nontreponemal titre is four-fold higher than the maternal titre, congenital syphilis is highly likely.

Consider lumbar puncture in all neonates with possible congenital syphilis.

For asymptomatic neonates born to mothers with confirmed syphilis (even if treated during pregnancy), use:

benzathine benzylpenicillin *50 000 units/kg IM, as a single dose.*

For infants with probable congenital syphilis (i.e. clinical evidence of syphilis and/or nontreponemal test four-fold higher than the maternal titre), use:

benzylpenicillin *30 mg/kg IV*

0 to 7 days of life: 12-hourly

8 to 28 days of life: 6-hourly

from 29 days of life: 4-hourly.

For an infant with normal physical examination and nontreponemal test less than four-fold the maternal titre if the mother was not treated, was inadequately treated, or has evidence of reinfection or relapse, consider treating as probable congenital syphilis.

Treat the mother and their sexual contacts – see 'Genital and sexually transmissible infections,' page 159.

Duration:

Neonates with suspected or confirmed congenital syphilis (including central nervous system [CNS] disease): treat for 14 days.

Repeat nontreponemal testing in all infants born to mothers with confirmed syphilis every 2 to 3 months until this becomes nonreactive or the titre has decreased four-fold. If this fails to decline or increases after 6 to 12 months, perform a lumbar puncture and repeat the 14-day treatment course.

Herpes simplex virus (HSV) prophylaxis/treatment

Give prophylaxis to asymptomatic infants born to mothers with a first episode of genital herpes around the time of delivery as they have a high risk (approximately 30%) of neonatal herpes disease.

Infants who become infected have a high risk (~30%) of severe, disseminated or CNS disease.

Perform a lumbar puncture for HSV testing, if available.

For both asymptomatic infants and the initial treatment for symptomatic infants, use:

aciclovir 20 mg/kg IV

gestational age < 30 weeks: 12-hourly

gestational age from 30 weeks: 8-hourly.

If IV aciclovir is unavailable, use oral aciclovir, even though oral aciclovir is not well absorbed. Use:

aciclovir 20 mg/kg orally, 5 times daily.

For suppressive therapy in symptomatic neonates after completing initial treatment, use:

aciclovir 20 mg/kg orally, 8-hourly.

Duration

Prophylaxis in asymptomatic neonates: treat for 10 days.

Initial treatment for neonates with disease affecting the skin, eyes or mouth: treat for 14 days.

Initial treatment for neonates with disseminated or CNS disease: treat for at least 21 days.

For suppressive therapy: continue for 6 months.

Varicella-zoster virus prophylaxis/treatment

Neonatal chickenpox is life-threatening, with an estimated case fatality rate of up to 30%. Features may include fever, vesicular rash, pneumonia, meningoencephalitis and hepatitis.

Isolate the infected neonate from other infants and use contact precautions.

The highest risk of neonatal chickenpox occurs when infants are born to mothers who have their first episode of chickenpox from 7 days before to 28 days after delivery. Horizontal transmission can also occur from other household members to an infant born to a mother with no prior history of chickenpox.

For symptomatic neonates, use:

aciclovir 20 mg/kg IV

gestational age < 30 weeks: 12-hourly

gestational age from 30 weeks: 8-hourly.

If IV aciclovir is unavailable, give oral aciclovir (even though it is not well absorbed), use:

aciclovir 20 mg/kg orally, 5 times daily.

Duration: Treat symptomatic neonates for 10 days

Hepatitis B

Hepatitis B transmission from mother-to-child is common in untreated mothers with hepatitis B e-antigen in the absence of vaccination (up to 90%). Birth dose hepatitis B vaccination prevents approximately 75% of transmission, while the addition of hepatitis B immunoglobulin may improve protection against transmission by approximately 90%.

Mothers with hepatitis B should be encouraged to breastfeed.

For infants born to a mother who is hepatitis B e-antigen positive, use:

hepatitis B vaccine IM, as soon as possible after birth, preferably within 12 hours of delivery

AND

hepatitis B immunoglobulin 100 units IM, as a single dose (if available).

Followed by the **full hepatitis B vaccination regimen**; see the latest childhood immunisation schedule.

Infants with low birthweight (< 2 kg) do not respond as well to the vaccine. Consider a booster of hepatitis B vaccine at 12 months in addition to the usual regimen.

Infants born to mothers with hepatitis B should be prioritised for administration of the hepatitis B vaccine, if vaccine supplies are limited.

Other conditions

Tetanus in neonates

Tetanus is caused by toxigenic strains of the bacterium *Clostridium tetani*, which is found in soil and dust. In neonates, tetanus infection is most often associated with cutting the umbilical cord with a non-sterile implement.

Pregnant women and their newborn infants are protected from tetanus if the mother is fully vaccinated against tetanus either before or during pregnancy. The majority of reported tetanus cases in neonates are birth-associated among newborn infants whose mothers who have not been sufficiently vaccinated with a tetanus-toxoid-containing vaccine.

Ensure routine cord care with twice-daily chlorhexidine application.

The diagnosis is clinical since laboratory testing for tetanus is not available in Papua New Guinea. For neonates or young infants with suspected tetanus infection, see *Paediatrics for Doctors in Papua New Guinea*.

Tetanus prophylaxis
For neonates at risk of tetanus, e.g. babies BBA if the cord was cut with a non-sterile implement, give tetanus immunoglobulin. If immunoglobulin can be given within 24 hours of exposure, use: *tetanus immunoglobulin 250 units IM, as a single dose.* If it has been more than 24 hours since exposure, use: *tetanus immunoglobulin 500 units IM, as a single dose.*

Neonatal/congenital tuberculosis (TB)

Congenital and perinatal TB transmission occurs rarely, but the associated mortality when transmission does occur is high (approximately 50%).

Refer any neonate with suspected or confirmed neonatal or congenital TB, or a neonate born to a mother with confirmed TB, to the paediatric TB team. For more information, see *Standard Treatment for Common Illnesses of Children in Papua New Guinea* and *National Tuberculosis Management Protocol*.

Malaria in neonates

For neonates with suspected or confirmed malaria, see the *Standard Treatment for Common Illnesses of Children in Papua New Guinea.*

Key additional references

Intrapartum care for women with existing medical conditions or obstetric complications and their babies (2023). NICE guideline 121. National Institute for Clinical Excellence. Available at: https://www.nice.org.uk/guidance/ng121

Palasanthiran P, Starr M, Jones C, Giles M, editors. Management of perinatal infections. Sydney: Australasian Society for Infectious Diseases; 2022. https://asid.net.au/publications.

Sepsis in neonates. Safer Care Victoria. Victorian Government, Melbourne. October 2017. Available at Safer Care Victoria <www.safercare.vic.gov.au

Respiratory tract infections

This topic includes advice on the management of the following conditions in adults and children older than 3 months:

- **community-acquired pneumonia** (CAP)
  - CAP in children, page 221
  - CAP in adults, page 225
- **hospital-acquired pneumonia** (HAP) including ventilator-associated pneumonia (VAP) and aspiration pneumonia, page 232
- **lung abscess and empyema**, page 235
  - lung abscess or empyema in adults, page 236
  - lung abscess or empyema in children, page 238
- **bronchiectasis - acute exacerbation**, page 239
- **acute exacerbation of chronic obstructive pulmonary disease**, page 241
- **pertussis** (whooping cough), page 242
- **other respiratory tract infections** including acute exacerbation of asthma, acute bronchitis and acute bronchiolitis, page 243.

Community-acquired pneumonia

Community-acquired pneumonia (CAP) in children

For management of infections in infants < 3 months, see 'Infections in neonates and young infants,' page 199.

Pneumonia is an acute inflammation of the lung parenchyma, usually caused by viral or bacterial infection. Children typically present with cough, difficulty breathing and fever. Clinical signs include bronchial breath sounds, chest indrawing (subcostal indrawing) and focal crackles.

In infants < 12 months, bronchiolitis is a more common cause of fast breathing and respiratory distress than pneumonia, see page 243 in this topic.

Take blood for culture and susceptibility testing prior to antibiotics in patients who are systemically unwell.

If cough has been present for more than 3 weeks, if there is associated weight loss or a known tuberculosis (TB) contact, consider TB in the differential diagnosis.

Moderate pneumonia in children is associated with fast breathing and chest indrawing while severe pneumonia is associated with grunting, chest indrawing, oxygen saturation < 90% or danger signs including inability to feed, lethargy or convulsions.

Fast breathing in children is defined as:

- age 0 to 2 months respiratory rate ≥ 60 breaths per minute
- age 2 to 12 months respiratory rate > 50 breaths per minute
- age > 12 months respiratory rate > 40 breaths per minute.

See **adults with severe CAP who do not improve on initial empirical therapy**, page 230 for information on when to suspect *Staphylococcus aureus* infection.

Infants may present with life-threatening severe pneumonia due to pertussis without a typical prodrome. Treat **all** infants (aged 12 months or younger) with severe CAP presumptively for pertussis with azithromycin (or clarithromycin), unless pertussis can be ruled out with polymerase chain reaction (PCR) testing.

Managing poor response to treatment

Most children with pneumonia will respond to first-line treatment within 48 hours, and clinical signs of improvement relative to initial presentation may include resolution of fever, less respiratory distress such as chest indrawing, improved oxygen saturation and improved feeding. Cough and fast breathing often persist beyond 48 hours even when there is a treatment response.

If the child is not improving or is deteriorating, consider alternative causes, such as:

- viral pneumonia – common and often associated with wheeze in infants or young children; may have an undulating rather than progressive clinical course, and the child may be systemically well
- staphylococcal pneumonia – progressive and systemically unwell
- empyema (see page 235) – may require drainage and antistaphylococcal treatment
- atypical pneumonia due to pathogens such as *Mycoplasma* or *Chlamydia* species – persistent symptoms, especially common in school-aged children
- tuberculosis - can present as acute pneumonia, especially in infants who are a TB contact or who are malnourished
- *Pneumocystis jirovecii* pneumonia – usually human immunodeficiency virus (HIV)-exposed young infants (2 to 6 months) with severe respiratory distress
- causes other than pneumonia, such as cardiac disease or cardiac failure.

A chest X-ray is not indicated at initial presentation for a child with CAP. However, chest X-ray is useful in a child with pneumonia when there is poor response to first-line antibiotics.

Classification of the severity of pneumonia in children

Table 8: Classification of the severity of pneumonia in children

Sign or symptom	Classification	Management
Cough or difficulty in breathing with: • oxygen saturation < 90% or central cyanosis • severe respiratory distress (e.g. grunting, very severe chest indrawing) • 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 (see next section) • Treat high fever if present
Fast breathing: • ≥ 50 breaths per minute in a child aged 3 to 11 months • ≥ 40 breaths per minute in a child aged 1 to 5 years. Chest indrawing	**Pneumonia**	• Home care • Give recommended antibiotic regimen (see next section) • Advise the carer to return immediately if there are 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 e.g. paracetamol • Advise the mother when to return • Follow up after 5 days if not improving • If coughing for more than 14 days, seek advice from a paediatrician.

Reproduced with permission from Pocket Book of Hospital Care for Children. Second edition, 2013. Geneva; World Health Organization.

Antibiotic therapy for pneumonia in children

Nonsevere CAP in children

Use:

amoxicillin *40 mg/kg up to 1 g orally, 12-hourly for 3 days*

OR

clarithromycin *7.5 mg/kg up to 500 mg orally, 12-hourly for 3 days*

OR

azithromycin *10 mg/kg up to 500 mg orally, daily for 3 days.*

Give the first dose at the clinic and teach carer how to give the other doses at home.

Severe CAP in children

Use:

benzylpenicillin *50 mg/kg up to 1.2 g IV, 6-hourly*

PLUS

gentamicin *IV, child 3 months and older: 7 mg/kg up to 560 mg, once daily for a maximum of 7 days.*

Alternatively, as a single agent, use:

ceftriaxone *50 mg/kg up to 2 g IV, daily; for children requiring intensive care support, use ceftriaxone 50 mg/kg up to 1 g IV, 12-hourly*

OR

cefotaxime *50 mg/kg up to 2 g IV, 8-hourly; for children requiring intensive care support, use cefotaxime 50 mg/kg up to 2 g IV, 6-hourly.*

If not improving after 48 hours of treatment or if *Staphylococcus aureus* is suspected (see page 230), add:

flucloxacillin *50 mg/kg up to 2 g IV, 6-hourly.*

For infants (aged 12 months or younger) or for a child of any age with suspected pertussis, **add**:

azithromycin

child 6 months or older: 10 mg/kg up to 500 mg orally, on day 1, then 5 mg/kg up to 250 mg daily for a further 4 days

infant younger than 6 months: 10 mg/kg orally, daily for 5 days.

cont...

If azithromycin not available, use:

clarithromycin *7.5 mg/kg up to 500 mg orally, 12-hourly for 7 days.*

Switch to oral antibiotics, as for nonsevere pneumonia, when improving.

If the patient is not improving after 48 to 72 hours, reassess the diagnosis. Consider infective and noninfective diagnoses. See comments in CAP in adults below, for further work-up if there is failure to improve despite broad-spectrum antibiotics.

Duration: Treat for a total of 5 to 7 days (IV + oral) but stop azithromycin after 5 days if used.

Community-acquired pneumonia in adults

CAP is commonly caused by *Streptococcus pneumoniae*. Atypical bacterial pathogens including *Mycoplasma pneumoniae*, *Chlamydophila pneumoniae* and *Legionella* species are also important causes of CAP. These atypical organisms are not adequately treated with beta-lactam antibiotics; this is the rationale for the inclusion of doxycycline or azithromycin in empirical treatment regimens.

Respiratory viruses (including COVID-19) can cause pneumonia as a sole pathogen, or as co-infection with bacterial pathogens. *Pneumocystis jirovecii* (PJP) is an important cause of pneumonia in immunocompromised patients (e.g. patients living with HIV, organ transplant recipients, patients with malignancy).

Signs and symptoms that are more likely to occur in a patient with CAP include:

- rigors
- pleuritic chest pain
- tachypnoea (respiratory rate 18 breaths per minute or more at rest)
- oxygen saturation less than 95% on room air
- heart rate higher than 100 beats per minute
- on chest examination:
  - dullness to percussion
  - bronchial breath sounds
  - crepitations (crackles) on auscultation that do not clear with coughing.

Send sputum specimens for culture in patients admitted with moderate or severe pneumonia, and patients with mild pneumonia who fail to respond to empirical therapy. Take blood specimens for culture prior to starting antibiotics in patients who are systemically unwell. Consider performing nose and/or throat swabs for influenza, respiratory syncytial virus and COVID (if available).

Disease severity assessment involves:

- identifying patients with low-severity CAP. These patients have a low risk of complications and are usually suitable for management in the community
- identifying patients who have high-severity CAP associated with a risk of acute organ failure. These patients usually require intensive care support and monitoring.

If cough persists for longer than 2 to 3 weeks, investigate for tuberculosis (TB).

Pneumonia severity scoring tools for community-acquired pneumonia in adults

Tools for scoring pneumonia severity should not be used in isolation to decide management; but they are useful as an aid to clinical judgement.

These tools can be used to:

- decide whether to admit the patient to hospital (CURB-65), and
- identify patients at higher risk of death or requiring intensive care support (CORB).

Figure 6: CURB-65 tool for assessing severity of community-acquired pneumonia in adults

	Risk factor	Points
C	acute-onset confusion	1
U	uraemia (serum urea greater than 7 mmol/L, or blood urea nitrogen greater than 19 mg/dL)	1
R	respiratory rate 30 breaths/minute or more	1
B	systolic blood pressure lower than 90 mmHg, or diastolic blood pressure 60 mmHg or lower	1
65	age 65 years or older	1

Interpretation of CURB-65 score		
Risk of death (30-day mortality)	Site of care [Note 1]	Total points
less than 3%	outpatient, unless there are factors for admission (eg comorbidities, social circumstances)	0 to 1
9%	inpatient	2
15 to 40%	inpatient, and consider if intensive care support is required (especially for patients with CURB-65 score of 4 to 5)	3 to 5

Note 1: When deciding if inpatient management is appropriate, consider the patient's social circumstances (in particular the availability of home support), age, comorbidities, ability to tolerate and absorb oral therapy, need for supportive oxygen therapy, functional status and goals of care.

Adapted from the following with permission from BMJ Publishing Group Ltd
Lim WS, van der Eerden MM, Laing R, Boersma WG, Karalus N, Town GI, et al. Defining community-acquired pneumonia severity on presentation to hospital: an international derivation and validation study. Thorax 2003;58(5):377-82. [URL]

Lim WS, Baudouin SV, George RC, Hill AT, Jamieson C, Le Jeune I, et al. BTS guidelines for the management of community-acquired pneumonia in adults: update 2009. Thorax 2009;64 Suppl 3:iii1-55. [URL]

Figure 7: CORB tool for assessing severity of community-acquired pneumonia in adults

	Risk factor	Points
C	acute-onset confusion	1
O	oxygen saturation 90% or lower	1
R	respiratory rate 30 breaths/minute or more	1
B	systolic blood pressure lower than 90 mmHg, or diastolic blood pressure 60 mmHg or lower	1

↓

Interpretation of CORB score [NB1]:

CORB score of 2 or more = high risk of death or needing IRVS

IVRS = intensive respiratory or vasopressor support

Note 1: In the Australian CAP Study (ACAPS) cohort, the accuracy of CORB for predicting death or the need of IVRS (two or more features of CORB present) was a sensitivity of 72%, specificity of 70%, positive predictive value of 27%, negative predictive value of 94% and an area under the receiver operating characteristic curve = 0.72.

Adapted with permission from 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.

Patient review, modification and duration of therapy

Once treatment for CAP has started, the patient's symptoms should steadily improve. The rate of recovery is influenced by the severity of pneumonia and the patient's general health and comorbidities. Fever should subside within 2 days of therapy, and appetite should improve. Cough, sputum production (if present), chest discomfort and breathlessness may take several weeks to resolve and are often due to exacerbations of comorbidities (e.g. heart failure). Patients can report fatigue for months after an episode of pneumonia. Prolonged symptoms are not an indication for extended antibiotic therapy. If pneumonia remains the likely diagnosis, reassess the need for hospital admission.

Nonsevere CAP in adults

Use:

amoxicillin *1 g orally, 8-hourly for 5 to 7 days.*

In patients with **immediate nonsevere** or **delayed nonsevere** hypersensitivity to penicillins, use:

cefuroxime *500 mg orally, 12-hourly for 5 to 7 days.*

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

doxycycline *100 mg orally, 12-hourly for 5 to 7 days*

OR

clarithromycin *500 mg orally, 12-hourly for 5 to 7 days.*

For patients with nonsevere CAP who are unable to take oral therapy, use:

benzylpenicillin *1.2 g IV, 6-hourly.*

For patients with hypersensitivity to penicillins who are unable to take oral therapy, use:

chloramphenicol *1 g IV, 6-hourly.*

When the patient is able to tolerate oral therapy, switch to an oral regimen, as above, to complete a total of 5 to 7 days of therapy (IV + oral).

Severe CAP in adults

Initial empirical therapy for severe CAP in adults

Use:

ceftriaxone *2 g IV, daily*

PLUS

azithromycin *500 mg IV/orally, daily.*

Alternatively, as a three-drug regimen use:

gentamicin *IV, 5 mg/kg (7 mg/kg in critical illness), see Table 14 (page 384) for dosing frequency for information on dosing frequency, maximum dose and maximum number of doses*

PLUS

benzylpenicillin *1.2 g IV, 4-hourly*

PLUS

cont...

azithromycin *500 mg IV/orally, daily.*

If azithromycin is not available, use doxycycline or clarithromycin as per oral switch options below.

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

For patients who do not improve on initial therapy, see escalation approaches in the next section.

Switch to oral antibiotics when clinically well, according to the results of susceptibility testing. If susceptibility results are not available, use:

amoxicillin *1 g orally, 8-hourly*

PLUS EITHER (unless the patient has had at least 3 days of azithromycin)

doxycycline *100 mg orally, 12-hourly*

OR

clarithromycin *500 mg orally, 12-hourly.*

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

cefuroxime *500 mg orally, 12-hourly*

PLUS EITHER (unless the patient has had at least 3 days of azithromycin)

doxycycline *100 mg orally, 12-hourly*

OR

clarithromycin *500 mg orally, 12-hourly.*

Duration: Treat for a total of 5 to 7 days (IV + oral), except for azithromycin, which is only required for 3 to 5 days. If the patient has had at least 3 days of azithromycin, ongoing oral therapy with doxycycline or clarithromycin (to treat atypical bacteria) is not required.

Adults with severe CAP who do not improve on initial empirical therapy

In patients with severe CAP, suspect *S. aureus* in any of the following circumstances:

- rapid progression to sepsis
- cavitary or necrotising pneumonia
- multilobar consolidation
- multiple lung abscesses or empyema

cont...

- significant history of staphylococcal skin and soft tissue infection
- Gram-positive cocci in clusters in sputum Gram stain.

Escalation approaches for severe CAP in adults

If *S. aureus* is suspected **add** to the initial regimen:

flucloxacillin *2 g IV, 6-hourly.*

If the patient does not improve 48 hours after adding flucloxacillin or is admitted to intensive care unit, use:

meropenem *1 g IV, 8-hourly*

PLUS

azithromycin *500 mg IV/orally, daily.*

Consider adding MRSA cover:

vancomycin *slow IV infusion,* ***consider a loading dose in critically ill adults****. See 'Appendix 2: Vancomycin dosing' (page 386) for information on loading dose, dosing frequency and infusion time*

adult ≥ 40 years: 15 mg/kg, see Table 18 for dosing frequency (page 390)

adult < 40 years 20 mg/kg, see Table 17 for dosing frequency (page 389).

Ongoing management and duration of therapy

If there is failure to improve despite broad-spectrum antibiotics, consider the following:

- viral pneumonia (including COVID-19)
- *P. jirovecii* pneumonia
- TB
- empyema, abscess, tumour (order chest X-ray and/or computed tomography to investigate)
- HIV
- noninfective causes such as pulmonary oedema or pulmonary thromboembolic disease.

Seek appropriate advice for oral therapy options and duration of therapy.

Hospital-acquired pneumonia in adults and children

For hospital-acquired pneumonia (HAP) in neonates, refer to **sepsis, septic shock and meningitis**, page 199 in 'Infections in neonates and young infants.'

HAP is pneumonia that develops more than 48 hours after admission to hospital. This typically presents with fever, purulent sputum, new radiological infiltrate, raised inflammatory markers and deterioration in gas exchange.

HAP is a diagnosis that is often made in error. Always consider these differential diagnoses in patients with hospital-onset respiratory symptoms:

- postoperative atelectasis without infection
- left-sided cardiac failure
- pulmonary embolus
- acute exacerbation of chronic airflow limitation
- pneumothorax
- hospital-acquired viral infection.

Take blood specimens for culture prior to starting antibiotics in patients who have overt sepsis and send tracheal aspirate for microscopy and culture in all patients with presumptive ventilator-associated pneumonia.

Most HAP is caused by aspiration of bacteria from the oropharynx. Prolonged hospitalisation can result in changes to the oropharyngeal flora, with an increase in Gram-negative colonisation.

Recent broad-spectrum antibiotic therapy is a risk factor for HAP caused by more resistant bacteria (e.g. methicillin-resistant *Staphylococcus aureus*, multidrug-resistant Gram-negative bacteria such as Enterobacterales, *Pseudomonas aeruginosa* and *Acinetobacter* species).

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and other respiratory viruses (e.g. influenza, respiratory syncytial virus) can cause HAP or CAP.

Atypical pathogens are a much less common cause of HAP than CAP.

If there is no improvement despite broad-spectrum antibiotics, consider repeat chest X-ray and/or CT to look for complications such as pleural effusion, empyema or abscess.

Nonsevere HAP

Patients with HAP without sepsis or septic shock and who do not have a marked deterioration in gas exchange.

Use:

amoxicillin+clavulanate *500+125 mg (child: 25+5 mg/kg up to 500+125 mg) orally, 8-hourly for 7 days.*

For patients with hypersensitivity to penicillins, use:

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

For patients unable to tolerate oral therapy, use:

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

Switch to an oral regimen when able to tolerate therapy for a total duration of 7 days (IV + oral).

If no improvement after 48 hours, treat as severe HAP.

Severe HAP

HAP with marked deterioration in gas exchange OR sepsis/septic shock OR ventilated in an intensive care unit.

Use:

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

For suspected *S. aureus* (see comments for severe CAP on page 230), add:

vancomycin *slow IV infusion,* ***consider a loading dose in critically ill adults and children****. See* 'Appendix 2: Vancomycin dosing' *(page 386) for information on loading dose, dosing frequency and infusion time*

adult ≥ 40 years: 15 mg/kg, see Table 18 for dosing frequency (page 390)

adult < 40 years 20 mg/kg, see Table 17 for dosing frequency (page 389)

child 3 months and older: 15 mg/kg, 6-hourly.

If not improving after 48 hours, consider differential diagnoses as described in the HAP introductory section and repeat chest X-ray and/or CT scan to assess for complications, e.g. effusion, pneumothorax, empyema or abscess. If the patient continues to deteriorate despite treatment, switch to:

meropenem *1 g (child: 25 mg/kg up to 1 g) IV, 8-hourly*

PLUS

vancomycin *(doses as above).*

Switch to an oral regimen (as for nonsevere HAP) when able to tolerate therapy.

Duration: Treat for 7 days (IV + oral).

Ventilator-associated pneumonia

Ventilator-associated pneumonia (VAP) is pneumonia that develops in patient who has been mechanically ventilated for longer than 48 hours. This typically presents as fever, increased or purulent lower respiratory track secretions, new radiological infiltrates, raised inflammatory markers and deterioration in gas exchange.

Treat as per nonsevere or severe HAP based on the severity of symptoms.

Aspiration pneumonia

This is a bacterial infection caused by aspiration of organisms from the oropharynx.

Causative organisms may be oral streptococci, anaerobes, occasionally Gram-negative bacilli, and *S. aureus*.

Minor aspirations and aspirations without evidence of infection do **not** require antibiotic treatment.

Avoid routine antibiotic use.

Take blood for culture prior to starting antibiotics in patients who are systemically unwell, and send sputum for culture in all cases.

If antibiotics are required, use:

benzylpenicillin *1.2 g (child: 50 mg/kg up to 1.2 g) IV, 6- hourly.*

Anaerobic cover should only be considered in the setting of severe periodontal disease, malodorous sputum or hazardous alcohol consumption; **add**:

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.*

If *S. aureus* is suspected, add:

vancomycin *slow IV infusion,* ***consider a loading dose in critically ill adults and children****. See 'Appendix 2: Vancomycin dosing' (page 386) for information on loading dose, dosing frequency and infusion time*

adult ≥ 40 years: 15 mg/kg, see Table 18 for dosing frequency (page 390)

adult < 40 years 20 mg/kg, see Table 17 for dosing frequency (page 389)

child 3 months and older: 15 mg/kg, 6-hourly

OR

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

cont...

For patients with hypersensitivity to penicillins, use:

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

Clindamycin has adequate activity against anaerobes so it is not necessary to add metronidazole to clindamycin.

For features suggestive of *S. aureus* pneumonia, see page 230.

Switch to oral antibiotics when the patient improves, and according to the results of susceptibility testing. If susceptibility results are not available, use:

amoxicillin *1 g orally, 8-hourly (child: 40 mg/kg up to 1 g orally, 12-hourly)*

OR (if *S. aureus* or anaerobes are suspected)

amoxicillin+clavulanate *500+125 mg (child: 25+5 mg/kg up to 500+125 mg) orally, 8-hourly.*

In patients with hypersensitivity to penicillins, use:

clindamycin *450 mg (child: 10 mg/kg up to 450 mg) orally, 8-hourly.*

Duration: Treat for 7 days (IV + oral).

Lung abscess and empyema

Lung abscess is due to pulmonary tissue necrosis and formation of cavities containing necrotic debris and purulent fluid. Lung abscesses may be caused by aspiration of oral bacteria (polymicrobial, including anaerobic organisms), a complication of pneumonia (e.g. *Klebsiella pneumoniae*, *Staphylococcus aureus*), or a metastatic complication of bacteraemia (e.g. *S. aureus*).

Empyema is a collection of pus in the pleural space and usually occurs as a complication of pneumonia. Adequate drainage is essential for cure of empyema. Seek surgical review.

Take blood and sputum for culture prior to starting antibiotics. Send pleural fluid aspirate for biochemistry, culture, and tuberculosis (TB) testing if indicated.

A lung abscess can be classified as nonsevere if:

- there is no evidence of bacteraemia
- there is no evidence of *S. aureus* infection
- the patient does not have sepsis or septic shock.

If blood culture results demonstrates *S. aureus* bacteraemia, see page 253 in 'Sepsis and bloodstream infections' for management.

If the patient fails to improve despite the use of broad-spectrum antibiotics, consider an alternative pathogen or diagnosis, including:

- TB
- *Nocardia* species
- *Cryptococcus* species
- melioidosis
- noninfective causes (e.g. tumour, vasculitis).

Lung abscess and empyema in adults

Nonsevere lung abscess or empyema in adults
Use: ***benzylpenicillin*** *1.2 g IV, 6-hourly* *PLUS either* ***metronidazole*** *500 mg IV, 12-hourly* OR ***metronidazole*** *400 mg orally, 12-hourly.* Alternatively, as a single agent, use: ***amoxicillin+clavulanate*** *1+0.2 g IV, 6-hourly.* In patients with hypersensitivity to penicillins, use: ***clindamycin*** *600 mg IV, 8-hourly.* Switch to oral antibiotics when the patient has improved and modify therapy based on the results of culture and susceptibility testing. If the results of susceptibility testing are not available, use: ***amoxicillin*** *1 g orally, 8-hourly* *PLUS* ***metronidazole*** *400 mg orally, 12-hourly.* Alternatively, as a single agent, use: ***amoxicillin+clavulanate*** *500+125 mg orally, 8-hourly.* For patients with hypersensitivity to penicillins, use: ***clindamycin*** *450 mg orally, 8-hourly.*
Duration: Treat for a total of 3 to 4 weeks (IV + oral)

Severe lung abscess or empyema in adults

Use:

ceftriaxone *2 g IV, daily*

PLUS

metronidazole *500 mg IV, 12-hourly.*

For patients with **immediate severe** or **delayed severe** hypersensitivity to penicillins, meropenem may be suitable[13] (add vancomycin if the patient has septic shock, as below).

If the infection is community-acquired and patient has **septic shock**, use a four-drug regimen and **add** to the above treatment:

gentamicin *IV, 5 mg/kg (7 mg/kg in critical illness), see Table 14 (page 384) for dosing frequency for information on dosing frequency, maximum dose and maximum number of doses*

PLUS

flucloxacillin *2 g IV, 4-hourly.*

For patients with hypersensitivity to penicillins, with a community-acquired infection and who have **septic shock**, meropenem may be suitable, use:

meropenem *1 g IV, 8-hourly*[13]

PLUS

vancomycin *slow IV infusion, see 'Appendix 2: Vancomycin dosing' (page 386) for information on timing of next dose after loading dose, dosing frequency and infusion time*

- *adult ≥ 40 years:* ***loading dose 25 mg/kg up to 3 g*** *then 15 mg/kg, see Table 18 for dosing frequency (page 390)*
- *adult < 40 years:* ***loading dose 25 mg/kg up to 3 g*** *then 20 mg/kg, see Table 17 for dosing frequency (page 389).*

Switch to oral antibiotics once the patient has improved and modify therapy based on the results of susceptibility testing. If the results of susceptibility testing are unavailable, use empirical oral regimens as recommended for nonsevere lung abscess or empyema.

Duration: Treat for a total of 3 to 4 weeks (IV plus oral).

13 In patients with penicillin hypersensitivity, the rate of immune-mediated cross-reactivity with carbapenems is approximately 1%; therefore, meropenem can be considered in supervised settings. However, in patients with a history of a severe cutaneous adverse reaction (eg drug rash with eosinophilia and systemic symptoms [DRESS], Stevens–Johnson syndrome / toxic epidermal necrolysis [SJS/TEN], acute generalised exanthematous pustulosis [AGEP]), consider meropenem only in a critical situation when there are limited treatment options.

Lung abscess or empyema in children

In children, lung abscess caused by *Streptococcus pneumoniae* or *S. aureus* is more common than lung abscess due to aspiration of oral bacteria.

Management of lung abscess or empyema in children
Adequate drainage is essential. Seek surgical opinion for consideration of intercostal drain insertion. Use: ***ceftriaxone*** *50 mg/kg up to 2 g IV, daily* *PLUS either* ***clindamycin*** *15 mg/kg up to 600 mg IV, 8-hourly* OR ***clindamycin*** *10 mg/kg up to 450 mg orally, 8-hourly.* If clindamycin is unavailable, substitute with: ***flucloxacillin*** *50 mg/kg up to 2 g IV, 6-hourly* OR ***vancomycin*** *slow IV infusion, child 3 months and older: 15 mg/kg, 6-hourly. Consider a* ***loading dose*** *in critically ill children. See page 392 in 'Appendix 2: Vancomycin dosing' for information on loading dose, dosing frequency and infusion time in children.* For patients with **immediate severe** or **delayed severe** hypersensitivity to penicillins, meropenem may be suitable[14], use: ***meropenem*** *20 mg/kg up to 1 g IV, 8-hourly* Switch to oral antibiotics based on the results of susceptibility testing once the patient has improved.
Duration: Treat for a total of 3 to 6 weeks (IV + oral).

14 In patients with penicillin hypersensitivity, the rate of immune-mediated cross-reactivity with carbapenems is approximately 1%; therefore, meropenem can be considered in supervised settings. However, in patients with a history of a severe cutaneous adverse reaction (eg drug rash with eosinophilia and systemic symptoms [DRESS], Stevens–Johnson syndrome / toxic epidermal necrolysis [SJS/TEN], acute generalised exanthematous pustulosis [AGEP]), consider meropenem only in a critical situation when there are limited treatment options.

Bronchiectasis – acute exacerbation

Bronchiectasis is a disease characterised by the abnormal dilatation of one or more bronchi and bronchioles with chronic airway inflammation. Clinical features include chronic sputum production, recurrent chest infections, and airflow obstruction.

An exacerbation of bronchiectasis is an acute deterioration in a patient's symptoms from their usual baseline as evidenced by increased cough, sputum volume or purulence, dyspnoea, hypoxia or fever. Patients should only be treated with antibiotics during an acute exacerbation.

Antibiotics are not indicated unless all three of the following clinical features of bacterial infection are present:

- increased sputum volume or change in sputum viscosity
- increased sputum purulence
- increased cough, which may be associated with wheeze, breathlessness or haemoptysis.

Collect sputum for culture and, if systemically unwell, also collect blood for culture prior to starting antibiotic therapy. Consider testing for influenza, respiratory syncytial virus (RSV) and COVID-19; collect nose and/or throat swabs as appropriate.

Ensure other aspects of bronchiectasis management are optimised, such as airway clearance, physical activity and, if appropriate, bronchodilator therapy.

Patients with bronchiectasis are commonly colonised with organisms including *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Moraxella catarrhalis*, *Pseudomonas aeruginosa* and *Staphylococcus aureus.* Sputum cultures need to be interpreted in the clinical context, because isolated organisms may be colonising rather than causing infection. If the patient is improving on empirical antibiotic therapy, there is **no need** to adjust therapy based on culture results even if a resistant organism is identified.

The mainstays of therapy for bronchiectasis exacerbations are antimicrobials and prompt management of acute infection with appropriately targeted therapies. This reduces inflammation, minimising new structural lung damage.

The optimal duration of antimicrobial therapy is not well defined. For patients who seldom have exacerbations, 10 to 14 days is adequate. Even for severe infections and those with frequent recurrences, the duration should not exceed 14 days except after careful review of the microbiology and the trajectory of improvement while taking the course of antibiotics.

Antibiotic treatment will not eradicate colonising organisms.

Antibiotic therapy for infective exacerbation of bronchiectasis

Nonsevere infective exacerbation of bronchiectasis

Use:

amoxicillin *1 g (child: 25 mg/kg) orally, 8-hourly for 10 to 14 days.*

OR including for patients with penicillin hypersensitivity

doxycycline *100 mg orally, 12-hourly for 10 to 14 days.*

Severe infective exacerbation of bronchiectasis

Use:

benzylpenicillin *1.2 g (child 50 mg/kg up to 1.2 g) IV, 6-hourly*

PLUS

ciprofloxacin *750 mg (child 20 mg/kg up to 750 mg) orally, 12-hourly.*

For patients with **immediate nonsevere** or **delayed nonsevere** hypersensitivity to penicillins, use the ceftriaxone escalation regimen below. For patients with **immediate severe** or **delayed severe** hypersensitivity to penicillins, use ciprofloxacin as a single agent.

If no improvement after 48 hours and microbiology results are not available change to:

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

PLUS

ciprofloxacin *750 mg (child: 20 mg/kg up to 750 mg) orally, 12-hourly.*

For severe bacterial exacerbations of bronchiectasis in adults with *P. aeruginosa* colonisation, use:

ceftazidime *2 g IV, 8-hourly.*

For patients who improve on empirical therapy, switch to oral antibiotic therapy, as for nonsevere exacerbation.

For patients who do not improve on empirical antibiotic therapy, modify treatment based on the results of susceptibility testing.

Duration: Treat for 10 to 14 days (IV + oral).

Acute exacerbation of chronic obstructive pulmonary disease

An exacerbation of chronic obstructive pulmonary disease (COPD) is an acute deterioration in a patient's symptoms from their usual baseline as evidenced by increased cough, sputum volume or purulence, dyspnoea, hypoxia or fever. Acute exacerbations may be triggered by viral or bacterial infection, or noninfective causes. Respiratory viruses are the most common cause.

Consider performing nose and/or throat swabs for influenza, respiratory syncytial virus and COVID-19.

Do not use antibiotic therapy unless the patient has clinical features suggestive of bacterial infection. Bacterial COPD exacerbations are more likely if the patient has at least two of the three following symptoms (particularly an increase in sputum purulence) and/or an elevated CRP (greater than 20 mg/L).

- increased dyspnoea
- increased sputum volume or change in sputum viscosity
- sputum purulence (i.e. a change in sputum colour).

Sputum culture is not routinely recommended for COPD as many patients are persistently colonised with *Haemophilus influenzae, Moraxella catarrhalis* or *Streptococcus pneumoniae*, and a positive sputum culture result is not necessarily indicative of infection.

Antibiotic therapy for exacerbations of COPD

If consolidation is seen on chest X-ray, treat as CAP.

For patients with less severe exacerbations, treatment with antibiotics does not consistently improve outcomes.

For patients managed in the intensive care unit, antibiotics significantly reduce the rate of treatment failure and reduce mortality.

If antibiotic therapy is indicated, use:

amoxicillin *500 mg orally, 8-hourly for 3 days.*

Alternatively, including for patients with hypersensitivity to penicillins, use:

doxycycline *100 mg orally, 12-hourly for 3 days.*

Pertussis (whooping cough)

Pertussis is a notifiable disease in Papua New Guinea.

Pertussis is caused by the bacterium *Bordetella pertussis*. The diagnosis is largely clinical and laboratory testing (polymerase chain reaction [PCR]) was unavailable in Papua New Guinea at the time of writing. Pertussis classically presents with a persistent cough and coryza for one week (catarrhal phase), followed by a more pronounced cough in spells or paroxysms (paroxysmal phase). However, pertussis can also present as a nonspecific persistent cough, especially in older children and adults.

Patients are infectious just prior to and for 21 days after the onset of cough, if untreated, so antibiotics are recommended in patients of any age to minimise transmission if a diagnosis is made within 3 weeks of symptom onset. Advise patients to avoid contact with others, especially young children and infants, until antibiotic therapy has been taken for at least 5 days.

Pertussis can occur in immunised children, but the illness is generally less severe.

Treat mild cases in an outpatient setting.

Admission to a hospital or health centre is recommended for children aged 6 months or younger, or if there are complications such as pneumonia, heart failure, convulsions and malnutrition.

Management of suspected pertussis

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.*

OR

erythromycin *250 mg (child: 10 mg/kg up to 250 mg) orally, 6-hourly for 7 days.*

Give a pertussis-containing vaccine (e.g. diphtheria, tetanus, pertussis, hepatitis B recombinant and *Haemophilus influenzae* (Hib) combined vaccine) to children in the household 5 years or younger) who are not immunised.

Infants may require hospitalisation for supportive care of complications, such as heart failure, convulsions and malnutrition.

For children with severe symptoms, treat as severe CAP with an azithromycin-containing regimen.

Other respiratory tract infections

Acute asthma – asthma exacerbation

If there is consolidation on chest X-ray, treat as CAP.

Avoid routine antibiotic use.

Most respiratory infections that trigger asthma exacerbations are viruses. Routine antibiotic use is not beneficial.

Consider testing for influenza, RSV and COVID-19.

Acute bronchitis

Characterised by inflammation and bronchospasm of the airways with coughing, wheeze and shortness of breath.

If there is consolidation on chest X-ray, purulent sputum and/or increased work of breathing, treat as CAP.

Avoid routine antibiotic use.

Most patients have a viral infection or history of exposure to cigarette smoke or other toxic inhaled substances.

Options for cough relief include throat lozenges, hot tea, honey, smoking cessation or avoidance of second-hand smoke and/or over-the-counter medicines.

In most patients, the cough persists for **1 to 3 weeks**.

Bronchiolitis

If evidence of sepsis, aspiration, or acute consolidation on chest X-ray, treat as CAP.

Acute bronchiolitis is a common lower respiratory viral infection in children 2 years or younger, which typically occurs in annual epidemics and is characterised by airways obstruction and chest wheeze. Respiratory syncytial virus (RSV) is the most common cause. Secondary bacterial infection is uncommon (occurs in less than 2% of cases).

Consider testing for influenza, RSV and COVID-19.

Resolution occurs over 7 to 10 days; however, cough may persist for weeks.

Antibiotics are not routinely indicated and should be reserved for severe disease in infants 2 months or younger or when secondary bacterial infection is suspected based on chest X-ray changes (treat as per CAP).

Key additional references

Mathur S, Fuchs A, Bielicki J, Van Den Anker J, Sharland M. Antibiotic use for community-acquired pneumonia in neonates and children: WHO evidence review. Paediatr Int Child Health 2018; 38 (suppl 1):S66-75. Doi: 10.1080/20469047.2017.1409455.

Pocket book of hospital care for children: guidelines for the management of common childhood illnesses – 2nd ed. Geneva: World Health Organization; 2013.

Sepsis and bloodstream infections

This topic includes advice on the management of the following conditions in adults and children older than 3 months:

- **empirical management of sepsis or septic shock**, page 247
  - community-acquired sepsis, page 248
  - hospital-acquired sepsis, page 250
  - escalation regimen for patients not improving on initial therapy, page 252
- **directed therapy for bloodstream infections including sepsis and septic shock** for:
  - *Staphylococcus aureus* (MSSA and MRSA), page 253
  - *Streptococcus pyogenes* and other beta-haemolytic streptococci, page 257
  - Gram-negative enteric organisms (*Escherichia coli, Klebsiella* species and *Proteus* species), page 259
  - *Pseudomonas aeruginosa*, page 260
  - infection with multidrug-resistant Gram-negative bacteria, page 261
  - *Brucella* species, page 262
  - *Candida* species, page 262
- intravascular line infections including **haemodialysis/central line infection** and **peripheral intravenous cannula infection**, page 263.

The following topics are not included in this section:

- **sepsis, septic shock and meningitis in neonates and young infants** (page 199) in 'Infections in neonates and young infants'
- **typhoid** (enteric fever) (page 148) in 'Gastrointestinal tract infections'
- **leptospirosis** (page 345) and **melioidosis** (page 348) in 'Miscellaneous infections.'

Overview of sepsis and bloodstream infections

Development of sepsis begins with infection (tissue invasion), which can then progress to bloodstream involvement, progressing to severe sepsis (infection with specific organ dysfunction[15]). Patients with severe sepsis may develop septic shock (with hypotension not responsive to fluids) and/or multiorgan dysfunction syndrome

15 Patients with sepsis might present dysfunction of virtually any system, regardless of the site of infection. The 6 organ systems frequently affected are the kidneys, liver, lungs, heart, central nervous and haematological systems.

with dysfunction of two or more organs. Symptoms and signs of sepsis may or may not include features specific to the particular source of sepsis (e.g. cough if the source is respiratory, or dysuria if the sources is the genitourinary tract).

Sepsis should be considered in a child with fever who is severely ill and has signs indicative of bacterial infection. It is usually associated with tachycardia, tachypnoea, raised white cell count and organ dysfunction. Hypotension is a late sign of septic shock in children. Warning signs in adults include arterial hypotension (< 90 mmHg systolic), fever > 38°C, tachycardia, tachypnoea and altered mental status.

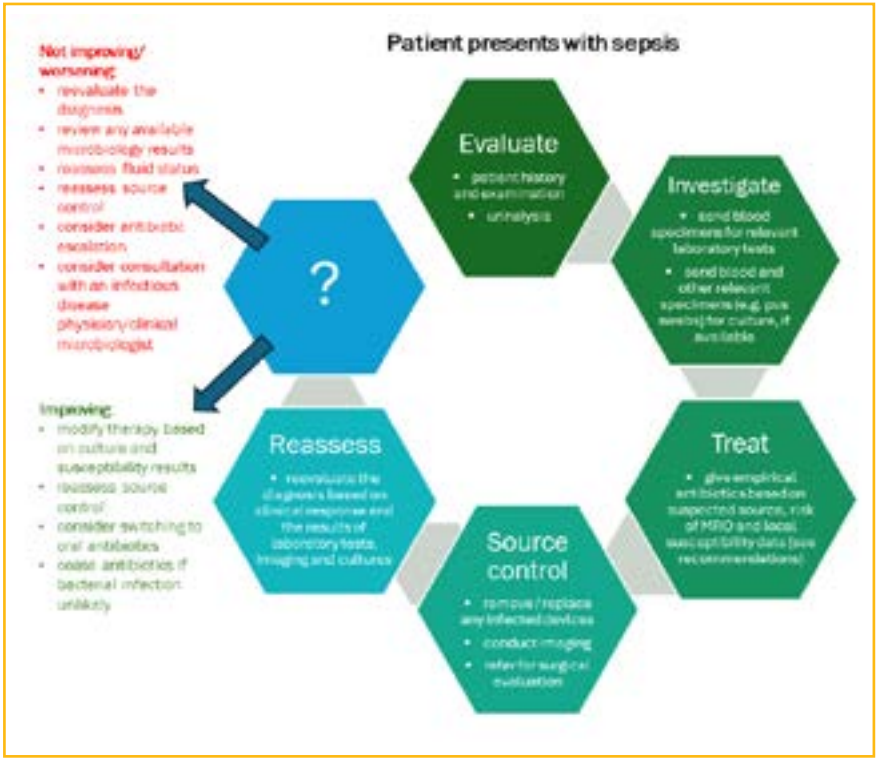
Importantly, many of these signs indicate decreased organ perfusion and can be improved with careful and early fluid resuscitation, appropriate antibiotic treatment and repeated reassessment (at least half-hourly). **Rapid treatment of sepsis saves lives.**

Common causative organisms across all ages include *Streptococcus pneumoniae, Staphylococcus aureus* (including methicillin-resistant S. aureus [MRSA]), *Streptococcus pyogenes* (especially in children aged 5 to 15 years), *Haemophilus influenzae, Neisseria meningitidis* and enteric Gram-negative organisms such as *Escherichia coli*, *Klebsiella pneumoniae* and *Salmonella* species (*S. Typhi* is prevalent in children in some regions).

Inpatients are prone to intravascular and other device-associated or healthcare-associated bloodstream infections with *Staphylococcus aureus* (including MRSA) and enteric Gram-negative organisms, including ceftriaxone-resistant strains of *Klebsiella* species and *E. coli* (those which produce extended-spectrum beta-lactamase (ESBL) enzymes). Intensive care patients are prone to healthcare-associated infections with *Staphylococcus aureus* (including MRSA) and enteric Gram-negative organisms, including *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, which may be multidrug-resistant. Candidaemia may be associated with indwelling central intravenous lines or urinary catheters. Patients with significant neutropenia are particularly at risk from *P. aeruginosa* bloodstream infection.

Approach to managing a patient presenting with sepsis

Figure 8: Approach to managing a patient presenting with sepsis



Empirical management of sepsis or septic shock

Patients with sepsis or septic shock require urgent intervention, including immediate resuscitation and prompt administration of antibiotics.

Take blood for culture and then administer antibiotics within 1 hour.

Continue repeated assessment and investigation for source of infection. Refer to relevant topic once a focus is found and direct antibiotics accordingly:

- For a lung/respiratory tract source, see **severe community-acquired pneumonia** (in children, page 224; in adults, page 229) or **hospital-acquired pneumonia** (page 233) in 'Respiratory tract infections'
- For a urinary tract source, see **severe pyelonephritis**, page 321 in 'Urinary tract infections'

- For a biliary or gastrointestinal tract source, see peritonitis due to **perforated bowel, intraperitoneal abscess**, page 181 in 'Intraabdominal infections'
- For a female genital tract source, see **severe pelvic inflammatory disease** (page 161) or **severe postprocedural pelvic infection** (page 163) in 'Genital and sexually transmissible infections' or **chorioamnionitis** (page 193) in 'Maternal infections associated with pregnancy'
- For a skin or soft tissue source, see **severe cellulitis** (page 274) in 'Skin infections,' or **severe diabetic foot infection** (page 305) or **necrotising soft tissue infections** (page 307) in 'Soft tissue infections.'

Septic shock is subtype of sepsis associated with circulatory, cellular and metabolic abnormalities. It presents as hypotension refractory to intravenous fluid replacement, requires vasopressor therapy to maintain mean arterial pressure (MAP) > 65 mmHg, and is associated with tissue hypoperfusion (lactate > 2 mmol/L) despite the absence of hypovolaemia.

A diagnosis of septic shock can be made in patients with mean arterial pressure (MAP) < 65 mmHg after adequate intravenous fluid replacement or who are on vasopressors.

Patients with septic shock require intensive care support.

The empirical regimens below are intended for initial therapy only (up to 48 hours) – modify as soon as additional information (e.g. source of infection or results of Gram stain, culture and susceptibility testing) is available.

Community-acquired sepsis or septic shock

Typhoid (enteric fever) may present as fever with few focal features, especially in children and adolescents – see **typhoid (enteric fever)**, page 148 in 'Gastrointestinal infections' for advice on the modification of antibiotic therapy. Note that a number of other infectious diseases that are prevalent in Papua New Guinea, including dengue, can present in a similar manner, see Table 1: Differential diagnosis of generalised or systemic infectious disease conditions, page 36.

Where relevant, test for malaria – and treat if confirmed. If rapid diagnostic tests for malaria are not available but malaria is suspected based on region (e.g. living in or recent travel to an area where malaria is endemic) and symptoms, start empirical treatment for malaria. See the *National Malaria Guidelines* for management information.

Empirical management of community-acquired sepsis or septic shock, without an immediately apparent source of infection

Consider patients high risk for multidrug-resistant organisms if they have had a recent hospital admission.

As a three-drug regimen, use:

gentamicin *IV, see Appendix 1: Gentamicin dosing (page 381) for information on dosing frequency, maximum dose and maximum number of doses*

adult: 5 mg/kg (7 mg/kg in critical illness), see Table 14 for dosing frequency (page 384)

child 3 months and older: 7 mg/kg up to 560 mg, once daily

PLUS

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

PLUS

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

For patients with an **immediate nonsevere** or **delayed nonsevere** hypersensitivity to penicillins, **substitute** flucloxacillin in the above regimen with:

cefazolin

adult: 2 g IV, 6-hourly

child: 50 mg/kg up to 2 g, 8-hourly.

For patients with sepsis or septic shock requiring intensive care support, who have had a recent admission to hospital or are significantly immunocompromised, **add** vancomycin (and use a four-drug regimen):

vancomycin *slow IV infusion, see 'Appendix 2: Vancomycin dosing' (page 386) for information on timing of next dose after loading dose, dosing frequency and infusion time*

adult ≥ 40 years: ***loading dose 25 mg/kg up to 3 g*** *then 15 mg/kg, see Table 18 for dosing frequency (page 390)*

adult < 40 years: ***loading dose 25 mg/kg up to 3 g*** *then 20 mg/kg, see Table 17 for dosing frequency (page 389)*

child 3 months and older: ***loading dose 25 mg/kg up to 3 g*** *then 15 mg/kg, 6-hourly.*

For patients with **immediate severe** or **delayed severe** hypersensitivity to penicillins, use (as a two-drug regimen):

gentamicin *(dosing as above)*

PLUS

vancomycin *(dosing as above).*

cont...

Alternatively, if vancomycin is not available or is contraindicated, use (as a two-drug regimen):

gentamicin *(dosing as above)*

PLUS

chloramphenicol *1 g (child: 25 mg/kg up to 1 g) IV, 6-hourly.*

However, note that the gentamicin and chloramphenicol regimen has inferior activity against *S. aureus*.

Monitoring and ongoing therapy for community-acquired sepsis or septic shock

When using gentamicin and/or vancomycin for sepsis or septic shock, monitor renal function (creatinine) at least every 72 hours.

Regimens with both gentamicin and vancomycin should not be continued for more than 72 hours due to an increased risk of nephrotoxicity; modify treatment according to microbiology results and the likely source of infection.

For patients who improve on empirical therapy

De-escalate antimicrobial therapy based on the final diagnosis of the source of infection and microbiology results. If microbiology is not available, de-escalate therapy based on additional information about the diagnosis and potential source of infection.

For patients who **worsen** or **do not improve** after 48 to 72 hours

Switch to the **escalation regimen for sepsis or septic shock**, page 252 in this topic.

Hospital-acquired sepsis

Common sources include:

- intravenous–device (peripheral or central; note that the device entry site may not appear infected)
- urinary tract (catheter-associated)
- pneumonia (aspiration- or ventilator- associated)
- surgical wound infection (postoperative fever is not necessarily indicative of bacterial infection)
- pressure ulcers.

Where possible, remove or replace existing intravascular devices and/or indwelling urinary catheters.

Empirical management of hospital-acquired sepsis or septic shock, source not apparent

As a two-drug regimen, use:

gentamicin *IV, see Appendix 1: Gentamicin dosing (page 381) for information on dosing frequency, maximum dose and maximum number of doses*

adult: 5 mg/kg (7 mg/kg in critical illness), see Table 14 for dosing frequency (page 384)

child 3 months and older: 7 mg/kg up to 560 mg, once daily

PLUS

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

In patients with **immediate nonsevere** or **delayed nonsevere** hypersensitivity to penicillins, use:

gentamicin *(dosing as above)*

PLUS

cefazolin

adult: 2 g IV,6-hourly

child: 50 mg/kg up to 2 g, 8-hourly.

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

gentamicin *(dosing as above)*

PLUS

chloramphenicol *1 g (child: 25 mg/kg up to 1 g) IV, 6-hourly.*

Ongoing therapy for hospital-acquired sepsis or septic shock

Review antimicrobial therapy according to newly available information (e.g. source of infection, Gram stain, results of culture and susceptibility testing) and the patient's clinical status.

cont...

For patients who improve on empirical therapy

The duration of treatment in the absence of positive cultures should be based on clinical assessment and is usually around 7 days. Patients who recover quickly may not have had a bacterial infection in the first place or had adequate source control (e.g. removal of an intravenous line) – shorten the duration of treatment or switch to a suitable oral antibiotic.

For patients who **worsen** or **do not improve** on empirical therapy

Switch to the **escalation regimen for sepsis or septic shock** (next section).

Escalation regimen for sepsis or septic shock

For patients with either community- or hospital-acquired sepsis or septic shock who, after 48 to 72 hours, have not improved or who have deteriorated:

- review the diagnosis and available microbiology
- reassess fluid status/adequacy of resuscitation
- reassess source control/devices
- consider consultation with a clinical microbiologist or infectious disease physician.

Escalation regimen for patients who worsen or do not improve on empirical therapy

Use as a two-drug regimen:

meropenem *1 g (child: 20 mg/kg up to 1 g) IV, 8-hourly*

PLUS

vancomycin *slow IV infusion, see Appendix 2: Vancomycin dosing' (page 386) for information on timing of next dose after loading dose, dosing frequency and infusion time*

adult ≥ 40 years: ***loading dose 25 mg/kg up to 3 g*** *then 15 mg/kg, see Table 18 for dosing frequency (page 390)*

adult < 40 years: ***loading dose 25 mg/kg up to 3 g*** *then 20 mg/kg, see Table 17 for dosing frequency (page 389)*

child 3 months and older: ***loading dose 25 mg/kg up to 3 g*** *then 15 mg/kg, 6-hourly.*

If meropenem is not available, use:

chloramphenicol *1 g (child: 25 mg/kg up to 1 g) IV, 6-hourly.*

Directed therapy for bloodstream infections

Gram-positive bacteria

Staphylococcus aureus

Staphylococcus aureus bacteraemia (SAB) – either methicillin-susceptible *S. aureus* [MSSA] or methicillin-resistant *S. aureus* [MRSA]) is a frequent cause of community- and hospital-acquired infection. The presentation is usually acute.

The commonest principal sources associated with SAB include:

- healthcare-associated events:
  - vascular access devices (e.g. intravenous cannula or central venous catheter); the entry site may not appear infected
  - skin and soft tissue infection (e.g. abscess, boil, postoperative wound infection)
  - infection with no apparent primary source or clear focus
- community-associated events (risk factors include diabetes, intravenous drug use):
  - infection with no apparent primary source or clear focus
  - skin and soft tissue infection (e.g. abscess, boil, deep abscess)
  - joint infection or spinal osteomyelitis
  - pneumonia or lung abscess
  - endocarditis (usually acute, may affect previously damaged or normal valves, or prosthetic valves).

General considerations:

- evaluate clinically for metastatic foci of infection (e.g. endocarditis, septic arthritis, osteomyelitis, abscesses)
- repeat one set of blood cultures after 48 to 72 hours of treatment to show clearance of bacteraemia
- where possible, control the infected sites/sources (e.g. cannula, abscess, necrotic bone)
- infective endocarditis can complicate *S. aureus* bacteraemia
- perform a transthoracic echocardiogram on all patients between days 5 and 7, if available.

Treat as **complicated** if any of the following are present:

- positive blood culture > 72 hours after starting appropriate antibiotics
- persistent fever > 72 hours after starting appropriate antibiotics
- identifiable focus of infection or a focus that has not been dealt with effectively (i.e. removal of a device, drainage of an abscess)
- evidence of significant metastatic foci of infection (endocarditis, vertebral osteomyelitis, visceral abscess)
- history of rheumatic heart disease (RHD) or abnormal cardiac valves on echocardiogram
- intravascular prosthetic material (cardiac valves, pacemaker, pacing wires, defibrillator, etc).

Management of clinically suspected *S. aureus* sepsis or septic shock

These recommendations apply to clinically suspected *S. aureus* bloodstream infection where no culture confirmation is available.

To provide cover against both MSSA and MRSA, use:

chloramphenicol *1 g (child: 25 mg/kg up to 1 g) IV, 6-hourly for at least 72 hours.*

When clinically improved, switch to:

trimethoprim+sulfamethoxazole *320+1600 mg (child: 8+40 mg/kg up to 320+1600 mg) orally, 12-hourly.*

Alternatively, if trimethoprim+sulfamethoxazole is not available or is contraindicated, use:

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

Duration of therapy for clinically suspected *S. aureus* sepsis or septic shock

Treat for a minimum of 14 days (IV + oral). The total duration will depend on the clinical situation including the presumed site of infection, source control, presence of sepsis and response to treatment.

Management of proven *S. aureus* bacteraemia (SAB)

For **MSSA**, use:

flucloxacillin *2 g (child 50 mg/kg up to 2 g) IV, 6-hourly.*

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

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

For patients with **immediate severe** or **delayed severe** hypersensitivity to penicillins, use vancomycin as for MRSA.

When switch to oral therapy is appropriate (see duration for further information), use:

flucloxacillin *1 g (child: 25 mg/kg up to 1 g) orally, 6-hourly.*

Alternatively, including for patients with **immediate nonsevere** or **delayed nonsevere** hypersensitivity to penicillins, use:

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

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

vancomycin *slow IV infusion, see 'Appendix 2: Vancomycin dosing' (page 386) for information on timing of next dose after loading dose, dosing frequency and infusion time*

- *adult ≥ 40 years:* ***loading dose 25 mg/kg up to 3 g*** *then 15 mg/kg, see Table 18 for dosing frequency (page 390)*
- *adult < 40 years:* ***loading dose 25 mg/kg up to 3 g*** *then 20 mg/kg, see Table 17 for dosing frequency (page 389)*
- *child 3 months and older:* ***loading dose 25 mg/kg up to 3 g*** *then 15 mg/kg, 6-hourly.*

If vancomycin is not available or contraindicated, use:

chloramphenicol *1 g (child: 25 mg/kg up to 1 g) IV, 6-hourly for at least 72 hours.*

When switch to oral therapy is appropriate (see duration of treatment for confirmed SAB for further information), use:

trimethoprim+sulfamethoxazole *320+1600 mg (child: 8+400 mg/kg up to 320+1600 mg) orally, 12-hourly.*

For **MRSA**, use:

vancomycin *slow IV infusion, see 'Appendix 2: Vancomycin dosing' (page 386) for information on timing of next dose after loading dose, dosing frequency and infusion time*

adult ≥ 40 years: ***loading dose 25 mg/kg up to 3 g*** *then 15 mg/kg, see Table 18 for dosing frequency (page 390)*

adult < 40 years: ***loading dose 25 mg/kg up to 3 g*** *then 20 mg/kg, see Table 17 for dosing frequency (page 389)*

child 3 months and older: ***loading dose 25 mg/kg up to 3 g*** *then 15 mg/kg, 6-hourly.*

If vancomycin is not available or contraindicated, use:

chloramphenicol *1 g (child: 25 mg/kg up to 1 g) IV, 6-hourly for at least 72 hours.*

When switch to oral therapy is appropriate (see duration of treatment for confirmed SAB for further information), if susceptibility is confirmed, use:

trimethoprim+sulfamethoxazole *160+800 mg (child: 4+20 mg/kg up to 160+800 mg) orally, 12-hourly.*

Management of proven *S. aureus* bacteraemia (SAB) in patients on dialysis

For patients on dialysis, for MSSA, use:

cefazolin *2 g IV, post dialysis.*

When switch to oral therapy is appropriate (see duration of treatment for confirmed SAB for further information), use:

cefalexin *1 g orally, 12-hourly.*

For patients with **immediate severe** or **delayed severe** hypersensitivity to penicillins, use vancomycin as for MRSA.

For MRSA use:

vancomycin *1 g IV weekly, after dialysis.*

When switch to oral therapy is appropriate (see duration of treatment for confirmed SAB for further information), if susceptibility is confirmed, use:

clindamycin *450 mg orally, 8-hourly.*

If the organism is not susceptible to clindamycin or if clindamycin is not available, continue weekly vancomycin and/or seek expert advice.

Duration of therapy for confirmed SAB in adults

Uncomplicated bacteraemia

Treat for 2 weeks total with at least 1 week of intravenous treatment.

Complicated bacteraemia and haemodialysis patients

Treat for at least 4 weeks with at least 2 weeks of intravenous therapy. Extend treatment to 6 weeks if response to antibiotics is slow.

Duration of therapy for confirmed SAB in children

The treatment course must be completed with intravenous therapy, except for bone and joint infections. For duration of complicated SAB, seek appropriate advice.

Uncomplicated SAB

For MSSA, continue intravenous treatment for at least 7 days after the first negative blood culture.

For MRSA, a minimum duration of 14 days of intravenous therapy is recommended.

While prolonged therapy is required for SAB associated with osteomyelitis or septic arthritis, the duration of intravenous therapy may be shortened to 4 days if **all** of the following criteria apply:

- bones or joints are the only focus of bacteraemia
- bacteraemia has resolved rapidly (blood culture results were negative at 48 to 72 hours)
- the child is clinically improving.

The remainder of the treatment course can be completed with oral therapy if a suitable oral antibiotic formulation is available.

Streptococcus pyogenes and other beta-haemolytic streptococci

Streptococcus pyogenes (group A streptococcus) bacteraemia 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. Related beta-haemolytic streptococcal species of groups B (*S. agalactiae*), C or G types are managed in the same manner.

When *S. pyogenes* bacteraemia is associated with necrotising fasciitis, urgent surgical debridement is required see **necrotising soft tissue infections** (page 307) in 'Soft tissue infections.'

Management of streptococcal bacteraemia

Use:

benzylpenicillin *1.8 g (child: 50 mg/kg up to 1.8 g) IV, 4-hourly.*

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

cefazolin *2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly; for adults with septic shock or requiring intensive care support, use a 6-hourly cefazolin dosing interval.*

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

vancomycin *slow IV infusion,* ***consider a loading dose in critically ill adults and children****. See 'Appendix 2: Vancomycin dosing' (page 386) for information on loading dose, dosing frequency and infusion time*

adult ≥ 40 years: 15 mg/kg, see Table 18 for dosing frequency (page 390)

adult < 40 years 20 mg/kg, see Table 17 for dosing frequency (page 389)

child 3 months and older: 15 mg/kg, 6-hourly.

For patients who have complicated *S. pyogenes* bacteraemia (sepsis, septic shock, toxic shock syndrome, pneumonia, meningitis or necrotising fasciitis), **add** to any of the regimens above:

clindamycin *600 mg (child: 15 mg/kg up to 600 mg) IV, 8-hourly for 72 hours.*

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 **immediate nonsevere** or **delayed nonsevere** hypersensitivity to penicillins, use:

cefalexin *500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly.*

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

clindamycin *450 mg (child: 10 mg/kg up to 450 mg) orally, 8-hourly.*

Duration of therapy for streptococcal bacteraemia

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

Gram-negative bacteria

The patient's presentation is usually acute; Gram-negative bacteria are a frequent cause of community- and healthcare-associated infection. The commonest principal sources include:

- healthcare-associated events:
  - urinary tract infection (in adults, this is most often associated with a urinary catheter)
  - febrile neutropenia (children and adults)
  - infection with no apparent primary source or clear focus (especially neonates)
  - vascular access device (especially central venous catheters); entry site may not appear infected
  - biliary tract infection (including cholangitis, cholecystitis, pancreatitis) or another intraabdominal focus, in adults this is most common following an intraabdominal procedure
  - pneumonia including ventilator-associated events in ICU
- community-associated events:
  - urinary tract infection (a common source in adults and children)
  - infection with no apparent primary source or clear focus
  - biliary tract infection (including cholangitis, cholecystitis, pancreatitis) (adults)
  - intraabdominal infection other than biliary tract (adults and children)
  - gastroenteritis including *Salmonella* and *Campylobacter* infection (adults and children)
  - pneumonia, skin and soft tissue – occurs less commonly (e.g. melioidosis – for *Burkholderia pseudomallei* bacteraemia, see **melioidosis,** page 348 in 'Miscellaneous infections').

Gram-negative enteric bacteria (e.g. *Escherichia coli, Klebsiella* species, *Proteus* species)

For *E. coli* or *K. pneumoniae* isolates resistant to broad-spectrum cephalosporins but susceptible to piperacillin+tazobactam and meropenem, use meropenem (if available) because the risk of mortality is increased in patients treated with piperacillin+tazobactam.

Treat according to the results of susceptibility testing, when available. Until then, use:

gentamicin *IV, see 'Appendix 1: Gentamicin dosing' (page 381) for information on dosing frequency, maximum dose and maximum number of doses*

adult: 5 mg/kg (7 mg/kg in critical illness), see Table 14 for dosing frequency (page 384)

child 3 months and older: 7 mg/kg up to 560 mg, once daily

OR

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

If gentamicin is used and the results of susceptibility testing are not available by 72 hours and empirical IV therapy is still required, switch to ceftriaxone.

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

chloramphenicol *1 g (child: 25 mg/kg up to 1 g) IV, 6-hourly.*

If site of infection is identified, refer to relevant section of these guidelines.

Effective source control with surgery, if necessary, is essential.

Duration of therapy for bloodstream infection with Gram-negative enteric bacteria

Switch to oral therapy when the source of infection is controlled and a sustained clinical response has been achieved. The treatment duration depends on the source of infection, see the relevant topic e.g. UTI or intraabdominal infections.

If the source of infection remains unknown, but response to treatment is rapid, the patient is not immunocompromised and there is no deep-seated or uncontrolled site of infection, a total duration of 5 to 7 days of antibiotic treatment (IV and oral) is adequate.

Pseudomonas aeruginosa

Commonest sources (community- and healthcare-associated):

- urinary tract
- skin/soft tissue
- no diagnosed focus, including febrile neutropenia
- intravenous–device-associated infection
- biliary tract
- pneumonia.

Treat according to the results of susceptibility testing, when available. Until then, use:

gentamicin *IV, see 'Appendix 1: Gentamicin dosing' (page 381) for information on dosing frequency, maximum dose and maximum number of doses*

adult: 5 mg/kg (7 mg/kg in critical illness), see Table 14 for dosing frequency (page 384)

child 3 months and older: 7 mg/kg up to 560 mg, once daily

PLUS either

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

OR

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

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

gentamicin *(dosing as above)*

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.

Duration of therapy for *P. aeruginosa* bloodstream infection

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.

Infection with multidrug-resistant Gram-negative bacteria

Meropenem-resistant Gram-negative organisms (e.g. *E. coli*, *Klebsiella* species, *Enterobacter* species, *P. aeruginosa* or *A. baumannii*) are frequently multi-resistant to most available agents. Expert advice is required for the management of infection with these organisms.

For a patient with a presumed **urinary** source of infection (organism identified in urine and/or blood cultures) that is not associated with hypotension or immune compromise, potential options include a single dose of aminoglycoside (amikacin is preferred if the organism is susceptible) and either nitrofurantoin, trimethoprim+sulfamethoxazole or ciprofloxacin (based on the results of susceptibility testing).

For patients with infection from a presumed **non-urinary** source (i.e. the organism is identified in blood or from another sterile site) or the infection is in an immunocompromised patient, the initial option is to use an extended infusion of meropenem – seek expert advice.

Discuss treatment with an infectious disease physician or medical microbiologist.

Brucellosis

Brucellosis is an uncommon zoonosis. It typically presents with insidious onset of fever, malaise, night sweats and arthralgias. There may be associated weight loss, low back pain, headache, cough and depression. Examination findings are variable, but may include hepatomegaly (in 50% of cases), splenomegaly (30%) and/or lymphadenopathy. Anaemia (in 29% of cases), raised alanine transaminase (33%) altered white cell counts (relative lymphocytosis [24%], leucopenia or leucocytosis) or thrombocytopaenia (12%) may occur. Complications include infection involving one or more focal organ sites (e.g. bone and joint including the spine, genitourinary tract, cardiovascular system, brain or skin).

Laboratory confirmation of brucellosis requires serological testing for specific antibody and/or recovery of *Brucellae* from blood or tissue culture. Microbiology laboratories in Papua New Guinea are able to grow the organism.

Consult with an infectious diseases or medical microbiology specialist for advice on an appropriate treatment regimen and duration for confirmed cases. A long duration of treatment may be required (e.g. 3 to 6 months).

Candida species sepsis (candidaemia)

The commonest source is the urinary tract, and *Candida* is especially associated with urinary catheters. Intravascular central line infection is also important (the line may not appear infected). Patients may have no diagnosed primary source.

General considerations

- where possible remove the source of candidaemia (e.g. central venous catheter, urinary catheter)
- evaluate clinically for metastatic foci of infection initially and during treatment
- perform regular ophthalmoscopy to detect possible metastatic endophthalmitis
- repeat one set of blood cultures after 48 to 72 hours of treatment
- if endocarditis is suspected, perform a transthoracic cardiac echo (if available).

Metastatic complications of candidaemia include:

- endocarditis
- endophthalmitis (may require vitrectomy – seek urgent advice from an ophthalmologist, see **endophthalmitis** (page 125) in ‘Eye infections’
- abscesses.

Treatment of candidaemia

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.

When clinically improved switch to:

fluconazole 400 mg (child: 6 mg/kg up to 400 mg) orally, daily.

Duration of therapy for candidaemia

If there are no metastatic complications, continue treatment for 2 weeks after blood culture results are negative and signs and symptoms of infection have resolved.

If metastatic complications such as endophthalmitis or liver abscess are present, prolonged treatment is required (e.g. 4 to 6 weeks).

Intravascular line infections

Intravascular line infections are a common cause of preventable sepsis and mortality in hospitalised patients. Standard preventative practices are important – see Table 21: Measures to prevent intravascular device-associated infections, page 394 in 'Appendix 3: Prevention of intravascular-device associated infections.'

Sterile dressings are a standard of care for both central and peripheral intravenous lines.

Peripheral intravenous cannula infection

Peripheral intravenous cannulas (PIVC) in adults should be changed after 72 hours regardless of signs of infection or complication. PIVCs in children can remain for longer (maximum of 5 days).

Note that the cubital fossa is a site of higher risk for infection and should therefore be avoided. Remove/replace cubital fossa cannulae within 24 hours.

Any PIVC must be removed if any signs of local site infection are found. In the presence of sepsis of uncertain source, remove/replace PIVC if present for > 48 to 72 hours and change the intravenous giving set. PIVC-associated infection may also be caused by colonisation of the internal cannula lumen which is not associated with inflammation of the skin entry site.

Collect at least one peripherally collected blood culture set (20 mL blood total for adults). Do **not** collect blood via the existing intravenous line.

If there is purulent discharge at the PIVC entry site, collect a pus swab for microscopy and culture.

PIVC infections are usually due to methicillin-susceptible *S. aureus* (MSSA) or MRSA – modify treatment based on blood or entry site cultures, if available.

Associated bloodstream infections with *S. aureus* bacteraemia require longer treatment – see directed treatment earlier in this topic.

Empirical treatment of PIVC infection

Use:

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

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

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

If patient is known to be colonised with MRSA or for patients with **immediate severe** or **delayed severe** hypersensitivity to penicillins, use:

vancomycin *slow IV infusion,* ***consider a loading dose in critically ill adults and children****. See 'Appendix 2: Vancomycin dosing' (page 386) for information on loading dose, dosing frequency and infusion time*

adult ≥ 40 years: 15 mg/kg, see Table 18 for dosing frequency (page 390)

adult < 40 years 20 mg/kg, see Table 17 for dosing frequency (page 389)

child 3 months and older: 15 mg/kg, 6-hourly.

Modify therapy according to the results of culture and susceptibility testing and switch to oral therapy when the patient has clinically improved. If blood cultures are negative or are unavailable, use:

flucloxacillin *1 g (child: 25 mg/kg up to 1 g) orally, 6-hourly*

Alternatively, including for patients with **immediate nonsevere** or **delayed nonsevere** hypersensitivity to penicillins, use:

cefalexin *500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly.*

For patients treated with vancomycin, switch to:

trimethoprim+sulfamethoxazole *160+800 mg (child: 4+20 mg/kg up to 160+800 mg) orally, 12-hourly.*

Duration of therapy for PIVC infection

Treat for 5 to 7 days (IV + oral), unless there is an associated bloodstream infection with *S. aureus* – see ***S. aureus* bacteraemia**, page 253 in this topic.

Haemodialysis/central line infection

Patients can present with clinical sepsis in the presence of a haemodialysis line or a central line. Note that the entry site of an infected line may not appear inflamed.

Take two sets of blood for culture before starting antibiotics. Take blood for cultures peripherally **not** from the line, as collecting from the line increases the risk of contamination during collection.

If there is purulent discharge at the intravenous entry site, send a swab to the laboratory for microscopy and culture.

Where possible, remove the line.

Lines infected with *Staphylococcus aureus*, *Pseudomonas* species or *Candida* species **must** be removed.

Management of central line infection

For patients with a central line (who are not receiving haemodialysis), use:

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

PLUS

gentamicin *IV, see Appendix 1: Gentamicin dosing (page 381) for information on dosing frequency, maximum dose and maximum number of doses*

adult: 5 mg/kg (7 mg/kg in critical illness), see Table 14 for dosing frequency (page 384)

child 3 months and older: 7 mg/kg up to 560 mg, once daily.

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

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

For patients with **immediate severe** or **delayed severe** hypersensitivity to penicillins or if methicillin-resistant *S. aureus* (MRSA) is identified, switch to:

vancomycin *slow IV infusion,* ***consider a loading dose in critically ill adults and children****. See 'Appendix 2: Vancomycin dosing' (page 386) for information on loading dose, dosing frequency and infusion time*

adult ≥ 40 years: 15 mg/kg, see Table 18 for dosing frequency (page 390)

adult < 40 years 20 mg/kg, see Table 17 for dosing frequency (page 389)

child 3 months and older: 15 mg/kg, 6-hourly.

Modify therapy according to the results of culture and susceptibility testing.

Duration of therapy

If there is rapid clinical improvement after removal of the line, treat for 5 to 7 days.

Associated bloodstream infections with *S. aureus* or Candida species require longer durations – see directed therapy for **S. aureus bacteraemia** (page 253) and **Candida species sepsis** (page 262) in this topic.

Management of haemodialysis access infection

For patients on haemodialysis, use:

cefazolin *2 g (child: 50 mg/kg up to 2 g) IV,* ***post dialysis*** *(3 times weekly on dialysis days)*

PLUS

gentamicin*, as a single dose as per Table 14 (page 384) in 'Appendix 1: Gentamicin dosing.'*

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

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

If methicillin-resistant *S. aureus* (MRSA) is identified, switch flucloxacillin or cefazolin to:

vancomycin *slow IV infusion,* ***consider a loading dose in critically ill adults and children****. See 'Appendix 2: Vancomycin dosing' (page 386) for information on loading dose, dosing frequency and infusion time*

adult ≥ 40 years: 15 mg/kg, see Table 18 for dosing frequency (page 390)

adult < 40 years 20 mg/kg, see Table 17 for dosing frequency (page 389)

child 3 months and older: 15 mg/kg, 6-hourly.

Modify therapy according to the results of culture and susceptibility testing.

Duration of therapy

If there is rapid clinical improvement after removal of the line, treat for 5 to 7 days.

Associated bloodstream infections with *S. aureus* or Candida species require longer durations – see directed therapy for ***S. aureus* bacteraemia in patients on dialysis** (page 256) and ***Candida* species sepsis** (page 262) in this topic.

Key additional resources

Fact sheet: Lactate in the deteriorating patient and sepsis. Australian Commission on Safety and Quality in Health Care (ACSQHC). 2022. Available from : https://www.safetyandquality.gov.au/sites/default/files/2022-06/lactate_in_the_deteriorating_patient_-_sepsis_clinical_care_standard.pdf

Microbiology documents. PNG Diagnostic Pathology Laboratories. Available from: http://path-png.org

WHO Fact Sheet: Sepsis. World Health Organization; July 2023. Available from: https://www.who.int/news-room/fact-sheets/detail/sepsis#:~:text=Sepsis%20is%20a%20life%2Dthreatening,multiple%20organ%20failure%20and%20death.

Diego-Yagüe I, Mora-Vargas A, Vázquez-Comendador JM, Santamarina-Alcantud B, Fernández-Cruz A, Múñez-Rubio E, Gutiérrez-Villanueva A, Sanchez-Romero I, Moreno-Torres V, Ramos-Martínez A, Calderón-Parra J. Sequential oral antibiotic in uncomplicated Staphylococcus aureus bacteraemia: a propensity-matched cohort analysis. Clin Microbiol Infect. 2023 Jun;29(6):744-750.

Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith C, French C, et al. Surviving Sepsis Campaign Guidelines 2021. Intensive Care Med 2021; 47(11):1181-1247.

Ferguson JK. Historical data from bacteraemic cases in patients at Hunter New England Health Service (personal communication, 2023).

Gavelli F, Castello L, Avanzi G. Management of sepsis and septic shock in the emergency department. Intern Emerg Med 2021; 16(6):1649-1661.

Harris PNA, Tambyah PA, Lye DC, Mo Y, Lee TH, Yilmaz M, et al. Effect of Piperacillin-Tazobactam vs Meropenem on 30-Day Mortality for Patients With E coli or Klebsiella pneumoniae Bloodstream Infection and Ceftriaxone Resistance: A Randomized Clinical Trial. JAMA 2018;320(10):984-94

Skin infections

This topic includes advice on the management of the following conditions in adults and children older than 3 months:

- bacterial skin infections
  - **impetigo**, page 270
  - **folliculitis, boils, carbuncles and skin abscesses**, page 272
  - **cellulitis and erysipelas**, page 273
  - **yaws**, page 276
  - **Buruli ulcer**, page 277
  - **leprosy**, page 278
- Viral skin infections
  - **herpes simplex virus infections** including oral mucocutaneous herpes and eczema herpeticum, page 279
  - **varicella-zoster virus infections** including varicella infection (chickenpox) and shingles (herpes zoster), page 281
- fungal skin infections
  - **tinea** including tinea of the trunk, limbs, face, fingers or toes, tinea capitis and kerion, onychomycosis (tinea of the nails) and tinea imbricata (grille), page 284
  - **cutaneous candidiasis**, page 288
  - **pityriasis versicolor** (tinea versicolor), page 289
- Insect and mite infestations
  - **lice** including head lice, body lice and pubic lice, page 290
  - **scabies** including non-crusted scabies and crusted scabies, page 292
  - **cutaneous larva migrans**, page 295
  - **filariasis**, page 296**.**

The following topic is not included in this section:

- **skin pustules in neonates and young infants** (page 210) in 'Infections in neonates and young infants.'

Other guidelines:

- *Guidelines for the Diagnosis, Treatment and Prevention of Leprosy* (WHO)

Bacterial skin infections

Impetigo

Impetigo

Impetigo is a superficial bacterial skin infection most often caused by *Streptococcus pyogenes* or *Staphylococcus aureus*. Children may also present with multiple crusting sores, usually on the face.

Nonbullous impetigo arises on the face, especially around the nares, or the extremities. It starts as erythematous papules that become vesicles, and then pustules that rupture and lead to honey-coloured crusted lesions on an erythematous base.

Bullous impetigo is characterised by the progression of vesicles to flaccid bullae that rupture easily, then become crusted. It is usually caused by *S. aureus*. Adults with bullous impetigo should be tested for human immunodeficiency virus.

Swab exudate for culture in patients that are not improving on empirical therapy. If any of the sores are raised, consider yaws as a possible cause – see **yaws** (page 276).

Treat scabies or head lice if present – see **scabies** (page 292) or **head lice** (page 290), in this topic.

Consider congenital syphilis in babies with a red rash, grey patches or flaccid bullous lesions associated with skin peeling off on their palms or under the soles of their feet – see **neonatal syphilis prophylaxis/treatment**, page 214 in 'Infections in neonates and young infants' for management.

It is important to eradicate streptococcus in order to minimise the risk of post-streptococcal diseases and transmission to other children.

Impetigo is contagious, requiring careful attention to hygiene. Advise patients/carers to:

- keep draining (discharging) lesions covered
- wash hands frequently
- keep fingernails cut short
- hot wash clothing, bedding and towels
- avoid sharing towels or face cloths
- avoid close contact with others until lesions have crusted over or the person has received at least 24 hours of treatment.

Staphylococcal scalded skin syndrome (SSSS) is a rare complication of localised infection caused by toxigenic strains of *S. aureus*. SSSS is predominantly seen in children younger than 5 years but cases have also been reported in older children and adults who are immunocompromised or who have severe renal impairment/chronic renal disease. It is characterised by the detachment of the outermost skin layer (epidermis) with the blistering of large areas of skin giving the appearance of a burn or scalding. A skin biopsy can help differentiate SSSS from toxic epidermal necrolysis.

Close observation, intravenous fluid resuscitation, pain relief and antibiotics are required. Seek appropriate advice for antibiotic choice; empirical therapy should treat both methicillin-susceptible and methicillin-resistant *S. aureus*. Where possible, manage patients in a high-dependency unit or ICU where close monitoring is possible.

Management of impetigo

Manage all impetigo by cleaning skin with soap and water. Crusts should be **gently** removed as causative organisms are hard to eradicate when crusts are present; however, advise patients and carers not to pick the crusts as this often results in wounds taking longer to heal and may sometimes cause scarring.

Topical antiseptics (e.g. chlorhexidine cream [such as Savlon] or gentian violet[16]) can be applied to the sores 2 to 3 times per day for 5 to 7 days.

For patients who have localised skin sores, topical antibiotics may be used if antiseptics do not work or are inappropriate (e.g. impetigo around the eyes). Use:

fusidic acid 2% ointment topically to crusted areas, two or three times daily for 5 days.

For moderate to severe disease (multiple skin sores or recurrent infection), use:

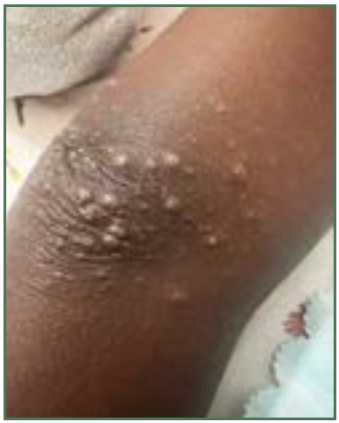
***flucloxacillin** 500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly for 7 days.*

Alternatively, including for patients with hypersensitivity to penicillins, use:

***trimethoprim+sulfamethoxazole** 160+800 mg (child: 4+20 mg/kg up to 160+800 mg) orally, 12-hourly for 3 days.*

16 Advise patients or carers to avoid applying gentian violet near the eyes.

Folliculitis, boils, carbuncles and skin abscesses



Folliculitis

Folliculitis is the inflammation of a hair follicle that presents as pustules. A boil (or furuncle) is a simple subcutaneous abscess. Carbuncles are deeper and wider lesions with interconnecting tracts from neighbouring hair follicles and present with multiple draining sinuses.

Boils and carbuncles are tender, painful and may be warm to the touch, but seldom cause systemic symptoms. In a patient with fever or spreading skin erythema, treat as for cellulitis – see next section.

The main pathogens are *Staphylococcus aureus* and *Streptococcus pyogenes.*

If pus is present (i.e. the boil is fluctuant), the treatment is incision and drainage. Antibiotics are not usually required for abscesses < 5 cm in diameter. Consider adjunctive antibiotic treatment for abscesses with a diameter ≥ 5 cm in diameter, where surgical drainage is incomplete (including for multiple boils) or of there is associated cellulitis.

If the patient is systemically unwell, treat as cellulitis. Consider osteomyelitis in a febrile patient with a hot, swollen and tender limb – see **long-bone osteomyelitis** in adults (page 40) and children (page 48) in 'Bone and joint infections.'

If a patient has signs of sepsis, see ***S. aureus* bacteraemia**, page 253 in 'Sepsis and bloodstream infections.'

Management of folliculitis, boils, carbuncles and skin abscesses

Send pus for culture. If systemically unwell, send blood for culture.

Incision and drainage is the key treatment for boils and carbuncles.

After adequate incision and drainage, if antibiotics are required, give:

flucloxacillin *1 g (child: 25 mg/kg up to 1 g) orally, 6-hourly.*

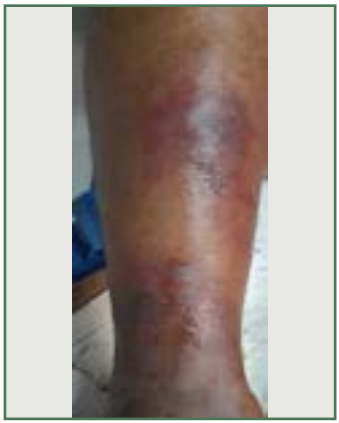
Alternatively, including for patients with hypersensitivity to penicillins, use:

trimethoprim+sulfamethoxazole *160+800 mg (child 4+20 mg/kg up to 160+800 mg) orally, 12-hourly.*

Duration

Treat for 5 to 7 days. Stop therapy earlier if infection has resolved.

Cellulitis and erysipelas



Cellulitis

In patients with cellulitis involving or surrounding an eye, see **periorbital (preseptal) and orbital cellulitis**, page 130 in 'Eye infections.'

Erysipelas is a superficial form of cellulitis affecting the upper dermis of the skin. It presents as a bright red, firm swelling with a clear line of demarcation between infected and noninfected tissue. Erysipelas mainly affects the lower limbs and face (often in a butterfly pattern). It is almost always caused by *S. pyogenes* (group A streptococcus).

Cellulitis is a common infection of the deep dermis and subcutaneous tissue. It presents as diffuse, spreading areas of skin erythema. Swelling, warmth, pain and fever or other systemic features may be present. *S. pyogenes*, or another *Streptococcus* species (e.g. group B, C or G), is the most common cause of nonpurulent recurrent cellulitis (e.g. associated with lymphoedema) or spontaneous, rapidly spreading cellulitis. Cellulitis caused by *S. aureus* (including methicillin-resistant strains [MRSA]) is less frequent and is often associated with penetrating trauma or ulceration. Purulent cellulitis (e.g. associated pustules or abscesses) is typically caused by *S. aureus*.

Treat predisposing factors for cellulitis such as tinea infection of the feet, lymphoedema and fissured dermatitis, if present to prevent recurrence. Consider testing for diabetes, and check glycaemic control in people known to have diabetes.

Incise and drain any abscesses. Rest and elevation of the affected area improves clinical response.

Send blood specimens for culture in patients that are systemically unwell and send swabs of pus for culture, if this is present.

In patients with septic shock, treat as for **necrotising soft tissue infections**, page 307 in 'Soft tissue infections.' Other features suggestive of necrotising fasciitis include:

- severe pain out of keeping with the apparent severity of infection
- rapid progression
- marked systemic features (e.g. high fever with rigors, tachycardia, tachypnoea, hypotension, confusion, vomiting).

Management of cellulitis and erysipelas

Mild cellulitis

Soft-tissue redness, warmth and swelling, pain or tenderness but no systemic features or significant comorbidities.

Use:

flucloxacillin *1 g (child: 25 mg/kg up to 1 g) orally, 6- hourly.*

Alternatively, including for patients with hypersensitivity to penicillins, use:

trimethoprim+sulfamethoxazole *160+800 mg (child 4+20 mg/kg up to 160+800 mg) orally, 12-hourly.*

Duration: Treat for 5 to 7 days.

It is usually appropriate to stop antibiotic therapy after 5 days, even if mild signs of inflammation remain; extend therapy if the infection has not clinically improved by the end of the treatment course.

Moderate to severe cellulitis

In addition to moderate swelling and tenderness, two or more systemic features e.g. temperature < 36 °C or > 38 °C, tachycardia (> 90 bpm), respiratory rate > 20 breaths per minute.

Assess patients for necrotising fasciitis or myonecrosis.

Patients with hypotension, septic shock or rapid progression of systemic features require broad-spectrum antibiotics – treat as for **necrotising soft tissue infection**, page 307 in 'Soft tissue infections.'

Urgently refer the patient to a higher level of health facility if very sick or not improving after 48 hours of standard treatment.

Rest and elevation of the affected area are important to improve the clinical response.

Use:

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

Alternatively, including in patients with **immediate nonsevere** or **delayed nonsevere** hypersensitivity to penicillins, use:

cefazolin *2 g (child 50 mg/kg up to 2 g) IV, 8-hourly.*

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

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

cont...

Switch to oral therapy as per mild cellulitis when systemic features have improved.

Local symptoms (e.g. erythematous rash) can worsen for up to 48 hours after effective therapy is started, but systemic features should improve. If systemic features do **not** improve after 48 to 72 hours of therapy, consider escalation of therapy. **Add**:

vancomycin *slow IV infusion,* ***consider a loading dose in critically ill adults and children****. See 'Appendix 2: Vancomycin dosing' (page 386) for information on loading dose, dosing frequency and infusion time*

adult ≥ 40 years: 15 mg/kg, see Table 18 for dosing frequency (page 390)

adult < 40 years 20 mg/kg, see Table 17 for dosing frequency (page 389)

child 3 months and older: 15 mg/kg, 6-hourly

OR (if vancomycin is not available), **add** to flucloxacillin or cefazolin:

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

Duration: Treat for a total of 7 to 10 days (IV + oral).

Cellulitis following water exposure

This refers to cellulitis that arises following exposure to water, as there is an increased risk of other organisms causing infection, e.g. *Aeromonas* species following fresh water or brackish water (slightly salty water e.g. in estuaries where a river meets the sea) exposure or *Vibrio* species following salt water (seawater) exposure.

This does not refer to water exposure from bathing in patients with existing cellulitis.

For cellulitis following water exposure that is not responding to empirical therapy, add an additional agent to the empirical regimen.

If fresh/brackish water exposure, **add**:

ciprofloxacin *500 mg (child: 10 mg/kg up to 500 mg) orally, 12-hourly.*

If saltwater exposure, **add**:

doxycycline *100 mg (child: 2 mg/kg up to 100 mg[17]) orally, 12-hourly*

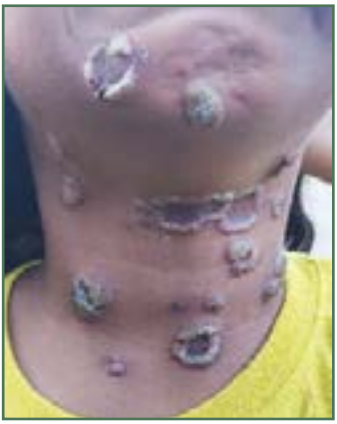
OR

ciprofloxacin *500 mg (child: 10 mg/kg up to 500 mg) orally, 12-hourly.*

Duration: The duration of therapy is determined by clinical response. For empirical therapy for localised infection, a duration of 5 days is likely to be appropriate.

17 Unlike older tetracyclines, doxycycline has not been associated with tooth discolouration, enamel hypoplasia or bone deposition with short-term use (< 21 days), even in children younger than 8 years, so is increasingly used in this age group. However, use may be limited by the lack of a suitable paediatric formulation.

Yaws



Yaws

Yaws is a skin infection caused by *Treponemal pallidum* subspecies *pertenue*, which is transmitted by skin-to-skin contact. Yaws is not known to cause congenital infection.

T. pallidum pertenue mostly causes a self-limiting primary infection with papules that enlarge into wart-like lesions with superficial erosion that heal spontaneously within 6 months. Weeks to months later, a generalised eruption of similar skin lesions occurs via haematogenous or lymphatic spread, and multiple relapses occur in the first 5 years.

Typically, lesions are painless, raised and reddish brown with a yellow crust. Yaws can be complicated by periostitis or paranasal maxillary erosions.

A recent study in Papua New Guinea found that *Haemophilus ducreyi* is a potential causative agent in chronic skin ulcers in children and young adults. While more commonly associated with sexual transmission, non-sexual transmission of *H. ducreyi* has also been described and co-infection with yaws is possible. For treatment, see **chancroid** (page 169) in 'Genital and sexually transmissible infections.'

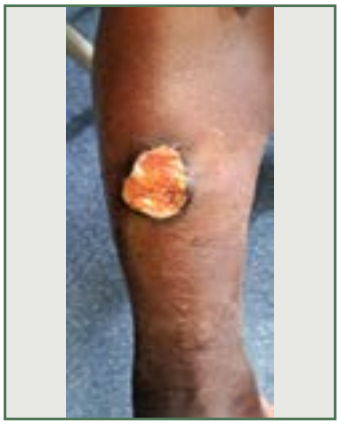
While syphilis serology can be used to assist in the diagnosis of yaws, serology cannot distinguish between the organisms that cause syphilis and yaws.

Polymerase chain reaction (PCR) testing for yaws is not currently available in Papua New Guinea. Rapid diagnostic tests (RDT) for yaws are available and are the recommended method of confirming infection.

Repeat testing with a nontreponemal RDT (e.g. RPR or Dual Path) should be performed 6 and 12 months following treatment; a four-fold decrease in titre should occur within 12 months of successful treatment.

Treatment of yaws
Use: ***azithromycin*** *30 mg/kg (maximum dose 2 g) orally, as a single dose.* Alternatively, use: ***benzathine benzylpenicillin*** *1.2 million units (child < 20 kg: 0.6 million units) IM, as a single dose.*

Buruli ulcer



Buruli ulcer

Buruli ulcer (caused by *Mycobacterium ulcerans*) is a chronic debilitating infection, often affecting the skin and sometimes bone, which can lead to permanent disfigurement and long-term disability. The mode of transmission is not known and there is no prevention for the disease.

Buruli ulcers usually begin as a painless dermal papule or subcutaneous swelling (nodule), a large painless area of induration (plaque) or a diffuse painless swelling of the legs, arms or face (oedema). The disease may progress with no pain and fever. Without treatment or sometimes during antibiotic treatment, the nodule, plaque or oedema will ulcerate within 4 weeks. Bone is occasionally affected, causing deformities.

Differential diagnoses should include extensive ulcerative yaws and ulcers caused by *Haemophilus ducreyi*.

Seek expert advice for diagnosis and treatment of Buruli ulcer.

Four standard laboratory methods can be used to aid in diagnosis of Buruli ulcer: PCR, direct microscopy, histopathology and culture. Send swabs and fine-needle aspiration sample to the lab for microscopy for acid-fast bacilli and seek advice from a medical microbiologist – PCR by referral may be possible.

The disease has been classified into three categories of severity:

- category I single small lesion less than 5 cm in diameter (32% of cases)
- category II non-ulcerative and ulcerative plaque and oedematous forms between 5 and 15 cm (35% of cases)
- category III lesions more than 15 cm in diameter including, disseminated and mixed forms such as osteomyelitis and joint involvement (33% of cases).

Treatment of Buruli ulcer

Treatment consists of a combination of antibiotics and other treatments; detailed guidance for health workers can be found in the WHO publication *Treatment of Mycobacterium ulcerans disease (Buruli ulcer).*

Recommended antibiotic treatment is:

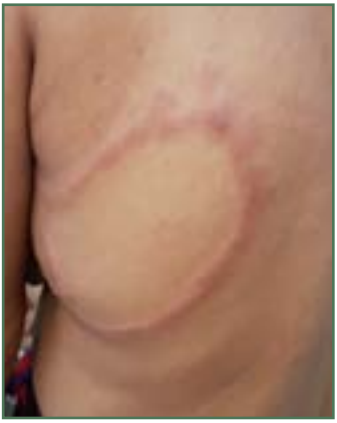
rifampicin *(adult and child) 10 mg/kg up to 600 mg orally, daily for 8 weeks*

PLUS

clarithromycin *500 mg (child: 7.5 mg/kg up to 500 mg) orally, 12-hourly for 8 weeks.*

Surgery may be necessary to remove necrotic tissue, cover skin defects, and correct deformities.

Leprosy



Leprosy

Details of the diagnosis and management of leprosy is beyond the scope of these guidelines. For more information on leprosy, see the WHO *Guidelines for the Diagnosis, Treatment and Prevention of Leprosy*.

Refer any person with suspected leprosy to a tuberculosis (TB)/Leprosy Program Officer.

Leprosy is a chronic bacterial infection primarily affecting the skin and peripheral nerves usually caused by *Mycobacterium leprae*. The most common first symptom noticed is numbness, which may precede the development of cutaneous lesions by years. The initial skin lesions are usually of the indeterminate type, presenting as a solitary or small number of hypopigmented patches.

Infection can present at any age, although it is rarely seen in infants and young children.

Leprosy should be included in the differential diagnosis of hypopigmented patches on the skin, particularly if the patient experiences diminished or altered sensation.

Transmission: The disease is transmitted through droplets from the nose and mouth. Prolonged, close contact over months with someone with untreated leprosy is needed to catch the disease. The disease is not spread through casual contact with a person who has leprosy, such as shaking hands or hugging, sharing meals or sitting next to each other. Moreover, the patient stops transmitting the disease when they begin treatment.

Diagnosis: The diagnosis of leprosy is done clinically. Laboratory-based services may be required in cases that are difficult to diagnose.

The disease manifests commonly through skin lesion and peripheral nerve involvement. Leprosy is diagnosed by finding at least one of the following **three cardinal signs**:

- definite loss of sensation in a pale (hypopigmented) or reddish skin patch; (including nodules and thickened skin lesions in multibacillary cases)
- thickened or enlarged peripheral nerve, with loss of sensation and/or weakness of the muscles supplied by that nerve
- microscopic detection of bacilli in a slit-skin smear.

Treatment: Leprosy is curable with multidrug therapy. Apart from the physical deformity, people affected by leprosy also face stigmatisation and discrimination. Early diagnosis and treatment can prevent disability. Refer any patient with suspected leprosy to a TB/Leprosy Program Officer.

Viral skin infections

Herpes simplex virus infections

See also: **encephalitis**, page 87 in 'CNS infections,' **dendritic corneal ulceration**, page 132 in 'Eye infections,' **genital herpes**, page 168 in 'Genital and sexually transmissible infections' or for neonates **herpes simplex virus prophylaxis/ treatment**, page 215 in 'Infections in neonates and young infants.'

Oral mucocutaneous herpes

Recurrent oral mucocutaneous herpes simplex virus (HSV) infection is common in children and adults. The primary episode generally occurs in childhood and may be associated with fever and lymphadenopathy.

Recurrent episodes are usually mild and infrequent. Lesions are usually preceded by pain, burning, or tingling for several hours to days (prodromal stage). The lesions begin as macules and rapidly become papular with vesicles appearing within 48 hours and scabs within 3 to 4 days.

Antiviral treatment is effective if started within 48 hours of symptoms.

See *Papua New Guinea National Guidelines for HIV Care and Treatment* for long-term suppression in patients living with HIV.

Management of acute oral mucocutaneous herpes

A barrier cream (e.g. petroleum jelly) applied to the lips can help prevent adhesions.

Mild: Symptomatic management (e.g. barrier cream) only.

Moderate to severe, use:

aciclovir 200 mg (child: 10 mg/kg up to 200 mg) orally, ***five times daily*** *for 7 days.*

Long-term suppression

Consider long-term suppression in patients with frequent disabling recurrences, erythema multiforme, or in immunocompromised patients.

Use:

aciclovir 400 mg orally, 12-hourly for up to 6 months.

Consider higher doses if prophylaxis unsuccessful.

Eczema herpeticum

Eczema herpeticum is a disseminated viral skin infection, usually caused by HSV-1 or HSV-2. It often complicates active or recently healed atopic dermatitis.

It presents with an acute eruption of itchy, painful vesicles or multiple crusted erosions in an area of dermatitis and may be associated with fever, lymphadenopathy and/or malaise.

Presentation of eczema herpeticum in children is more likely to be severe than in adults; hospitalisation may be required if the eruption is generalised.

Clinical diagnosis can be challenging; most diagnosis is based on experience.

Treatment of eczema herpeticum

Take swabs for culture to rule out bacterial infection, as this condition resembles impetigo.

Consult an ophthalmologist if the eyes are involved.

Prompt antiviral therapy is indicated while awaiting culture results, use:

aciclovir 400 mg (child 10 mg/kg) orally, 8-hourly.

For disseminated disease or for patients unable to tolerate oral therapy, use:

aciclovir 10 mg/kg IV, 8-hourly.

If intravenous aciclovir is not available, use a higher dose of tablets orally or via nasogastric tube (NGT):

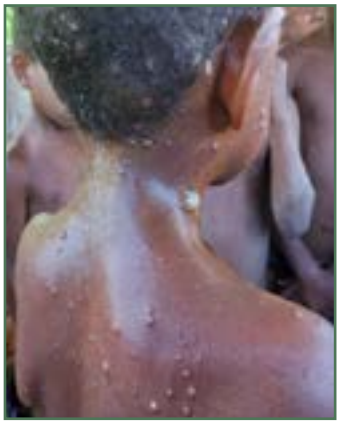
aciclovir 800 mg (child: 20 mg/kg up to 800 mg), orally or via NGT, ***5 times daily****.*

If secondary bacterial infection is present, treat as cellulitis.

Duration

Treat for 7 to 10 days. Extend duration if lesions have not healed or crusted by day 10.

Varicella-zoster virus infections



Varicella (chickenpox)

Varicella infection (chickenpox)

Neonates are at increased risk of severe disease – see page 216 in 'Infections in neonates and young infants' for management.

Chickenpox is caused by primary infection with the varicella-zoster virus and usually presents with a pruritic, vesicular rash that later crusts.

Most cases occur in children. Chickenpox is usually more severe in adults; if chickenpox is suspected or diagnosed in an adult, rule out causes of immunocompromise such as HIV. Perinatal infection may put babies at risk of infection if the mother develops chickenpox just before delivery or during the 28 days after delivery.

Chickenpox is highly contagious and is easily spread from person to person by breathing in airborne respiratory droplets from an infected person's coughing or sneezing or through direct contact with the fluid from the open sores. A person with chickenpox is contagious 1 to 2 days before the rash appears and until all the blisters have formed scabs; advise patients to avoid contact with anyone who is immunocompromised or pregnant during this period.

Most patients do not require treatment.

In healthy children, chickenpox infection is usually an uncomplicated, self-limiting disease. Complications may include:

- secondary bacterial infection of skin lesions caused by scratching
  - infection may lead to abscess, cellulitis, necrotising fasciitis and gangrene
- dehydration from vomiting and diarrhoea
- exacerbation of asthma
- viral pneumonia
- chickenpox lesions may heal with scarring.

Some complications are more commonly seen in immunocompromised and adult patients with chickenpox:

- disseminated primary varicella infection; this carries high morbidity
- central nervous system complications such as Reye's syndrome, Guillain–Barré syndrome and encephalitis
- thrombocytopenia and purpura.

For patients with secondary bacterial infection, see **cellulitis**, page 273 in this topic or **necrotising soft tissue infections**, page 307 in 'Soft tissue infections,' for management recommendations.

Management of varicella (chickenpox)

Most healthy patients with chickenpox only require symptomatic management. This may include:

- trimming children's fingernails to minimise scratching
- paracetamol to reduce fever and pain
- calamine lotion and/or oral antihistamines to relieve itching.

Give oral antiviral treatment to immunocompromised patients with mild symptoms and all pregnant women who have presented within 72 hours of rash onset. Use:

aciclovir 800 mg (child: 20 mg/kg up to 800 mg) orally, ***5 times daily****.*

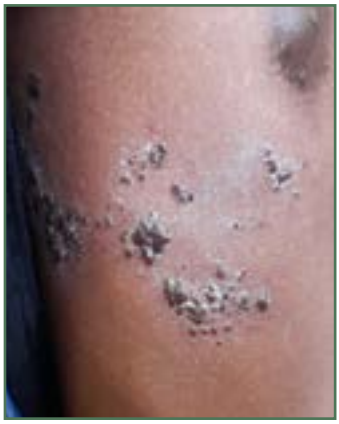
Give intravenous antiviral treatment to patients with severe disease or complicated disease (e.g. pneumonitis, encephalitis, or hepatitis) irrespective of the duration of rash. Use:

aciclovir 10 mg/kg (child 12 years or younger: 500 mg/m^2) IV, 8-hourly.

Switch to oral aciclovir after clinical improvement.

Duration: Treat for 7 days (IV + oral). In those with slow improvement and for those with significant immune compromise, therapy may be required for a total of up to 14 days.

Shingles (herpes zoster)



Shingles (herpes zoster)

Shingles (herpes zoster) is caused by reactivation of the varicella-zoster virus (chickenpox virus). Shingles and its complications can be prevented by vaccination. The shingles vaccine is recommended for older adults and immunocompromised people, even if the person has previously had shingles. The vaccine is not on the Medical and Dental Catalogue but may be available from private healthcare providers.

Shingles is characterised by unilateral dermatomal pain, with a vesicular rash on an erythematous base in a dermatomal distribution. It is more common in older adults, can be haemorrhagic in immunocompromised patients, and may be complicated by postherpetic neuralgia. Management of this complication is more likely to be successful if analgesia is commenced early.

If secondary bacterial infection is present treat as **cellulitis**, see page 273 in this topic.

Test for HIV in disseminated disease, see *Papua New Guinea National Guidelines for HIV Care and Treatment* for management.

Postherpetic neuralgia

Postherpetic neuralgia is pain persisting for at least 3 months after shingles (herpes zoster) infection. It occurs in about 10% of all patients with shingles, and in over 70% of patients older than 50 years.

Consider using an oral adjuvant (e.g. amitriptyline), see *PNG Adult Standard Treatment Manual* for further information on managing post-herpetic neuralgia.

Shingles management

If the rash has been present for less than 72 hours, antiviral treatment reduces acute pain, duration of the rash, viral shedding and ocular complications.

Treat nociceptive shingles pain with oral paracetamol or nonsteroidal anti-inflammatory drugs. In **adults**, an oral corticosteroid can be added for moderate to severe pain; use:

prednisolone 50 mg orally, once daily in the morning for 7 days.

Antiviral treatment is indicated for immunocompetent adults and adolescents who present within 72 hours of rash onset and for all immunocompromised patients **regardless of the duration of the rash**.

In children, herpes zoster (shingles) is generally less painful and most children do not require treatment. However, treat all immunocompromised children and children with severe or rapidly progressing infection.

If oral antiviral treatment is indicated, use:

aciclovir 800 mg (child: 20 mg/kg up to 800 mg), orally 5 times daily for 7 days.

Shingles management for immunocompromised patients or those with disseminated disease

Admit to hospital and use:

aciclovir 10 mg/kg (child < 5 years: 20 mg/kg) IV, 8-hourly.

Change to oral therapy (as above) when clinically improving and treat for a total of 10 to 14 days (IV + oral).

Fungal skin infections

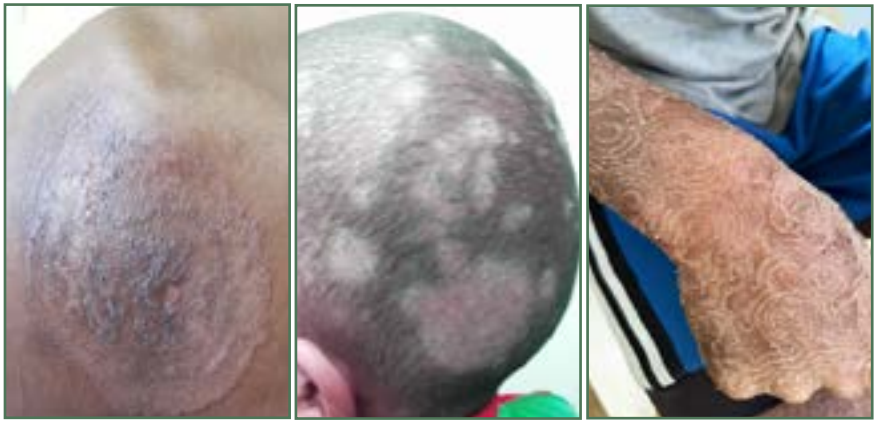
Conducting a potassium hydroxide (KOH) test on a skin scraping, if available, can be useful to assist in the diagnosis and differentiation of fungal skin infections. If the diagnosis remains uncertain, send a skin scraping to the laboratory for microscopy and/or culture.

Tinea

Tinea (ringworm) is caused by dermatophytes, which can infect the skin, scalp or nails. The typical rash is annular (ring-shaped), itchy and scaly with a definite edge and central clearing.

Topical antifungal therapy is appropriate for recent onset of localised tinea affecting the trunk (including groin), limbs, face, or between the fingers or toes. Tinea of the scalp (tinea capitis), including kerion, and tinea of the nails (onychomycosis) require treatment with oral antifungals.

Onychomycosis (tinea of the nails)



Left: tinea corporis, middle: tinea capitis, right: tinea imbricata (grille)

If the diagnosis is uncertain, take a skin scraping and send to the laboratory for microscopy and culture, prior to antifungal treatment.

In tinea pedis, keep feet dry, particularly between toes (advise patients to dry meticulously after bathing), avoid wearing occlusive footwear for long periods and dry footwear in the sun.

Advise all patients to:

- bath daily and wear clean clothes
- avoid sharing towel/clothes and sheets
- investigate household contacts, pets and farm animals for evidence of infection and treat appropriately, if required.

Treatment of tinea of the trunk, limbs, face, fingers or toes

Tinea corporis: dermatophyte infection of skin excluding palms, soles, groin, and face.

Tinea cruris: dermatophyte infection of inguinal area and crural fold.

Tinea pedis: dermatophyte infection of feet.

Tinea manuum: dermatophyte infection of hand.

Use:

miconazole 2% cream topically, twice daily for 2 to 4 weeks

OR

terbinafine 1% cream topically, once or twice daily for 7 to 14 days.

Use oral antifungal therapy for tinea that is widespread or established, has not responded to topical antifungal therapy or recurs soon after treatment, is on the scalp, palms or soles, is inflammatory, hyperkeratotic, vesicular or pustular. Use:

*fluconazole 150 mg orally, once **weekly**.*

Duration

Topical therapy: Topical azoles should be continued for 2 weeks after the fungal rash disappears (usually 2 to 4 weeks in total). Topical terbinafine allows a shorter duration of treatment.

Oral therapy: Treat for 2 to 6 weeks depending on severity. Monitor liver function weekly.

Treatment of tinea capitis and kerion

Tinea capitis: dermatophyte infection of hair and scalp. Predominantly affects children.

Kerion: an inflammatory abscess, especially on the scalp, caused by dermatophyte fungal infection. Often associated with alopecia.

To confirm diagnosis, send skin scrapings and hair for microscopy.

Higher doses of oral antifungal drugs are usually used in tinea of the scalp compared to tinea elsewhere. Topical antifungal therapy is ineffective.

Bacterial superinfection in kerion is common – if suspected, take a swab for microscopy and bacterial culture. Commence antibiotics as for cellulitis if indicated.

Use:

griseofulvin 20 mg/kg (up to 500 mg) orally, once daily for 6 to 8 weeks

OR

terbinafine 250 mg (child less than 20 kg: 62.5 mg; child 20 to 40 kg: 125 mg) orally, once daily for 4 weeks.

Ketoconazole or selenium sulfide shampoos reduce spore shedding. They are ineffective when used alone but can be used as an adjunct to therapy.

Onychomycosis (tinea of the nails)

Most commonly cause by dermatophytes (e.g. *Trichophyton rubrum*, *T. mentagrophytes* var. *interdigitale*).

Many disorders mimic onychomycosis. Ideally, diagnosis should be confirmed by microbiology before starting treatment.

Onychomycosis needs oral antifungal treatment. Use:

terbinafine 250 mg (child less than 20 kg: 62.5 mg; child 20 to 40 kg: 125 mg) orally, once daily for 12 weeks for toenails or 6 weeks for fingernails

OR

fluconazole 150 to 300 mg orally, once weekly for 24 to 52 weeks for toenails and 12 to 24 weeks for fingernails.

For onychomycosis in pregnant women, initiate treatment after delivery, if possible, due to limited safety information of oral antifungal agents in pregnancy.

Duration

Onychomycosis is frequently chronic and may be hard to treat. Most nails with extensive onychomycosis still look abnormal after 3 months' treatment, as a new nail takes up to 9 months to grow.

For moderate to severe onychomycosis, give a second course if healthy clear nail starts to appear at the proximal (posterior) nail fold after one course of treatment. If no clear nail appears after one course of treatment, refer to an expert.

Tinea imbricata (grille)

A variant of tinea corporis caused by *Trichophyton concentricum.*

Advise all patients to clean their skin with soap and water daily.

Treat with an oral antifungal, use:

terbinafine 250 mg (child less than 20 kg: 62.5 mg; child 20 to 40 kg: 125 mg) orally, once daily for 1 to 4 weeks according to patient response

OR

griseofulvin 20 mg/kg (up to 500 mg) orally, once daily for 2 to 4 weeks according to patient response.

Add a keratolytic agent to oral antifungal treatment:

Whitfield's ointment (3% salicylic acid, 6% benzoic acid) topically, once daily for 4 weeks.

In children, Whitfield's ointment should be applied to no more than one-quarter of the body on any one day and should not applied to the face.

Cutaneous candidiasis

See also **candida vulvovaginitis**, page 164 in 'Genital and sexually transmissible infections;' **oral candidiasis**, page 137 and **oesophageal candidiasis**, page 139 in 'Gastrointestinal infections.'

Candida infection presents as patches of moist, confluent erythematous macules with overlying curd-like material. It usually occurs on mucosal surfaces or in skin folds (e.g. under breasts, in the inguinal fold). It most commonly occurs in patients with predisposing factors such as therapy with broad-spectrum antibiotics or diabetes.

Treatment of cutaneous candidiasis

The diagnosis can be confirmed with a fungal skin scraping and potassium hydroxide test, if available. If the diagnosis remains unclear, send skin scrapings and a swab for microscopy and culture.

Use:

miconazole 2% cream topically, 12-hourly.

A mild steroid cream can be added to the antifungal cream if required to relieve itching.

Duration: Continue treatment until 2 weeks after symptoms have resolved.

Pityriasis versicolor (tinea versicolor)

Pityriasis versicolor

Pityriasis versicolor is a common chronic condition caused by *Malassezia* yeasts and is most commonly seen in adolescents and young adults. It presents with patches of hypopigmentation or hyperpigmentation, with fine scale usually on the neck, chest, back and upper arms. The rash is usually asymptomatic.

Treatment of pityriasis versicolor (tinea versicolor)

The diagnosis can be confirmed with a fungal skin scraping and potassium hydroxide test, if available. If the diagnosis remains uncertain, send a fungal skin scraping to the laboratory for microscopy prior to starting antifungal treatment.

Use:

ketoconazole shampoo 2% topically, once daily (leave for 3 to 5 minutes and then wash off) for 3 consecutive days.

OR

terbinafine 1% cream topically, twice daily for 1 week.

If there is no response to topical therapy, use:

fluconazole 400 mg orally, as a single dose.

Do **not** use **oral** terbinafine or griseofulvin because they are ineffective against *Malassezia* yeasts.

While the condition does not leave scars, pigmentary changes may take several months to return to normal.

Patients who experience frequent recurrences can use ketoconazole shampoo applied to the entire body for 10 minutes once a month to prevent recurrences.

Insect and mite infestations

Lice

Head lice (*Pediculus humanus* var. *capitis*)

Head lice are crawling insects that live on the scalp and lay eggs on hair. Bites may produce erythematous macules, papules, excoriations and scaling with accompanying pruritus.

Severe or persistent head lice may warrant HIV testing.

'Wet combing' is a physical method of removing nits and lice; however, this method only has about a 40% success rate when used alone. Nit combs (which can be purchased at pharmacies) are very fine-toothed combs which can remove both lice and nits.

Advise caregivers to:

- wet the hair and apply conditioner
- comb down the hair shaft from the scalp to the ends
- work through the scalp in sections
- expect nit removal to take at least half an hour
- repeat until no lice are found on three consecutive occasions.

For topical treatment of head lice, use:

permethrin 1% lotion topically to damp hair and scalp. Leave for 20 minutes before washing out. Repeat application 7 days after first treatment.

Wash pillowcases, combs and brushes in hot water (≥ 60 °C) followed by ironing (if possible) or dry in the sun or, if not feasible, seal in a plastic bag for 14 days.

Examine family and close contacts; only treat those with live lice and/or nits. Preventative treatment of noninfected persons is ineffective and increases the risk of resistance.

If head lice are refractory to topical treatments, use:

ivermectin 200 micrograms/kg (rounded up to the nearest 1.5 mg) orally with fatty food, as a single dose. Repeat dose after 7 days.[18]

18 Ivermectin is not currently licensed for use in children weighing less than 15 kg because of a lack of safety data. However, limited data suggest that oral ivermectin in children weighing less than 15 kg is well tolerated with no serious or long-term adverse effects. Ivermectin should not be used in pregnancy.

Body lice (pediculosis corporis)

Caused by *Pediculus humanus* var. *corporis,* lice that live in clothing. Patients complain of pruritus, and present with excoriations, often linier, primarily on the neck, shoulders, back and wrist. In chronic cases, patients may have hyperpigmentation macules.

Pediculus humanus can be a vector for typhus and trench fever (*Bartonella quintana*).

Use:

permethrin 1% lotion topically to body. Leave on for 20 minutes before washing off. Repeat application after 7 days.

If lice are refractory to topical treatments, use:

ivermectin 200 mcg/kg (rounded up to the nearest 1.5 mg) orally with fatty food, as a single dose (not in pregnant people). Repeat dose after 7 days.

Clothing and bedding should be discarded or washed in hot water (≥60°C) or sealed in plastic bags for 14 days.

Pubic lice (pediculosis pubis)

Caused by *Phthirus pubis,* lice that live in pubic, axillary, beard and other body hair. The main symptom is itch. Eggs are visible on hairs. Examine all hair-baring surfaces.

Pediculosis pubis is commonly transmitted by sexual or close contact – examine contacts. Consider testing for other sexually transmissible infections.

Use:

permethrin 1% lotion topically to hair. Leave for 20 minutes before washing out.

Repeat application after 7 days.

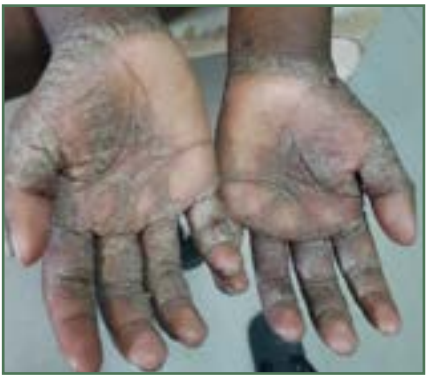
Shaving hair may be helpful.

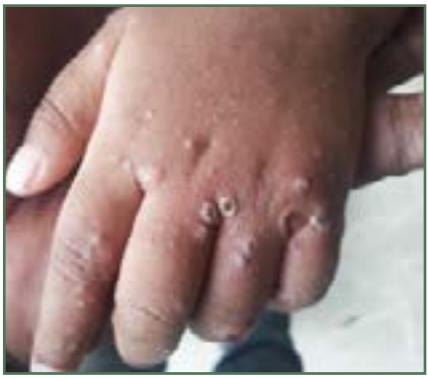
If lice are refractory to topical treatments, use:

ivermectin 200 mcg/kg (rounded up to the nearest 1.5 mg) orally, with fatty food, as a single dose. Repeat dose after 7 days.[19]

19 Ivermectin is not currently licensed for use in children weighing less than 15 kg because of a lack of safety data. However, limited data suggest that oral ivermectin in children weighing less than 15 kg is well tolerated with no serious or long-term adverse effects. Ivermectin should not be used in pregnancy.

Scabies





Left: crusted scabies, right: scabies (non-crusted).

Scabies is caused by the mite *Sarcoptes scabiei var. hominis,* a human pathogen that is spread by close physical contact. An allergic reaction to the mite causes inflammation and itch, particularly at night. Excoriations appear in the interdigital webs, sides of fingers, wrists, lateral palms, elbows, axillae, scrotum, penis, labia and areola mammae in women. Scaly burrows in the finger web spaces are pathognomonic. In infants, elderly and immunocompromised individuals, all skin surfaces are susceptible.

Send skin scraping from multiple sites for microscopy if diagnosis is unclear. However, in non-crusted scabies, this may be falsely negative due to the low mite burden in scabies. Skin scrapings will usually be positive in crusted scabies due to the high mite burden.

Wash all clothing, pillows, towels and bedding used during the previous week in hot water and dry in the sun (wash the morning after treatment). For items that cannot be washed, store in a sealed plastic bag for 8 days. This period of time ensures that the scabies mites and any larvae hatched from eggs die.

Encourage patients to wash their whole body every day.

Treat secondary bacterial infection with antibiotics as for **cellulitis**, page 273 in this topic.

Itch may initially worsen with treatment and may take 3 weeks to resolve after treatment completion. Topical steroids and/or antihistamines can be used to relieve symptoms.

Using scabies treatments in infants and children

Ivermectin is not currently licensed for use in children weighing less than 15 kg because of a lack of safety data. However, limited data suggest that oral ivermectin in children weighing less than 15 kg is well tolerated with no serious or long-term adverse effects.

Permethrin is the recommended treatment for infants, despite currently not being approved for use in children less than 6 months. The risk must be balanced against the serious morbidity of untreated scabies.

Treatment of scabies

Note that a 5% concentration of permethrin lotion or cream is required for the treatment of scabies; permethrin 1% lotion is for the treatment of lice only.

Box 3: Advice on application of topical scabicides for the patient or carer

Topical application advice for the patient or carer (applies to all topical scabicide preparations)

- wash (with soap and water) and dry skin before application
- apply a thin layer of the cream/lotion to the whole body, from the neck down; pay particular attention to the hands (including under the nails) and genitalia
- if scabies mites are present above the neck, apply to the face and scalp but avoid the eyes, nose and mouth
- reapply the cream/lotion to the hands if they are washed
- for infants and young children, recommend mittens to stop them sucking their fingers after the treatment is applied.

Scabies (non-crusted)

Treat all household members and close contacts. See Box 3 (above) for detailed instructions for application of topical scabicides.

Use:

*permethrin **5% lotion** topically to dry skin from neck down. Leave on for a minimum for 8 hours (usually overnight) and reapply to hands if washed.*

If there is a history of failure, leave permethrin lotion on for 24 hours.

Alternatively, use:

ivermectin 200 mcg/kg (rounded up to the nearest 1.5 mg) orally with fatty food, as a single dose.[20]

20 Ivermectin is not currently licensed for use in children weighing less than 15 kg because of a lack of safety data. However, limited data suggest that oral ivermectin in children weighing less than 15 kg is well tolerated with no serious or long-term adverse effects. Ivermectin should not be used in pregnancy.

cont...

Benzyl benzoate is effective if used correctly; however, skin irritation occurs more frequently with benzyl benzoate than with permethrin, and this can affect adherence. If ivermectin or permethrin are not available or not tolerated, use:

benzyl benzoate 25% emulsion, topically (child 6 months to 2 years: dilute with 3 parts water; child 2 to 12 years: dilute with equal parts of water) topically to dry skin from the neck down. Leave on for 24 hours and reapply to hands if washed.

If skin irritation occurs in adults with undiluted benzyl benzoate, dilute with equal parts water.

In patients who are pregnant or breastfeeding, permethrin 5% is the preferred treatment.

In infants < 6 months (including neonates), use:

permethrin 5% lotion, topically applied to the entire body including the scalp, but avoiding eyes and mouth. Cover hands to prevent oral ingestion. Leave on for 8 hours.

In infants with permethrin allergy, sulfur 5% in white soft paraffin can be used instead: apply topically, once daily for 3 days. However, this product is less effective than permethrin.

Note: Increased itch with treatment usually represents increased mite activity and should **not** be routinely considered allergy unless other features of allergy present.

Duration: For all treatments, repeat application or dose 7 days after first treatment.

Crusted scabies (Norwegian scabies)

In crusted scabies, the mite population on the patient is very high due to an inadequate host immune response. It occurs in immunocompromised patients and presents as hyperkeratotic plaques. There may be associated thickening and dystrophy of the toenails and fingernails.

Test patients for HIV.

Provide patients advice on topical application for topical scabicide, see Box 3 on the previous page.

Refer to a dermatologist and infectious diseases physician, if available.

Treatment of crusted scabies is difficult. A combination of 3 treatments is required: oral ivermectin plus a topical scabicide plus a topical keratolytic agent to reduce scaling.

Use:

ivermectin 200 mcg/kg (rounded up to the nearest 1.5 mg) orally with fatty food (see dosing frequency below)[21]

PLUS a topical scabicide:

permethrin 5% lotion, topically (see dosing frequency below)

OR

benzyl benzoate 25% emulsion, topically (see dosing frequency below)

PLUS a topical keratolytic agent:

Whitfield's solution (3% salicylic acid and 6% benzoic acid), topically

OR alternatively:

salicylic acid 5 to 10% in sorbolene cream, topically.

Frequency and duration

Apply the scabicide every second day for the first week, then apply twice weekly until cured.

Apply the topical keratolytic after washing on days when the topical scabicide is not applied.

Mild: Give ivermectin on days 1 and 8 of treatment course.

Moderate: Give ivermectin on days 1, 2 and 8 of treatment course.

Severe: Give ivermectin on days 1, 2, 8, 9 and 15 of treatment course.

Cutaneous larva migrans

Cutaneous larva migrans is caused by animal hookworms. It presents with erythematous, intensely pruritic, serpiginous (snake-like) tracks due to migrating larvae that progress a few centimetres per day. It commonly involves the feet, legs and buttocks.

Diagnosis is based on clinical history and examination. Patients typically have a history of exposure to contaminated sand or soil.

21 Ivermectin is not currently licensed for use in children weighing less than 15 kg because of a lack of safety data. However, limited data suggest that oral ivermectin in children weighing less than 15 kg is well tolerated with no serious or long-term adverse effects. Ivermectin should not be used in pregnancy.

Treatment of cutaneous larva migrans
Use: *ivermectin 200 mcg/kg (rounded up to the nearest 1.5 mg) orally with fatty food, daily for 1 to 2 days.*[22] OR *albendazole 400 mg (child ≤10 kg: 200 mg) orally, daily for 3 days.*

Filariasis

Lymphatic filariasis is caused by the mosquito-borne nematode *Wuchereria Bancrofti*, which inhabits the lymphatics and subcutaneous tissues. It is usually acquired in childhood, but as it is often unrecognised (and therefore untreated), it causes damage to lymphatic vessels with disfiguring visible manifestations of disease, such as lymphoedema (tissue swelling), elephantiasis (thickening of skin/tissue) and hydrocele (scrotal swelling), occurring later in life and leading to permanent disability.

Symptoms and clinical presentations depend on several factors, including the host immune response, and individuals with detectable circulating microfilariae are often asymptomatic while severe clinical symptoms may be seen among individuals without detectable microfilaremia.

Acute inflammatory manifestations include red, warm, tender oedema along the length of a lymphatic channel with or without systemic signs (e.g. fever, nausea, vomiting). The inflammation may involve the lower limbs, external genitalia, breasts, spermatic cord (funiculitis), epididymis and testicle (epididymo-orchitis). Attacks resolve spontaneously within a week and recur regularly in patients with chronic disease.

Chronic filariasis is characterised by lymphoedema of the arms and legs (‘elephantiasis’), hydrocele and long-term disability.

In Papua New Guinea, filariasis is being targeted for elimination by mass drug administration with a three-drug regimen (ivermectin plus diethylcarbamazine (DEC) plus albendazole). Mass drug administration programs are managed by the public health team, and details are not included in these guidelines.

The management of lymphatic filariasis is based on the three clinical stages of disease:

- asymptomatic infection
- acute attacks
- lymphoedema/elephantiasis.

22 Ivermectin is not currently licensed for use in children weighing less than 15 kg because of a lack of safety data. However, limited data suggest that oral ivermectin in children weighing less than 15 kg is well tolerated with no serious or long-term adverse effects. Ivermectin should not be used in pregnancy.

Management of asymptomatic infections

Asymptomatic infections are those without external signs of infection but with a peripheral blood film showing microfilariae or a positive antigen test.

Use a triple-drug regimen (commonly referred to as 'IDA'):

ivermectin 200 mcg/kg (rounded up to the nearest 1.5 mg) orally, as a single dose[23]

PLUS

diethylcarbamazine 6 mg/kg orally, as a single dose

PLUS

albendazole 400 mg (child > 6 months and < 10 kg, 200 mg) orally, as a single dose.

Alternatively, if ivermectin is not available, use as a two-drug regimen:

ivermectin 200 mcg/kg (rounded up to the nearest 1.5 mg) orally, as a single dose[23]

PLUS

albendazole 400 mg (child > 6 months and < 10 kg, 200 mg) orally, as a single dose.

Management of acute attacks

Acute attacks can occur in both the asymptomatic and chronic stages; in the asymptomatic stage it can lead to lymphoedema. Acute attacks are caused by:

- an inflammatory reaction to the adult worms, involving the skin, lymph nodes and lymphatic vessels and associated with fever, chills, malaise and pain
- secondary bacterial infection by *Staphylococcus aureus* or *Streptococcus* species.

Management of acute attacks can prevent the progression to advanced stages.

For patients with secondary bacterial infection, provide antibiotic treatment as for **cellulitis**, see page 273 in this topic.

Refer any patient with an acute attack that does not improve after 48 hours of administering antibiotics.

cont...

23 Ivermectin should not be used in pregnancy.

For all patients with an acute attack, provide symptomatic management with:

- an antipyretic and analgesic (e.g. paracetamol)
- supportive measures:
  - rest
  - elevation of the affected area.

During acute attacks:

- do not administer antifilarial treatment (e.g. IDA)
- do not cut or peel the skin
- do not bandage the affected area
- do not exercise the affected area.

Lymphoedema/elephantiasis

Chronic manifestations of lymphatic filariasis usually take 10 to 15 years to develop and include lymphoedema/elephantiasis, hydrocele and permanent deformity.

Hydrocele requires surgery.

Most patients with lymphoedema or elephantiasis are not actively infected with a filarial parasite and are therefore not likely to benefit from DEC or other antifilarial treatment. However, for patients who test positive for microfilariae on peripheral blood film or antigen test, treat as for asymptomatic infections (see previous page).

Treatment should concentrate on the management of lymphoedema – hygiene, elevation, exercise, skin care and footwear. Daily hygiene has shown to have the largest positive impact on lymphoedema.

Advise all patients about supportive management:

- **hygiene** – daily washing of the affected area with soap and clean, warm water. Avoid using a brush or abrasive material. (Diligent washing may reduce acute attacks and prevent progression of lymphoedema)
- **skin and wound care** – inspect skin for entry points of potential infection and treat. Do not cut or peel skin or blister and/or apply traditional herbs
- **elevation** of the affected area. (Patients with lymphoedema of the legs and who have heart problems should not elevate their legs while sleeping unless advised by their doctor)
- **exercises** - including the affected and unaffected limbs to promote lymph flow, but **do not exercise during an acute attack**
- advise the patient to wear comfortable shoes.

cont...

Patients with lymphoedema should be referred to a primary healthcare unit when:

- non-filarial lymphoedema is suspected.

Key additional references

El-Gohary M, van Zuuren EJ, Fedorowicz Z, Burgess H, Doney L, Stuart B, et al. Topical antifungal treatments for tinea cruris and tinea corporis. Cochrane Database Syst Rev 2014;(8):CD009992.

Fact sheet: Lymphatic filariasis. 1 June 2023. World Health Organization. Available from: https://www.who.int/news-room/fact-sheets/detail/lymphatic-filariasis.

Horton, J., Klarmann-Schulz, U., Stephens, M. et al. The design and development of a multicentric protocol to investigate the impact of adjunctive doxycycline on the management of peripheral lymphoedema caused by lymphatic filariasis and podoconiosis. Parasites Vectors 13, 155 (2020). https://doi.org/10.1186/s13071-020-04024-2.

Kreijkamp-Kaspers S, Hawke K, Guo L, Kerin G, Bell-Syer SE, Magin P, et al. Oral antifungal medication for toenail onychomycosis. Cochrane Database Syst Rev 2017;7:CD010031.

May PJ, Tong SYC, Steer AC, Currie BJ, Andrews RM, Carapetis JR, et al. Treatment, prevention and public health management of impetigo, scabies, crusted scabies and fungal skin infections in endemic populations: a systematic review. Trop Med Int Health 2019;24(3):280-93.

Mitjà O, Lukehart SA, Pokowas G, Moses P, Kapa A, Godornes C, Robson J, Cherian S, Houinei W, Kazadi W, Siba P, de Lazzari E, Bassat Q. Haemophilus ducreyi as a cause of skin ulcers in children from a yaws-endemic area of Papua New Guinea: a prospective cohort study. Lancet Glob Health. 2014 Apr;2(4):e235-41. doi: 10.1016/S2214-109X(14)70019-1. Epub 2014 Mar 27. PMID: 25103064.

Parasites - Lymphatic Filariasis. Centers for Disease Control. March 16, 2018. Available from: https://www.cdc.gov/parasites/lymphaticfilariasis/treatment.html.

Rosumeck S, Nast A, Dressler C. Ivermectin and permethrin for treating scabies. Cochrane Database Syst Rev 2018;4:CD012994.

Sharquie KE, Al-Rawi JR, Noaimi AA, Al-Hassany HM: Treatment of scabies using 8% and 10% topical sulfur ointment in different regimens of application. PMID: 22395587.

Simple, complicated and crusted scabies. Norther Territory (NT) Health Guideline. NT Health; 2023.

Singalavanija S, Limpongsanurak W, Soponsakunkul S: A comparative study between 10 per cent sulfur ointment and 0.3 per cent gamma benzene hexachloride gel in the treatment of scabies in children. PMID: 14700144.

Soft tissue infections

This topic includes advice on the management of the following conditions in adults and children older than 3 months:

- **diabetic foot infection**, page 301
- **necrotising soft tissue infections**, page 307
- **mastitis** including lactational mastitis and nonlactational mastitis, page 312
- **cervical lymphadenitis** including tuberculosis lymphadenitis and nontuberculosis mycobacterial lymphadenitis, page 315.

The following topics are not included in this section:

- **neonatal mastitis and breast abscess** (page 211) in 'Infections in neonates and young infants.'
- **cellulitis and erysipelas** (page 273) in 'Skin infections'

Diabetic foot infection

Assessing diabetic foot ulcers for infection

Diabetic foot infections may involve skin and soft tissue or extend deeper to underlying muscle and bone. They commonly involve ulcers that have commenced over pressure points or after local trauma. Diabetic foot infections are often worse than they appear. Complications that should be considered include osteomyelitis and necrotising soft tissue infection. If a patient is in **septic shock**, treat as **necrotising soft tissue infection** (see page 307 in this topic).

For an ulcer to be considered infected, **at least two** of the following features should be present (IWGDF, IDSA)[19]:

- local swelling or induration
- erythema extending more than 0.5 cm in any direction from the wound
- local tenderness or pain
- local warmth
- purulent discharge.

Other causes of inflammation should be considered in the differential diagnosis, e.g. Charcot process, gout, trauma.

An **acute Charcot process** arises silently within a neuropathic foot over several months and displays skin warmth and redness together with non-tender foot swelling. The process is usually unilateral and often involves bony changes that can

19 IWFDF = International Working Group on the Diabetic Foot, IDSA = Infectious Diseases Society of America.

be confused for osteomyelitis. Radiographic (X-ray or CT scan) findings may show characteristic findings.

Culture of tissue samples obtained during surgery, by biopsy or aspiration can guide antibiotic therapy. Take blood for cultures if the patient is systemically unwell. Organisms isolated from ulcer swabs usually reflect colonisation rather than infection. An exception is detection of methicillin-resistant *Staphylococcus aureus* (MRSA), which usually requires specific treatment.

Always obtain surgical opinion for the potential need for debridement.

Proper wound care and dressings attended with asepsis are important as is effective offloading of pressure and foot elevation. Provide deep venous thrombosis prophylaxis, if available.

Optimising nutrition and control of diabetes is important.

Many patients may have bony changes consistent with osteomyelitis on X-ray (see also Charcot process above). See Table 3: Suggested duration of antibiotic therapy for osteomyeltis in adults, page 47 in 'Bone and joint infections' for treatment duration if this is present.

Antibiotic choice

Choice of empiric antibiotics should consider the infection severity, ulcer duration and recent use of antibiotics.

S. aureus and streptococci are the most common causes of acute diabetic foot infections in patients who have not recently been treated with antibiotics. Gram-negative pathogens are more likely with recent antibiotic use. Infections of chronic ulcers (present for 4 weeks or more) are often polymicrobial, involving Gram-positive, Gram-negative aerobic and anaerobic bacteria. Empiric antibiotics with activity against MRSA, e.g. trimethoprim+sulfamethoxazole, should be considered for patients not improving with empirical therapy. Modify therapy based on the results of culture and susceptibility testing, when available.

Treatment of diabetic foot infection

Mild diabetic foot infection

Mild infection involves only the skin and subcutaneous tissue. Erythema extends no more than 2 cm from the wound margin and there are no systemic features of infection.

Treatment targets *S. aureus* or pyogenic streptococci (e.g. streptococcus groups A, B, C or G) and anaerobic bacterial species.

In a neuropathic foot, also consider Charcot process as a differential diagnosis (see previous page).

For patients with an acute, mild diabetes-related foot ulcer (present < 30 days) who have not recently received antibiotics, use:

flucloxacillin *1 g orally, 6-hourly.*

For patients with hypersensitivity to penicillins or for patients failing to improve after 72 hours of treatment with flucloxacillin, use:

trimethoprim+sulfamethoxazole *160+800 mg orally, 12-hourly.*

For patients with infection of a chronic ulcer (present for ≥ 30 days) or who have recently received antibiotics, use:

amoxicillin+clavulanate *500+125 mg orally, 8-hourly*

OR

flucloxacillin *1 g orally, 6-hourly*

PLUS

metronidazole *400 mg orally, 12-hourly.*

For patients with hypersensitivity to penicillins or for patients failing to improve after 72 hours of treatment with any of the above regimens, use:

trimethoprim+sulfamethoxazole *160+800 mg orally, 12-hourly*

PLUS

metronidazole *500 mg orally, 12-hourly.*

Duration

Treat for 10 days unless signs of infection persist (in that case, obtain an X-ray and surgical opinion).

Note that antibiotic therapy is not expected to cause the ulcer to heal.

Moderate diabetic foot infection

Moderate infection involves structures deeper than the skin or subcutaneous tissues (e.g. muscle, bone, joint, tendon) or erythema that extends more than 2 cm from the wound margin, but the infection is not associated with systemic inflammatory response syndrome (SIRS) (as described for severe infection).

For patients with moderate infection of a diabetes-related foot ulcer, use:

amoxicillin+clavulanate *1+0.2g IV, 6-hourly*

OR, as a two-drug regimen, including for patients with **immediate nonsevere** or **delayed nonsevere** hypersensitivity to penicillins:

cefazolin *2 g IV, 8-hourly*

PLUS

metronidazole *400 mg orally (preferred) or 500 mg IV, 12-hourly.*

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

chloramphenicol *500 mg orally, 6-hourly*

PLUS

metronidazole *400 mg orally (preferred) or 500 mg IV, 12-hourly.*

If a patient is systemically well but fails to improve within 72 hours of starting this regimen, assess the need for surgical debridement and switch to the regimen below, which provides coverage for MRSA and *Pseudomonas*, use:

chloramphenicol *500 mg orally, 6-hourly.*

PLUS

ciprofloxacin *500 mg orally, 12-hourly (or if the patient is unable to tolerate oral therapy, use 400 mg IV, 8-hourly).*

However, if systemic symptoms have developed, treat as **severe diabetic foot infection** (next section).

Duration

Treat for total of 3 weeks (IV + oral). However, a longer duration of therapy is needed for wounds involving the deeper tissues (e.g. suspected osteomyelitis). Consider further surgical opinion, if relevant, and evaluate X-rays.

Note that antibiotic therapy is not expected to cause the ulcer to heal.

Severe diabetic foot infection

Severe infection is associated with a systemic inflammatory response syndrome (SIRS) (i.e. 2 or more of: abnormal temperature [more than 38 °C or less than 36 °C]; heart rate more than 90 beats per minute; respiratory rate more than 20 breaths per minute; white cell count more than 12 × 109/L or less than 4 × 109/L.

For patients with sepsis or septic shock (e.g. BP < 90/60 mmHg), take appropriate samples for cultures and start antibiotic therapy **within 1 hour**.

Use:

flucloxacillin *2 g IV, 6-hourly*

PLUS

ciprofloxacin *500 mg orally (preferred), 12-hourly (or if the patient is unable to tolerate oral therapy, use 400 mg IV, 8-hourly)*

PLUS

metronidazole *400 mg orally (preferred), or 500 mg IV, 12-hourly.*

For patients with hypersensitivity to penicillins, as a two-drug regimen, use:

ciprofloxacin *500 mg orally, 12-hourly (or 400 mg IV, 8-hourly)*

PLUS either

clindamycin *600 mg IV, 8-hourly*

OR

chloramphenicol *1 g IV, 6-hourly.*

If the patient has sepsis or septic shock or known previous infection/colonisation MRSA, **add** to the above regimens:

vancomycin *slow IV infusion,* ***consider a loading dose in critically ill adults.*** *See 'Appendix 2: Vancomycin dosing' (page 386) for information on loading dose, dosing frequency and infusion time*

adult ≥ 40 years: 15 mg/kg, see Table 18 for dosing frequency (page 390)

adult < 40 years 20 mg/kg, see Table 17 for dosing frequency (page 389).

If vancomycin is not available, use the chloramphenicol and ciprofloxacin combination above.

Modify therapy based on the results of culture and susceptibility testing, if available.

cont...

After significant improvement, switch to oral therapy. If the results of culture and susceptibility testing are unavailable, see **mild diabetic foot infection** for antibiotic choice.

For patients who do **not** improve on empirical antibiotic therapy, obtain repeat surgical review as amputation for source control may need to be considered. Consider switching to the escalation regimen (below).

Duration

The optimal duration of antibiotics depends on the infection severity, presence of osteoarticular involvement and whether debridement or amputation of necrotic tissue has been performed.

If there has been complete resection of all infected bone (this can be assumed if the surgical resection extends proximally at least one joint from the affected bone/joint) – cease antibiotics after surgery.

In patients who have undergone appropriate debridement of all necrotic tissue or partial amputations but have residual osteomyelitis, 3 weeks of total therapy may be reasonable (IV + oral).

In patients who have more extensive bony or soft tissue infection despite debridement, more prolonged treatment may be required. Further surgical opinion and diagnostic imaging may be required.

Note that antibiotic therapy is not expected to cause the ulcer to heal.

Escalation regimen for severe diabetic foot infection not improving on empirical therapy

For patients who do not improve on empirical antibiotic therapy, obtain repeat surgical review as amputation for source control may need to be considered.

Consider escalating to:

ceftazidime *2 g IV, 8-hourly*

PLUS

metronidazole *500 mg IV, 12-hourly*

PLUS

vancomycin *slow IV infusion,* ***consider a loading dose in critically ill adults.*** See *'Appendix 2: Vancomycin dosing' (page 386) for information on loading dose, dosing frequency and infusion time*

cont...

adult ≥ 40 years: 15 mg/kg, see Table 18 for dosing frequency (page 390)

adult < 40 years 20 mg/kg, see Table 17 for dosing frequency (page 389).

If an organism with an extended-spectrum beta-lactamase (ESBL) enzyme is cultured from tissue, switch to:

***meropenem** 1 g IV, 8-hourly*

PLUS

***vancomycin** (dosing as above).*

Necrotising soft tissue infections

A number of clinical syndromes can be associated with rapidly progressive necrotising skin and soft tissue infections, such as necrotising fasciitis (necrosis of the soft tissues), myonecrosis (necrosis of the muscles) or gangrene (extensive necrosis).

Diagnosis is difficult and expert advice is essential.

Penetrating and crush injuries are particularly likely to lead to necrotising skin and soft tissue infection, but necrotising infection can also follow surgical procedures. Life-threatening *Streptococcus pyogenes* necrotising fasciitis can occur spontaneously or follow varicella infection (chickenpox). Diabetes is also a risk factor for necrotising skin and soft tissue infection.

Clinical features that suggest a necrotising skin and soft tissue infection include:

- constant severe pain, even if skin inflammation is initially limited
- skin necrosis or bruising
- hard ('wooden') subcutaneous tissue that is painful on palpation
- oedema beyond the margin of erythema
- cutaneous anaesthesia
- gas in the soft tissues (detected by palpation [skin or soft tissue crepitus] or imaging)
- systemic features, including fever, leucocytosis, elevated C-reactive protein (CRP), delirium or acute kidney impairment
- rapidly spreading infection.

If the diagnosis is uncertain, early surgical consultation is recommended; surgical exploration and collection of deep tissue samples for microscopy and culture can provide a definitive diagnosis.

Consider necrotising skin and soft tissue infections in patients who are critically ill with a skin and soft tissue infection.

Surgical removal of devitalised tissue and urgent antibiotic therapy are essential for management; typically, multiple debridements are required. Empirical antibiotic therapy is used while the pathogen(s) and affected tissues are determined.

Clindamycin is included in the treatment of necrotising soft tissue infections for its theoretical anti-toxin effects. It should be stopped after 3 days (72 hours) of treatment.

Treatment of necrotising soft tissue infections

Empirical treatment of necrotising soft tissue infection

Necrotising fasciitis, myonecrosis, gas gangrene, Fournier gangrene.

Take blood specimens for culture prior to starting antibiotics. Send tissue specimens from the operating theatre for culture.

Change to directed antibiotics as soon as culture results are available.

Urgent surgical debridement is essential.

Give antibiotics within **1 hour of presentation**. Use:

meropenem *1 g (child: 40 mg/kg up to 1 g) IV, 8-hourly*

PLUS

vancomycin *slow IV infusion, see 'Appendix 2: Vancomycin dosing' (page 386) for information on timing of next dose after loading dose, dosing frequency and infusion time*

- *adult ≥ 40 years:* ***loading dose 25 mg/kg up to 3 g*** *then 15 mg/kg, see Table 18 for dosing frequency (page 390)*
- *adult < 40 years:* ***loading dose 25 mg/kg up to 3 g*** *then 20 mg/kg, see Table 17 for dosing frequency (page 389)*
- *child 3 months and older:* ***loading dose 25 mg/kg up to 3 g*** *then 15 mg/kg, 6-hourly*

PLUS

clindamycin *600 mg (child: 15 mg/kg up to 600 mg) IV/orally, 8-hourly.*

Alternatively, replace meropenem in the above regime with:

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

However, do not use piperacillin+tazobactam with vancomycin for more than 72 hours as this combination is associated with an increase risk of nephrotoxicity.

cont...

If these antimicrobials are not available, use:

chloramphenicol *1 g IV, 6-hourly*

PLUS

ciprofloxacin *500 mg orally (preferred), 12-hourly (or 400 mg IV, 8-hourly).*

Switch to oral antibiotics, guided by the results of culture and susceptibility testing, when further debridement is no longer necessary, there has been clinical improvement and the patient has been afebrile for 48 to 72 hours.

If the results of culture and susceptibility testing are unavailable, switch to:

chloramphenicol *500 mg orally, 6-hourly*

PLUS

ciprofloxacin *500 mg orally, 12-hourly.*

Empirical treatment of necrotising soft tissue infection associated with a wound that has been immersed in water

This refers to an infection following an injury received in a marine (salt water), river/stream (fresh water) or estuary (brackish water) environment as there is an increased risk of other organisms causing infection e.g. *Aeromonas* species.

Ciprofloxacin is included in the empirical regimen because *Aeromonas* isolates often produce carbapenemase enzymes.

Take blood specimens for culture prior to starting antibiotics. Send tissue specimens from operating theatre for culture.

Switch to directed antibiotics as soon as the results of culture and susceptibility testing are available.

If the wound has been immersed in water, as a four-drug regimen, use:

meropenem *1 g (child: 20 mg/kg up to 1 g) IV, 8-hourly*

OR

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

PLUS

vancomycin *slow IV infusion, see 'Appendix 2: Vancomycin dosing' (page 386) for information on timing of next dose after loading dose, dosing frequency and infusion time*

cont...

adult ≥ 40 years: **loading dose 25 mg/kg up to 3 g** *then 15 mg/kg, see Table 18 for dosing frequency (page 390)*

adult < 40 years: **loading dose 25 mg/kg up to 3 g** *then 20 mg/kg, see Table 17 for dosing frequency (page 389)*

child 3 months and older: **loading dose 25 mg/kg up to 3 g** *then 15 mg/kg, 6-hourly*

PLUS

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.*

Switch to oral antibiotics, based on the results of culture and susceptibility testing, when further debridement is no longer necessary, there has been clinical improvement, and the patient has been afebrile for 48 to 72 hours.

If the results of culture and susceptibility testing are unavailable, switch to:

chloramphenicol *500 mg orally, 6-hourly*

PLUS

ciprofloxacin *500 mg orally, 12-hourly.*

Duration:

Stop clindamycin after 72 hours. Continue oral antibiotics until the infection has resolved, but not necessarily until the wound has healed. Usually 2 to 4 weeks of therapy is required.

Streptococcus pyogenes necrotising soft tissue infection

Also see directed therapy for *Streptococcus pyogenes* bloodstream infection, page 257 in 'Sepsis and bloodstream infections.'

Use:

benzylpenicillin *2.4 g (child: 50 mg/kg up to 2.4 g) IV, 4-hourly*

PLUS

clindamycin *600 mg (child: 15 mg/kg up to 600 mg) IV, or 450 mg (child: 10 mg/kg up to 450 mg) orally, 8-hourly.*

cont...

In patients with **immediate nonsevere** or **delayed nonsevere** hypersensitivity to penicillins, replace benzylpenicillin with:

cefazolin
adult: 2 g IV, 6-hourly
child: 50 mg/kg up to 2 g IV, 8-hourly.

Seek appropriate advice for appropriate alternatives for patients with **immediate severe** or **delayed severe** hypersensitivity to penicillins.

Switch to oral therapy, based on susceptibility results, when further debridement is no longer necessary, there has been clinical improvement and the patient has been afebrile for 48 to 72 hours. If susceptibility results are not available to guide therapy, use:

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

Seek appropriate advice for oral stepdown options for patients with hypersensitivity to penicillins.

Duration

Stop clindamycin after 72 hours. Continue oral amoxicillin until the infection has resolved but not necessarily until the wound has healed; generally, a minimum of 10 to 14 days.

Clostridium species necrotising soft tissue infection (gas gangrene)

Use:

benzylpenicillin *2.4 g (child: 50 mg/kg up to 2.4 g) IV, 4-hourly*

PLUS

clindamycin *600 mg (child: 15 mg/kg up to 600 mg) IV, or 450 mg (child: 10 mg/kg up to 450 mg) orally, 8-hourly.*

For patients with hypersensitivity to penicillins, replace benzylpenicillin with metronidazole. Use:

metronidazole *500 mg (child: 12.5 mg/kg up to 500 mg) IV, 8-hourly.*

Switch to oral therapy, guided by the results of susceptibility testing, when further debridement is no longer necessary, there has been clinical improvement, and the patient has been afebrile for 48 to 72 hours. If susceptibility results are not available to guide therapy, use:

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

Duration

Stop clindamycin after 72 hours. Continue oral antibiotics until infection has resolved but not necessarily until the wound has healed; generally a minimum of 10 to 14 days.

Methicillin-resistant *Staphylococcus aureus* necrotising soft tissue infection

If the infection is associated with *S. aureus* bacteraemia, treat as *S. aureus* bacteraemia, see page 253 in 'Sepsis and bloodstream infections.'

Use:

vancomycin *slow IV infusion, see 'Appendix 2: Vancomycin dosing' (page 386) for information on timing of next dose after loading dose, dosing frequency and infusion time*

adult ≥ 40 years: ***loading dose 25 mg/kg up to 3 g*** *then 15 mg/kg, see Table 18 for dosing frequency (page 390)*

adult < 40 years: ***loading dose 25 mg/kg up to 3 g*** *then 20 mg/kg, see Table 17 for dosing frequency (page 389)*

child 3 months and older: ***loading dose 25 mg/kg up to 3 g*** *then 15 mg/kg, 6-hourly*

PLUS

clindamycin *600 mg (child: 15 mg/kg up to 600 mg) IV, or 450 mg (child: 10 mg/kg up to 450 mg) orally, 8-hourly.*

Switch to oral antibiotics based on the results of susceptibility testing, when further debridement is no longer necessary, there has been clinical improvement, and the patient has been afebrile for 48 to 72 hours.

Duration

Stop clindamycin after 72 hours. Continue oral antibiotics until infection has resolved but not necessarily until the wound has healed. Usually 4 weeks minimum.

Mastitis

For mastitis in neonates, see page 211 in 'Infections in neonates and young infants.'

Mastitis is an inflammation of the breast that can lead to infection. Mastitis most commonly affects people who are breastfeeding (lactational mastitis) but can also occur in people who are not breastfeeding.

Consider tuberculous as it is a possible, but uncommon, cause of mastitis that generally has a more indolent presentation.

If *Staphylococcus aureus* is identified in blood cultures, treat as for *S. aureus* bacteraemia, see page 253 in 'Sepsis and bloodstream infections.'

Lactational mastitis

Acute mastitis is usually associated with lactation and is frequently due to *S. aureus.*

Breastfeeding or expressing milk (manually or via a pump) from the infected breast is safe and should be continued.

Provide advice for pain relief, such as using cold or warm compresses, a warm shower or bath, and/or paracetamol or ibuprofen.

Take blood specimens for culture if the patient is systemically unwell.

Avoid trimethoprim+sulfamethoxazole in people who are breastfeeding newborn infants (< 1 month old) or infants with glucose-6-phosphate dehydrogenase deficiency. Use cautiously in people who are breastfeeding infants who are jaundiced, premature or ill.

Treatment of lactational mastitis (mild infection)

In patients without systemic symptoms, increased breastfeeding or expressing milk from the affected breast may prevent progression and resolve infection without antibiotics.

In patients with systemic symptoms, or symptoms or signs that have not resolved after 24 to 48 hours of increased breastfeeding and expressing of milk, early antibiotic therapy is important to prevent abscess formation.

For mild infection, use:

trimethoprim+sulfamethoxazole *160+800 mg orally, 12-hourly.*

This regimen is preferred as it includes some cover for methicillin-resistant *Staphylococcus aureus*. Alternatively, use:

flucloxacillin *500 mg orally, 6-hourly.*

Duration

Treat for 5 to 7 days.

Treatment of lactational mastitis (moderate to severe infection)

Use:

flucloxacillin *2 g IV, 6-hourly*

PLUS either

trimethoprim+sulfamethoxazole *160+800 mg orally, 12-hourly*

OR

vancomycin *slow IV infusion,* ***consider a loading dose in critically ill adults****. See 'Appendix 2: Vancomycin dosing' (page 386) for information on loading dose, dosing frequency and infusion time*

adult ≥ 40 years: 15 mg/kg, see Table 18 for dosing frequency (page 390)

adult < 40 years 20 mg/kg, see Table 17 for dosing frequency (page 389).

Alternatively, including in patients with **immediate nonsevere** or **delayed nonsevere** hypersensitivity to penicillins, use:

cefazolin *2 g IV, 8-hourly*

PLUS either

trimethoprim+sulfamethoxazole *160+800 mg orally, 12-hourly*

OR

vancomycin *IV (dosing as above).*

Step down to oral antibiotics as for mild infection when clinically improved.

Duration

Treat for a total of 7 to 10 days (IV + oral).

If infection does not resolve with antibiotic therapy, evaluate the patient for an abscess and consider whether infection is caused by a different pathogen.

Nonlactational mastitis

Not all mastitis has an infective cause.

Forms of nonlactational mastitis include periductal mastitis and idiopathic granulomatous mastitis.

Empirical therapy for periductal mastitis

Use:

flucloxacillin *500 mg orally, 6-hourly*

PLUS

metronidazole *500 mg orally, 12-hourly*

OR including in patients with **immediate nonsevere** or **delayed nonsevere** hypersensitivity to penicillins, use:

cefalexin *500 mg orally, 6-hourly*

PLUS

metronidazole *500 mg orally, 12-hourly.*

Modify therapy based on the results of Gram stain and culture, when available.

It is important to consider breast cancer as a differential diagnosis, especially if there is a lack of response to antimicrobial therapy.

Most patients with periductal mastitis are smokers; smoking cessation is helpful for reducing the risk of repeat infection.

Duration

The optimal length of therapy is not certain; a 5- to 7-day course can be used if the response to therapy is rapid and complete; if necessary, the duration may be extended to 10 to 14 days.

Cervical lymphadenitis

Cervical lymphadenitis (cervical lymphadenopathy) may be associated with viral or bacterial infection, or noninfective causes. Noninfective causes include Kawasaki disease; Kikuchi disease; periodic fever, aphthous stomatitis, pharyngitis and cervical adenitis (PFAPA) syndrome; and malignancy (e.g. lymphoma).

For acute cervical lymphadenitis that is secondary to infection at another site, manage as for the primary source of infection (e.g. tonsillitis, quinsy, odontogenic infection).

Chronic cervical lymphadenitis may be caused by tuberculosis or nontuberculous mycobacteria, *Bartonella henselae* or, less commonly, *Toxoplasma gondii*. Perform fine-needle aspiration of a lymph node and send the aspirate for cytology and nucleic acid amplification testing (e.g. polymerase chain reaction [GeneXpert-TB]).

Test any patient presenting with chronic cervical lymphadenitis for HIV.

Tuberculosis lymphadenitis

Treat as per the *National Tuberculosis Management Protocol*.

Tuberculous lymphadenitis is characteristically slow to respond to effective treatment, and nodes may enlarge during treatment or after cessation of treatment.

Nontuberculous mycobacterial lymphadenitis

Nontuberculous mycobacteria (NTM) are transmitted through environmental sources. *Mycobacterium avium* complex (MAC), the most common cause of lymphadenitis, is found in soil and water (from both natural and treated water).

Identification of NTM can be difficult. Tuberculosis (TB) should be ruled out either through microbiological testing or, if unavailable, through consideration of the clinical picture including family history and exclusion of HIV infection – for people living with HIV, treat as TB.

Surgical excision is the mainstay of management and is usually curative. Antimycobacterial therapy may be indicated for complicated or recurrent lymphadenitis. Seek appropriate advice.

Key references

Hand, R., Manning, L., Ritter, J.C., Norman, P., Lamb, L., Makepeace, A., Sankhesara, D., Hamilton, E. and Ingram, P. (2019), Antimicrobial stewardship opportunities among inpatients with diabetic foot infections: microbiology results from a tertiary hospital multidisciplinary unit. Intern Med J, 49: 533-536. https://doi.org/10.1111/imj.14251

Lipsky BA, Aragon-Sanchez J, Diggle M, Embil J, Kono S, Lavery L, et al. IWGDF guidance on the diagnosis and management of foot infections in persons with diabetes. Diabetes Metab Res Rev 2016;32 Suppl 1:45-74.

Lipsky BA, Berendt AR, Cornia PB, Pile JC, Peters EJ, Armstrong DG, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis 2012;54(12):e132-73.

Urbina T, Razazi K, Ourghanlian C, Woerther P-L, Chosidow O, Lepeule R, et al. Antibiotics in necrotizing soft tissue infections. Antibiotics (Basel)- 2021; 10(9):1104. Doi: 10.3390/antibiotics10091104.

Wukich, DK, Schaper, NC, Gooday, C, et al. Guidelines on the diagnosis and treatment of active Charcot neuro-osteoarthropathy in persons with diabetes mellitus (IWGDF 2023). Diabetes Metab Res Rev. 2023;e3646. https://doi.org/10.1002/dmrr.3646.

Urinary tract infections (UTI)

This topic includes advice on the management of the following conditions in adults and children older than 3 months:

- **empirical antibiotic choice for UTI**, page 317
- **cystitis** including cystitis in nonpregnant women, cystitis in men and cystitis in children 3 months or older, page 318
- **pyelonephritis and complicated urinary tract infection**, page 321
- **candiduria**, page 323
- **asymptomatic bacteriuria**, page 323
- **recurrent UTI**, page 324
- **catheter-associated UTI**, page 325
- **bacterial prostatitis** including acute bacterial prostatitis and chronic bacterial prostatitis, page 326.

The following topics are not included in this section:

- **vulvovaginitis** (page 164) and **epididymitis and epididymo-orchitis** (page 174) in 'Genital and sexually transmissible infections'
- **sepsis, septic shock and meningitis in neonates** (page 199) in 'Infections in neonates and young infants'
- **urinary tract infections during pregnancy** (page 189) in 'Maternal infections associated with pregnancy.'

Empirical antibiotic choice for UTI

Recommendations for empirical antibiotic therapy for a UTI are mainly guided by two factors: the local resistance rates of common pathogens (in particular *Escherichia coli*), and the risk and severity of adverse outcomes from initial treatment failure. The use of narrow-spectrum drugs is always preferable but if the prevalence of resistance is high, the likelihood of treatment failure outweighs the benefits of their use. Pyelonephritis has a higher likelihood of serious complications than cystitis, so a higher likelihood of efficacy is required for its treatment.

Amoxicillin+clavulanate and ciprofloxacin have unnecessarily broad spectrums of activity for empirical therapy of cystitis. The use of broad-spectrum antibiotics selects for antibiotic-resistant organisms and increases the risk of *Clostridioides difficile* (formerly known as *Clostridium difficile*) infection.

Do not use nitrofurantoin to treat pyelonephritis; this drug does not achieve adequate concentrations in kidney tissue.

Gentamicin in combination with amoxicillin (or ampicillin) is recommended when empirical intravenous therapy is required for a severe UTI. This combination is preferred to broad-spectrum cephalosporins because:

- gentamicin is active against a greater percentage of Enterobacterales, and is more rapidly bactericidal
- ceftriaxone and cefotaxime do not have any activity against *Pseudomonas aeruginosa* or enterococci
- gentamicin with amoxicillin (or ampicillin) is less likely to contribute to the development of *C. difficile* infection and the selection of antibiotic-resistant bacteria.

UTI caused by multidrug-resistant Gram-negative organisms

There is worldwide emergence of multidrug-resistant *Escherichia coli*, particularly extended-spectrum beta-lactamase (ESBL)-producing strains, causing UTIs and associated bacteraemias.

Risk factors for UTI caused by a multidrug-resistant Gram-negative bacterium include recent stay in hospital, previous colonisation or infection with multidrug-resistant Gram-negative bacterium, recent antibiotic exposure or lack of response to initial antibiotic therapy.

If a multidrug-resistant organism is identified, **discuss treatment with a medical microbiologist or infectious diseases physician.** For more information, see **infection with multidrug-resistant Gram-negative bacteria**, page 261 in 'Sepsis and bloodstream infections.'

Cystitis

Symptoms of cystitis may include dysuria, urinary frequency or haematuria and lower abdominal discomfort. Fever (38°C or higher), vomiting or renal angle tenderness suggests upper UTI – see pyelonephritis.

In children, symptoms of cystitis may be nonspecific e.g. irritability and lethargy.

Uncomplicated cystitis is defined as acute, sporadic or recurrent cystitis in nonpregnant women with no comorbidities and no known relevant anatomical or functional abnormalities within the urinary tract. Cystitis in men, children and pregnant women is considered complicated.

Acute uncomplicated cystitis is most frequently caused by *Escherichia coli* (75 to 95% of cases), with occasional infections caused by other bacteria such as *Klebsiella pneumoniae*, *Proteus mirabilis* and *Staphylococcus saprophyticus*.

For nonpregnant women with a first episode of acute uncomplicated cystitis, urine culture and susceptibility testing may not be necessary; empirical therapy can be started based on symptoms alone.

Obtain a urine sample for culture and susceptibility testing from:

- men
- patients with recurrent UTIs (two or more episodes within the last 6 months)
- patients with recent antibiotic use (within the last 30 days)
- patients who have not improved with empirical treatment
- children (collect via an in-and-out catheter or suprapubic aspiration).

Men should be examined for evidence of prostatitis, particularly in cases of obstructive urinary symptoms or prostate tenderness on gentle digital rectal examination – see **bacterial prostatitis**, page 326 in this topic.

In symptomatic infants < 12 months old, have a low threshold for treating as for pyelonephritis.

It is unnecessary to perform post-treatment urine culture to confirm resolution of infection for asymptomatic people, except for pregnant women and men with prostatitis.

High fluid intake and complete bladder emptying may aid resolution of UTI.

Strategies to manage symptoms include:

- drinking plenty of liquids
- taking a commercial urinary alkaliniser or one teaspoon of baking soda (bicarbonate of soda) in water
- avoiding acidic foods or drinks as they cancel out the effect of urinary alkalinisers and can aggravate burning symptoms when passing urine
- using paracetamol or a nonsteroidal anti-inflammatory drug (if appropriate) for patients with symptoms of acute cystitis.

Urinary alkalinising agents significantly reduce the antimicrobial effect of nitrofurantoin. If prescribing a patient nitrofurantoin, advise the patient not to use an alkalinising agent.

If a patient has persistent lower urinary tract symptoms, such as dysuria, despite adequate compliance with empirical therapy, collect a urine sample for culture and sensitivity testing to establish or exclude the presence of a drug-resistant organism.

Older women may have nonspecific urinary symptoms, such as dysuria, without evidence of infection. Ongoing lower urinary tract symptoms without evidence of a causative bacterial organism on culture may represent interstitial cystitis, vaginal prolapse, vulval candidiasis, sexually transmissible infection or prior pelvic surgery or trauma. Consider gynaecology or urology review.

Treatment of cystitis

If patient has a catheter, see **catheter-associated UTI** (CA-UTI), page 325 in this topic.

Treatment of cystitis in nonpregnant women

Most women under the age of 65 years who are treated symptomatically (without antibiotic therapy) for acute uncomplicated cystitis become symptom free within 1 week.

If empirical therapy is required for acute uncomplicated cystitis in nonpregnant women, use:

nitrofurantoin *100 mg orally, 6-hourly for 5 days*

OR

trimethoprim+sulfamethoxazole *160+800 mg orally, 12-hourly for 3 days*

OR

cefalexin *500 mg orally, 12-hourly for 5 days.*

Treatment of cystitis in men

For empirical therapy of acute cystitis in men in whom prostatitis is unlikely, while awaiting the results of urine culture, use:

nitrofurantoin *100 mg orally, 6-hourly for 7 days*

OR

trimethoprim+sulfamethoxazole *160+800 mg orally, 12-hourly for 7 days*

OR

cefalexin *500 mg orally, 12-hourly for 7 days.*

Only use a fluroquinolone (e.g. ciprofloxacin) if it is the only appropriate option based on the results of culture and susceptibility testing.

Modify antibiotic therapy based on the results of culture and susceptibility testing, when available.

Treatment of cystitis in children 3 months or older

Treat all children with systemic symptoms as severe pyelonephritis.

Use:

nitrofurantoin *1.5 mg/kg up to 100 mg orally, 6-hourly for 5 days*

OR

trimethoprim+sulfamethoxazole *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 5 days.*

Modify antibiotic therapy based on the results of culture and susceptibility testing, when available.

Pyelonephritis and complicated UTI

For management of **acute pyelonephritis in pregnancy**, see page 190 in 'Maternal infections associated with pregnancy' and page 199 'Infections in neonates and young infants' for the management of infections in neonates.

Pyelonephritis usually presents with fever (> 38 °C), chills, dysuria and unilateral costovertebral angle tenderness. In young children, the symptoms and signs may be more nonspecific, with fever, vomiting and poor feeding common in infants < 12 months.

Uncomplicated pyelonephritis is defined as pyelonephritis limited to nonpregnant, premenopausal women with no known relevant urological abnormalities or comorbidities.

Complicated UTI is a UTI in the presence of:

- obstruction
- immunocompromise
- renal stones
- anatomical urinary tract abnormality.

Take a urine specimen for culture in all patients with pyelonephritis or complicated UTI.

If the patient is systemically unwell, collect blood specimens for culture prior to starting antibiotics. **If a patient has signs of sepsis, give antibiotics within 1 hour of presentation.** See 'Sepsis and bloodstream infections,' page 245, for more information.

For children < 12 months with pyelonephritis, there should be a low threshold for treating with intravenous antibiotics initially, due to an increased risk of secondary bacteraemia. Treat all children with systemic symptoms as severe pyelonephritis.

Consider imaging the renal tract to define or exclude underlying anatomical or functional abnormality, including renal or perinephric abscess.

Do **not** use nitrofurantoin to treat pyelonephritis as it does not achieve adequate concentrations in kidney tissue.

Treatment of pyelonephritis in adults and children

Mild to moderate pyelonephritis

Use:

trimethoprim+sulfamethoxazole *160+800 mg (child: 4+20 mg/kg up to 160+800 mg) orally, 12-hourly for 7 to 10 days*

OR

amoxicillin+clavulanate *500+125 mg (child: 25+5 mg/kg up to 500+125 mg) orally, 8-hourly for 7 to 10 days.*

Severe pyelonephritis

Use:

gentamicin *IV, see 'Appendix 1: Gentamicin dosing' (page 381) for information on dosing frequency, maximum dose and maximum number of doses*

adult: 5 mg/kg (7 mg/kg in critical illness), see Table 14 for dosing frequency (page 384)

child 3 months and older: 7 mg/kg up to 560 mg, once daily

PLUS

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

For patients with hypersensitivity to penicillins, use gentamicin as a single drug for empirical therapy.

For patients still requiring intravenous therapy after 72 hours, switch to:

ceftriaxone *1 g (child: 50 mg/kg up to 1 g) IV, daily*

for patients with septic shock or requiring intensive care support, increase the dose to

ceftriaxone *1 g (child: 50 mg/kg up to 1 g) IV, 12-hourly.*

cont...

If the patient is not improving after 48 to 72 hours of treatment with ceftriaxone, consider escalating to:

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

Switch to oral antibiotics when clinically improved, based on the results of culture and susceptibility testing. If susceptibility results are unavailable, use an empirical oral regimen as for mild to moderate pyelonephritis.

Duration

Treat for a total of 7 to 10 days (IV + oral).

Candiduria

The presence of *Candida* in urine is common, particularly in patients with indwelling catheters, and does not necessarily indicate UTI. Antifungal therapy is not usually indicated and should not be initiated without expert advice.

In children or immunocompromised patients, change (or remove) the catheter and send a second specimen for culture. If *Candida* is isolated from the new sample, perform kidney ultrasound to evaluate renal involvement, which may be indicated by the presence of fungal balls.

Only consider treatment with oral fluconazole in patients with symptoms of acute candidal pyelonephritis (e.g. flank pain and fever 38 °C or higher), if *Candida* is isolated from two different sites or if fungal balls are seen on imaging – seek appropriate advice.

The risk of candiduria is increased by the continued use of urinary catheters, urinary stents or nephrostomy tubes – remove these devices if possible.

Asymptomatic bacteriuria

Asymptomatic bacteriuria refers to the presence of uropathogenic bacteria (e.g. *E. coli*) in the urine, identified by a positive urinary culture, in the absence of any symptoms of a UTI. The incidence of asymptomatic bacteriuria is more common in elderly patients and patients with urinary catheters, see CA-UTI, page 325 in this topic.

Screening for and treatment of asymptomatic bacteriuria is **not** recommended, except for patients undergoing some urological procedures, see **urological surgery** (page 363) in 'Surgical antibiotic prophylaxis' for further information.

Recurrent UTI

Recurrent UTI in adults

Recurrent UTI is defined as two or more episodes of symptomatic infection within 6 months.

Always take a history and examine the patient. Consider alternative diagnoses such as sexually transmissible infections or vulvovaginitis.

Take urine samples for culture and susceptibility testing.

Assess patients for diabetes.

Urological evaluation is recommended for men with recurrent UTI as chronic bacterial prostatitis is a common cause of recurrent UTI. For women with recurrent UTI, investigations including cystoscopy and diagnostic imaging have limited value.

Acute treatment of recurrent UTI in adults

Treat an acute episode of recurrent UTI as for cystitis or pyelonephritis, as appropriate.

Prevention of recurrent UTI in adults

Antibiotic-sparing approaches are preferred prior to using antibiotic prophylaxis. These include:

- increasing fluid intake to a target of 2 to 3 litres daily
- postcoital voiding
- hygiene (wiping from front to back to avoid perineal contamination with faecal flora)
- intravaginal oestrogen in postmenopausal women (not available on the Papua New Guinea Medical and Dental Catalogue but may be available from private healthcare providers).

Patient-initiated standby antibiotics (i.e. antibiotics prescribed to be taken at the onset of symptoms) may be appropriate for some women who have frequent symptomatic UTIs. This strategy is appropriate if the person has had the diagnosis confirmed at least once with a urine culture and is able to easily recognise the symptoms. Advise patients to seek medical review if symptoms do not resolve within 48 hours of completing treatment.

Antibiotic prophylaxis could be considered for women who have frequent symptomatic infections (e.g. two or more infections during a 6-month period or three or more infections over a 12-month period) in whom symptoms are problematic and conservative measures have failed.

If used, suitable options for antibiotic prophylaxis are nitrofurantoin (50 to 100 mg orally, at night) or cefalexin (250 mg orally, at night).

Typically, continuous prophylaxis is used for 6 months and then stopped.

Recurrent UTI in children

For children with recurrent UTI, further investigations, such as renal ultrasound and/or computed tomography, are needed. If potential underlying issues are identified, refer to a urologist for further investigation and management. Also consider possible abuse.

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. 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 severe UTI (i.e. infections that require hospital admission) or vesicoureteric reflux grades III to V – seek appropriate advice.

Catheter-associated UTI

Catheter-associated UTI (CA-UTI) refers to a UTI occurring in a person who is currently catheterised or has been catheterised within the last 48 hours. It is the leading cause of secondary healthcare-associated bacteraemia.

Consider the diagnosis of CA-UTI in catheterised patients with signs and symptoms, including fever (38°C or higher), rigors, acute mental state change, flank pain, acute haematuria, or pelvic discomfort.

Do **not** investigate (with urinalysis or urine culture) catheterised patients with symptoms which are not specific for CA-UTI.

Asymptomatic bacteriuria, i.e. the presence of uropathogenic bacteria (e.g. *E. coli*) in the urine in the absence of any symptoms of a UTI, is frequently found in patients with indwelling urinary catheters. There may be an associated positive urinalysis test for white cells, protein, and/or nitrates. Asymptomatic bacteriuria should **not** be treated with antibiotics, although the catheter should be removed if possible.

Guide to collecting urine samples in patients with indwelling urinary catheters:

- do **not** collect a urine sample from the drainage bag for culture
- **remove** the indwelling catheter and obtain a midstream urine sample, do **not** send the catheter tip for culture
- if ongoing catheterisation is required, **replace** the catheter, then collect a urine sample from the port in the drainage system, or if this is not possible, by separating the catheter from the drainage system.

The rationale for avoiding collection of urine from an existing catheter is that the internal surfaces of the catheter tubing are coated with a bacterial biofilm which contaminates the microbiological sample.

Antibiotic therapy for CA-UTI is often only transiently effective if the catheter is not removed or replaced, because most antibiotics penetrate poorly into catheter biofilm. Treatment without catheter removal can lead to superinfection with resistant organisms.

Use the results of urine culture and susceptibility testing to guide choice of antimicrobial therapy.

The recommended duration of therapy is 7 days; if response to treatment is delayed, 10 to 14 days of therapy may be required.

Do not give antibiotic prophylaxis to prevent CA-UTIs.

Bacterial prostatitis

Acute bacterial prostatitis

While prostatitis is a common diagnosis, less than 10% of cases are due to bacterial infection.

Acute bacterial prostatitis usually presents with symptoms associated with UTI (e.g. acute dysuria, urinary frequency and urgency), and systemic features (e.g. fever [38°C or higher], chills, sweats). Obstructive urinary symptoms (e.g. weak stream, dribbling, hesitancy or urinary retention) and symptoms suggestive of prostatic involvement (e.g. pelvic or perineal pressure, or prostate tenderness on gentle digital rectal examination) may also be present.

Obtain urine samples for culture and susceptibility testing for patients with acute bacterial prostatitis. For patients in hospital, also collect blood samples for culture and susceptibility testing.

Refer any man with one or more of the following symptoms to a urologist for further investigations:

- frequency, dysuria and/or weak urine flow
- chronic pelvic pain, including pain in the testes or perineum
- painful ejaculation or blood in semen.

Management of nonsevere acute bacterial prostatitis

While awaiting the results of culture and susceptibility testing, use:

trimethoprim+sulfamethoxazole *160+800 mg orally, 12-hourly for 2 weeks.*

OR

ciprofloxacin *500 mg orally, 12-hourly for 2 weeks.*

Confirm the infection has resolved by repeating urine culture 1 week after treatment is completed.

Management of severe acute bacterial prostatitis

Acute bacterial prostatitis is considered severe if the patient has fever (38 °C or higher), systemic features (e.g. chills, sweats), or sepsis or septic shock.

During acute infection, most antibiotics (except nitrofurantoin) have good penetration into the inflamed prostate.

While awaiting the results of culture and susceptibility testing, use:

gentamicin *IV, 5 mg/kg (7 mg/kg in critical illness), see Table 14 (page 384) for dosing frequency for information on dosing frequency, maximum dose and maximum number of doses*

PLUS

amoxicillin *2 g IV, 8-hourly.*

If gentamicin is contraindicated, or for patients with immediate nonsevere or delayed nonsevere hypersensitivity to penicillins, or if intravenous therapy is still required at 72 hours, use:

ceftriaxone *1 g IV, daily.*

After 48 to 72 hours of treatment with ceftriaxone, if the patient is not improving, consider escalating to:

ciprofloxacin *400 mg IV, 8-hourly.*

Modify empirical therapy based on the results of culture and sensitivity testing. Switch to oral therapy once the patient is clinically stable. If the results of culture and susceptibility tests are unavailable, use a regimen as for nonsevere acute bacterial prostatitis.

Duration

The total duration of therapy (intravenous + oral) is usually 4 weeks; but if the patient is treated with ciprofloxacin, only 2 weeks of treatment is required. Confirm the infection has resolved by repeating urine culture 1 week after treatment is completed.

Chronic bacterial prostatitis

Recurrent infection of the prostate, usually with Gram-negative organisms.

Presentation may include low-grade fever, urgency or perineal discomfort. Most cases of what is thought to be 'chronic prostatitis,' characterised by chronic pelvic pain, are not due to infection and repeated courses of antibiotic treatment should be avoided.

Chronic bacterial prostatitis is rare.

Consider noninfectious causes, such as bladder malignancy, or other infections including sexually transmissible infections.

Management of chronic bacterial prostatitis

If antibiotic treatment is necessary, take cultures prior to starting treatment and refer patients who fail initial therapy to urology.

Antibiotics should be guided by the results of culture and susceptibility testing, however fluroquinolones and trimethoprim+sulfamethoxazole are preferred agents due to good prostate penetration.

Use:

trimethoprim+sulfamethoxazole *160+800 mg orally, 12-hourly for 4 weeks.*

Alternative therapy:

ciprofloxacin *500 mg orally, 12-hourly for 4 weeks.*

Wound infections

This topic includes advice on the management of the following conditions in adults and children older than 3 months

- **bite wounds**, page 329
- **traumatic wound infections**, page 333
- **surgical site infections**, page 335
- **burns**, page 338**.**

The following topics are not included in this section:

- **open fractures** (page 56) and **maxilla and mandible fractures** (page 60) in 'Bone and joint infections'
- **necrotising soft tissue infections** (page 307) in 'Soft tissue infections'
- **tetanus prophylaxis following traumatic wounds** (page 378) in 'Prevention of infection for medical conditions.'

Bite wounds

Bites, including clenched-fist injuries (in which the hand is lacerated by contact with another person's teeth), often become infected.

Consider tetanus prophylaxis for all bite wounds – ensure that tetanus immunisation is up-to-date. See requirement for **tetanus prophylaxis following traumatic wounds**, page 378 in 'Prevention of infection for medical conditions.'

Bite wound infections are caused by bacteria associated with human skin (*Staphylococcus aureus*), and animal oral flora (*Pasteurella* species, *Capnocytophaga canimorsus*, *Streptococcus* species and anaerobic bacteria). Marine bite infections are associated with *Aeromonas* species, *Shewanella putrefaciens*, and *Vibrio* species.

Antibiotics are required for infected bites. If there is evidence of infection, take a wound swab for culture. If the patient is systemically unwell, collect blood specimens for culture. If the wound is debrided, send a tissue specimen for culture. Seek surgical advice for wounds where pain appears to be disproportionate to the injury as this may be due to an abscess or complications such as acute compartment syndrome.

For bites that are not clinically infected, antibiotics are only required if the risk of developing a wound infection is high. Bite wounds are **high risk** for infection if any of the following are present:

- delayed presentation for debridement (> 8 hours)
- puncture wound that cannot be adequately debrided

- wound on hands, feet or face
- wound involving bones, joints or tendons
- the patient is immunocompromised
- the wound is from a cat.

If patient is in **septic shock** treat as for **necrotising soft tissue infections**, page 307 in 'Soft tissue infections.'

Antibiotic therapy for bite wounds

Mild infection associated with human bite (including clenched-fist injuries), cat or dog bites

Clenched-fist injuries are injuries in which the hand is lacerated by contact with another person's teeth.

Mild infections have localised symptoms only.

Presumptive treatment for high-risk wounds or treatment of mild infection:

amoxicillin+clavulanate *500+125 mg (child: 25+5 mg/kg up to 500+125 mg) orally, 8-hourly.*

For patients with hypersensitivity to penicillins, use:

doxycycline *100 mg (child ≥8 years: 2 mg/kg up to 100 mg) orally, 12-hourly*[20]

PLUS

metronidazole *400 mg (child: 10 mg/kg up to 400 mg) orally, 12-hourly*

OR

trimethoprim+sulfamethoxazole *160+800 mg (child: 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.*

Duration

Presumptive treatment for high-risk wounds: treat for 3 days.

Mild infection: treat for 5 to 7 days depending on clinical response.

20 Unlike older tetracyclines, doxycycline has not been associated with tooth discolouration, enamel hypoplasia or bone deposition with short-term use (< 21 days), even in children younger than 8 years, so is increasingly used in this age group. However, use is limited by the lack of a suitable paediatric formulation.

Moderate to severe infection associated with human bite (including clenched-fist injuries), cat or dog bites

Clenched-fist injuries are injuries in which the hand is lacerated by contact with another person's teeth.

Moderate to severe infections are associated with systemic features or involving deeper tissues (such as bones, joints or tendons).

Use:

ceftriaxone *2 g (child: 25 mg/kg up to 2 g) IV, daily*

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 hypersensitivity to penicillins, use:

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

PLUS

clindamycin *450 mg (child: 10 mg/kg up to 450 mg) orally, 8-hourly.*

If oral therapy is not possible, use:

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

PLUS

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

Switch to oral antibiotics as for mild infection once clinically improved.

Duration: treat for a total of 10 to 14 days (IV + oral).

Mild infection associated with marine bites or bite wounds contaminated by water

Mild infections have localised symptoms only.

Presumptive treatment for high-risk wounds or mild infection:

flucloxacillin *500 mg (child: 15 mg/kg up to 500 mg) orally, 6-hourly*

PLUS

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

cont...

For patients with hypersensitivity to penicillins, use:

trimethoprim+sulfamethoxazole *160+800 mg (child: 4+20 mg/kg up to 160+800 mg) orally, 12-hourly.*

Duration

For presumptive treatment of high-risk wounds: treat for 3 days.

Mild infection: treat for 5 to 7 days depending on clinical response.

Moderate to severe infection associated with marine bites or bite wounds contaminated by water

Moderate to severe infections are associated with systemic features or involving deeper tissues (such as bones, joints or tendons).

Use:

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

PLUS either

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

OR

doxycycline *100 mg (child: 10 mg/kg up to 100 mg) orally, 12-hourly.*

For patients with hypersensitivity to penicillins, use:

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

PLUS

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

Switch to oral antibiotics as for mild infections once clinically improved.

Duration: treat for a total of 10 to 14 days (IV + oral).

Traumatic wound infections

If a patient has an open fracture, see **open fractures** (page 56) in 'Bone and joint infections.'

If patient is in **septic shock** treat as for **necrotising soft tissue infections** (page 307) in 'Soft tissue infections.'

This section provides advice for patients with extremity wounds. For patients with other wounds (e.g. penetrating abdominal wounds, chest trauma), seek appropriate advice.

For patients with traumatic wounds, ensure that tetanus immunisation is up-to-date. See **tetanus prophylaxis following traumatic wounds**, page 378 in 'Prevention of infection for medical conditions.'

Careful cleaning and debridement of traumatic wounds is important to prevent infection; use at least 1 L of normal saline for wound washout before surgery. Immobilisation and elevation are also beneficial.

Antibiotics are **not** routinely required for traumatic wounds. They are used as:

- prophylaxis for wounds requiring surgical management or that are significantly contaminated (e.g. penetrating injuries through footwear, stab wounds)
- treatment of established infection.

If antibiotic therapy is indicated for a traumatic wound that has been immersed in water, see water-immersed wound infections for antibiotic choice.

Likely pathogens in post-traumatic wound infection include *Staphylococcus aureus* and *Streptococcus pyogenes* (group A streptococcus). Anaerobic post-traumatic wound infection (e.g. *Clostridium perfringens* infection) is rare but may follow severe injuries if the wound is heavily contaminated. A broader range of pathogens are seen in infections of traumatic wounds that have been immersed in water, including soil- or sewage-contaminated water (e.g. injuries sustained in a natural disaster, marine injuries).

Collect samples for Gram stain and culture before antibiotic therapy is started.

Antibiotic therapy for traumatic wound infections

Mild traumatic wound infection

Heavily contaminated wounds that do not require surgery.

Mild infection, i.e. localised post-traumatic wound infection not associated with systemic symptoms or involving deeper tissues (such as bones, joints or tendons).

If there is evidence of infection, take a wound swab for culture. If there are systemic features of infection, take blood specimens for culture.

Use:

flucloxacillin *500 mg (child: 15 mg/kg up to 500 mg) orally, 6-hourly.*

For patients with hypersensitivity to penicillins, use:

trimethoprim+sulfamethoxazole *160+800 mg (child: 4+20 mg/kg up to 160+800 mg) orally, 12-hourly*

OR

clindamycin *450 mg (child: 10 mg/kg up to 450 mg) orally, 8-hourly.*

Duration

Treat for 5 to 7 days depending on clinical response.

Moderate to severe traumatic wound infection

For wounds that require surgery.

Moderate to severe infection, i.e. post-traumatic wound infection associated with systemic features or deeper tissues (such as bones, joints or tendons).

Swab wound for culture. If there are systemic features of infection, send blood cultures.

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

Alternatively, use:

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

OR, including in patients with hypersensitivity to penicillins:

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

OR

vancomycin *slow IV infusion,* ***consider a loading dose in critically ill adults and children****. See 'Appendix 2: Vancomycin dosing' (page 386) for information on loading dose, dosing frequency and infusion time*

adult ≥ 40 years: 15 mg/kg, see Table 18 for dosing frequency (page 390)

adult < 40 years 20 mg/kg, see Table 17 for dosing frequency (page 389)

child 3 months and older: 15 mg/kg, 6-hourly.

cont...

If wound is heavily contaminated or has penetrated to a hollow viscus, **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.*

Duration

Change to oral antibiotics based on culture and susceptibility results when clinically improving to complete a total of 10 to 14 days (IV + oral). If cultures are not available, use an oral regimen as for mild traumatic wound infections.

Surgical site infections

If patient is in **septic shock**, treat as for **necrotising soft tissue infections**, page 307 in 'Soft tissue infections.'

A surgical site infection refers to a postoperative patient who has developed an infection at the operation site, either on the ward or after being discharged.

Diabetes is a common patient factor that increases the risk for surgery, including the risk of surgical site infections. Test all surgical patients for diabetes on admission, control blood sugars before surgery where possible and check blood sugar levels for all patients prior to surgery.

Most surgical site infections are caused by organisms already colonising the patient at the time of surgery. Infection is most commonly caused by skin flora, including *Staphylococcus aureus*, other *Staphylococcal* species, *Streptococcal* species. and, in clean-contaminated procedures (where the gastrointestinal, respiratory or genitourinary tracts are entered), *Enterococcus* species, and Gram-negative bacilli and anaerobes. Empirical antibiotic choice depends on whether Gram-positive bacteria or Gram-negative or anaerobic bacteria are suspected.

Collect samples for Gram stain and culture before starting antibiotic therapy. More severe surgical site infections (including those involving the deep soft tissues) may require removal of stiches, surgical exploration, drainage, removal of implanted material (e.g. mesh, orthopaedic hardware), irrigation and debridement; delayed wound closure is often necessary.

Septic patients need urgent surgical intervention and source control. If there is a poor response to empirical therapy, consider ultrasound to look for an abscess or other collection.

Antibiotic therapy for surgical site infections

Mild (superficial) surgical site infection

For minor skin infections, measures such as surgical drainage and irrigation with sodium chloride 0.9% are often adequate for cure. Antibiotic therapy is necessary for skin infection with associated cellulitis or infection of the subcutaneous tissues.

If the procedure did not enter the gastrointestinal, respiratory or genitourinary tracts, suspect Gram-positive bacteria. Use:

flucloxacillin *500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly.*

Alternatively, including for patients with **immediate nonsevere** or **delayed nonsevere** hypersensitivity to penicillins, use:

cefalexin *500 mg (child: 12.5 mg/kg up to 500 mg) orally, 6-hourly.*

For patients with **immediate severe** 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.*

If the procedure entered the gastrointestinal, respiratory or genitourinary tracts, suspect Gram-negative or anaerobic bacteria. **Add** metronidazole to one of the above regimens:

metronidazole *400 mg (child: 10 mg/kg up to 400 mg) orally, 12-hourly.*

Duration

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.

Moderate to severe surgical site infection

For deep incisional surgical site infections (involving the fascia or muscle) or surgical site infections with systemic features, but not sepsis or septic shock, it is usually necessary to combine antibiotic therapy with source control (e.g. drainage, irrigation, debridement).

Swab the wound for culture and take blood for culture if systemically unwell. Debride the wound if necrotic tissue or deep collection is present. Send tissue for culture.

cont...

If the procedure did not enter the gastrointestinal, respiratory or genitourinary tracts, suspect Gram-positive bacteria. Use:

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

Alternatively, for patients with **immediate nonsevere** or **delayed nonsevere** hypersensitivity to penicillins, use:

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

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

vancomycin *slow IV infusion,* **consider a loading dose in critically ill adults and children**. *See 'Appendix 2: Vancomycin dosing' (page 386) for information on loading dose, dosing frequency and infusion time*

adult ≥ 40 years: 15 mg/kg, see Table 18 for dosing frequency (page 390)

adult < 40 years 20 mg/kg, see Table 17 for dosing frequency (page 389)

child 3 months and older: 15 mg/kg, 6-hourly.

If the procedure entered the gastrointestinal, respiratory or genitourinary tracts, suspect Gram-negative or anaerobic bacteria and **add** to one of the above agents (and use a three-drug regimen):

gentamicin *IV, see Appendix 1: Gentamicin dosing (page 381) for information on dosing frequency, maximum dose and maximum number of doses*

adult: 5 mg/kg (7 mg/kg in critical illness), see Table 14 for dosing frequency (page 384)

child 3 months and older: 7 mg/kg up to 560 mg, once daily

PLUS

metronidazole *500 mg (child: 12.5 mg/kg up to 500 mg) IV, 12-hourly.*

If the patient is not responding to empirical therapy, assess surgical source control (based on clinical assessment and imaging if relevant). Remove any prosthetic material if indicated. If escalation of antibiotic treatment is required, **add** an agent with activity against methicillin-resistant *Staphylococcus aureus*, use:

vancomycin *(dosing as above).*

OR

chloramphenicol *1 g (child: 25 mg/kg up to 1 g) IV, 6-hourly*

OR

cont...

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

For patients that still do not respond, consider expert consultation and escalate therapy by **switching** to (as a two-drug regimen):

meropenem *1 g (child: 20 mg/kg up to 1 g) IV, 8-hourly*

PLUS

vancomycin *(dosing as above).*

Duration

Modify therapy based on the results of culture and susceptibility testing when systemic features have resolved and source control has been achieved. If culture results are unavailable, see mild (superficial) infection for appropriate regimens.

Treat for 7 to 14 days depending on the severity of infection and clinical response.

Burns

Consider tetanus prophylaxis for all burns. See **tetanus prophylaxis following traumatic wounds**, page 378 in 'Prevention of infection for medical conditions.'

Antibiotic prophylaxis is not indicated for patients with burns that do not require immediate debridement surgery (e.g. superficial hot water burns).

For all burns cases, proper debridement and/or escharotomy is paramount.

For patients who require debridement use routine surgical prophylaxis, see **plastic and reconstructive surgery** (page 362) in Table 11: Surgical antibiotic prophylaxis for specific procedures in 'Antibiotic prophylaxis in surgical procedures.' There is no evidence to support the use of systemic prophylactic antibiotics after debridement. Monitor patients closely for evidence of infection and treat if this occurs.

Superficial wound swab cultures can be helpful to direct therapy when infection is present; however, they should be interpreted in the clinical context, as organisms isolated may be colonising rather than infecting the wound.

Send blood specimens for culture if systemically unwell. Send tissue specimens for culture from debridement if infection is suspected.

If there are signs of surrounding cellulitis, treat as **cellulitis** (page 273) in 'Skin infections.'

Management of burns

Wound care for burns can be extremely painful. For smaller wounds, provide paracetamol, nonsteroidal anti-inflammatory drugs and / or oral opioids for pain during dressing changes.

For larger burns, intravenous opioids are typically required.

For minor burns, use:

sterilised gauze dressing impregnated with white soft paraffin.

For burns with moderate to severe with signs of infection, use:

silver sulfadiazine 1% cream topically (note: this cream does not penetrate eschar).

Key additional references

Berríos-Torres SI, Umscheid CA, Bratzler DW, et al. Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, 2017. JAMA Surg 2017; 152:784.

Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, Fish DN, Napolitano LM, Sawyer RG, Slain D, Steinberg JP, Weinstein RA; American Society of Health-System Pharmacists; Infectious Disease Society of America; Surgical Infection Society; Society for Healthcare Epidemiology of America. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health Syst Pharm. 2013 Feb 1;70(3):195-283.

Miscellaneous infections

This topic includes advice on the management of the following conditions in adults and children older than 3 months

- **acute rheumatic fever**, page 341
- **leptospirosis**, page 345
- **scrub typhus and other rickettsial infections**, page 346
- **tetanus**, page 347
- **melioidosis**, page 348**.**

The following topics are not included in this section:

- **secondary prevention of rheumatic fever** (page 367) and **tetanus prophylaxis following traumatic wounds** (page 378) in 'Prevention of infection for medical conditions.'

Acute rheumatic fever

Acute rheumatic fever (ARF) is a multisystem inflammatory disease resulting from an autoimmune response to recurrent *Streptococcus pyogenes* (group A streptococcus [GAS]) infection of throat or skin.

It most frequently affects children and can lead to the development of rheumatic heart disease (RHD).

Diagnosis of acute rheumatic fever

Clinical signs may include arthritis (swollen and painful joints), carditis (heart murmurs), erythema marginatum (red rash), chorea (abnormal movements) and subcutaneous nodules (raised swellings in skin), along with fever and arthralgia (joint pain).

Consider other causes of a swollen joint in a child or adolescent (e.g. septic arthritis).

Diagnosis of ARF can be complex. A combination of clinical features (revised Jones criteria) and evidence of preceding GAS infection is used. Samples should be collected and sent to the lab for throat culture and serology for GAS, if available. Throat culture may be negative by the time of onset of ARF.

Patients with suspected rheumatic fever should be admitted to hospital. If possible, echocardiography should be performed.

Table 9: Major and minor manifestations for the diagnosis of acute rheumatic fever

	High-risk groups [Note 1]	Low risk groups
definite initial episode of ARF	2 major manifestations + evidence of preceding GAS infection, OR 1 major + 2 minor manifestations + evidence of preceding GAS infection [Note 2]	
definite recurrent [Note 3] episode of ARF in a patient with a documented history of ARF or RHD	2 major manifestations + evidence of preceding GAS infection, [Note 2], OR 1 major + 2 minor manifestations + evidence of preceding GAS infection [Note 2], OR 3 minor manifestations + evidence of a preceding GAS infection [Note 2]	
probable or possible ARF (first episode or recurrence) [Note 3]	A clinical presentation in which ARF is considered a likely diagnosis but falls short in meeting the criteria by either: • one major or one minor manifestation, OR • no evidence of preceding Strep A infection (streptococcal titres within normal limits or titres not measured) Such cases should be further categorised according to the level of confidence with which the diagnosis is made: • probable ARF (where ARF is considered the most likely diagnosis) • possible ARF (where ARF is considered less likely than other diagnoses but cannot be excluded)	
major manifestations	carditis (including subclinical evidence of rheumatic valvulitis on echocardiogram) polyarthritis [Note 4] or aseptic monoarthritis or polyarthralgia Sydenham chorea [Note 5] erythema marginatum [Note 6] subcutaneous nodules	carditis (including subclinical evidence of rheumatic valvulitis on echocardiogram) polyarthritis [Note 4] Sydenham chorea [Note 5] erythema marginatum [Note 6] subcutaneous nodules
minor manifestations	fever of 38°C or higher [Note 7] monoarthralgia [Note 8] ESR 30 mm/hour or more, or CRP 30 mg/L or more prolonged PR interval on ECG [Note 9]	fever of 38.5°C or higher polyarthralgia or aseptic monoarthritis [Note 8] ESR 60 mm/hour or more, or CRP 30 mg/L or more prolonged PR interval on ECG [Note 9]

cont...

ARF = acute rheumatic fever; CRP = C-reactive protein; ECG = electrocardiogram; ESR = erythrocyte sedimentation rate; GAS = group A streptococcus, RHD = rheumatic heart disease.

Note 1: For determination of risk of acute rheumatic fever, see below.

Note 2: Elevated or rising antistreptolysin O or other streptococcal antibody, or a positive throat culture or rapid antigen or nucleic acid test for GAS infection.

Note 3: Recurrent definite, probable or possible ARF requires a time period of more than 90 days after the onset of symptoms from the previous episode of definite, probable or possible ARF.

Note 4: A definite history of arthritis is sufficient to satisfy this manifestation. Note that if polyarthritis is present as a major manifestation, polyarthralgia or aseptic monoarthritis cannot be considered an additional minor manifestation in the same person.

Note 5: Chorea does not require other manifestations or evidence of preceding GAS infection, provided other causes of chorea are excluded.

Note 6: Care should be taken not to label other rashes, particularly non-specific viral exanthems, as erythema marginatum.

Note 7: In high-risk groups, fever can be considered a minor manifestation based on a reliable history (in the absence of documented temperature) if anti-inflammatory medication has already been administered.

Note 8: If polyarthritis is present as a major criterion, monoarthritis or arthralgia cannot be considered an additional minor manifestation.

Note 9. If carditis is present as a major criterion, prolonged PR interval cannot be considered as an additional minor manifestation.

Adapted with permission from: The 2020 Australian guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease (3.2 edition, March 2022); 2020, Reproduced with permission from Menzies School of Health Research. https://www.rhdaustralia.org.au/

An individual is at high risk of developing ARF if they are:

- younger than 40 years and any one of the following:
  - a person living in a rural or remote area in Papua New Guinea
  - a person living in a household affected by overcrowding or experiencing socioeconomic disadvantage
  - a person with a history of ARF or RHD
  - part of a family or household in which a member has a recent history of ARF or RHD.
- For individuals younger than 40 years, but particularly between 5 and 20 years, other factors that could put them at high risk of developing ARF include:
  - current or prior residence in, or frequent or recent travel to, a setting with a high rate of ARF (e.g. refugees, migrants).

Management of definite, probable and possible ARF

See *Standard Treatment for Common Illnesses of Children in Papua New Guinea* for more information on non-antimicrobial management, including management of heart failure and arthritis or severe arthralgia.

Following the first episode of ARF or a diagnosis of RHD, patients should be treated with **ongoing** penicillin to prevent recurrence and prevent development of progression of RHD, see **secondary prevention of rheumatic fever** (page 367) in 'Prevention of infection for medical conditions.'

Treatment of ARF

Antibiotics are used to treat any residual GAS infection and eliminate carriage of the organism. Use:

benzathine benzylpenicillin *IM, as a single dose*

adult: 1.2 million units (2.3 mL)

child 10 kg to less than 20 kg: 0.6 million units (1.2 mL)

child 20 kg or more: 1.2 million units (2.3 mL).

If a patient cannot tolerate injections, an oral formulation can be given instead. Use:

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

Penicillin is the drug of choice for the treatment of GAS infection and elimination of carriage. If patients report hypersensitivity, they should be carefully assessed to confirm immune-mediated hypersensitivity.

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

cefalexin *1 g (child: 25 mg/kg up to 1 g) orally, 12-hourly for 10 days.*

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

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

To treat arthritis or severe arthralgia (joint pain and swelling), use:

aspirin (adult or child) 12.5 to 15 mg/kg up to 900 mg orally, 6-hourly. If needed for severe pain, increase temporarily to 20 to 25 mg/kg orally, 6-hourly

OR

ibuprofen 200 to 400 mg (child: 5 to 10 mg/kg [for overweight children, use ideal body weight] up to 400 mg) orally, three times daily.

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 (e.g. farmwork, livestock contact, local flooding) are commonly present. Ideally, serology testing can be used to confirm the diagnosis, but this was not available in Papua New Guinea at the time of writing.

Management of leptospirosis

Management of mild leptospirosis

Start treatment if leptospirosis is suspected clinically. Send blood specimens to confirm the diagnosis, if serology testing is available.

Doxycycline is the preferred drug for empirical therapy because it also treats rickettsial infections, which have a similar presentation to leptospirosis. However, avoid doxycycline in pregnant people.

For mild cases, where oral therapy is tolerated, use:

doxycycline *100 mg (child: 2 mg/kg up to 100 mg) orally, 12-hourly for 7 days* [21]

OR

amoxicillin *500 mg (child: 15 mg/kg up to 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 up to 500 mg) orally, 6-hourly (child: 8-hourly) for 7 days*

OR

azithromycin

adult: 1 g orally, as a single dose on day 1, then 500 mg orally, daily on days 2 and 3

child: 10 mg/kg up to 500 mg orally, as a single dose on day 1, then 5 mg/kg up to 250 mg orally, daily on days 2 and 3

OR

clarithromycin *500 mg orally, 12-hourly for 7 days.*

21 Unlike older tetracyclines, doxycycline has not been associated with tooth discolouration, enamel hypoplasia or bone deposition with short-term use (< 21 days), even in children younger than 8 years, so is increasingly used in this age group and should be used when it is the drug of choice. However, use is limited by the lack of a suitable paediatric formulation.

Management of severe leptospirosis

Start treatment if leptospirosis is suspected clinically. Send blood specimens to confirm the diagnosis, if serology testing is available.

All severe cases require early referral to hospital for inpatient care. Use:

benzylpenicillin *1.2 g (child: 50 mg/kg up to 1.2 g) IV, 6-hourly*

OR

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

Alternative agents are:

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

In cases requiring ICU admission, ceftriaxone is the preferred agent.

Duration: treat for at least 7 days (IV + oral).

Scrub typhus and other rickettsial infections

Suspect in patients with headache, fevers, elevated transaminases, thrombocytopaenia and leucocytosis. Examine for eschar, painful lymphadenopathy, and rash.

Management of scrub typhus and other rickettsial infections

Use:

doxycycline *100 mg (child: 2 mg/kg up to 100 mg) orally, 12-hourly*[22] *for 7 days.*

Doxycycline is recommended to treat rickettsial infections in children of all ages because it is the most effective treatment. However, its use is limited by the availability of suitable paediatric formulations.

Alternatively, use:

azithromycin *500 mg (child: 10 mg/kg up to 500 mg) on day 1, then 250 mg (child: 5 mg/kg up to 250 mg) for a further 4 days.*

22 Unlike older tetracyclines, doxycycline has not been associated with tooth discolouration, enamel hypoplasia or bone deposition with short-term use (< 21 days), even in children younger than 8 years, so is increasingly used in this age group. Doxycycline should be used when it is the drug of choice, regardless of the patient's age, if there is a suitable formulation available.

Tetanus

See also: **tetanus prophylaxis following traumatic wounds** (page 378) in 'Prevention of infection for medical conditions.'

Clostridium tetani inoculation of a dirty wound causes disease by toxin production. After infection of a wound, the incubation period of tetanus is usually around 1 week but ranges from 1 day to 2 months. Many patients may not remember the wound, so this should not put clinicians off the diagnosis.

Generalised spasms are the most common presentation – symptoms usually begin with trismus and progress to involve the rest of the muscles of the body. The spasms and autonomic dysfunction of tetanus should be controlled with diazepam and magnesium sulfate in a similar manner to convulsions.

Disease may take weeks to resolve.

Management of tetanus

Nurse patients in a calm, dim, quiet environment (movement, wind, bright lights or emotional distress can all trigger spasms).

All patients will need a full course of vaccination against tetanus in addition to antitoxin (immunoglobulin) and antibiotics as acute tetanus infection does **not** confer immunity following recovery.

Clean and debride all contaminated wounds early and thoroughly.

Protect the airway and ventilate patients who have severe disease with uncontrolled spasms and risk of airway and or respiratory compromise.

To halt further production of toxin, use antibiotics with activity against *C. tetani*; give:

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.*

Alternatively, use:

benzylpenicillin *1.8 g (child: 50 mg/kg up to 1.8 g) IV, 6-hourly*

OR

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

To neutralise toxin already in circulation

Use **either**:

human tetanus immunoglobulin (for intramuscular administration) 500 units IM

OR if available

cont...

human tetanus immunoglobulin (for intravenous administration) 4000 units IV

To reduce muscle spasm and distress

Use:

diazepam 5 to 20 mg orally/IV, 8-hourly (doses up to 20 mg, 2-hourly may be required). At high doses (80 mg/24 hours), monitor for respiratory suppression.

To reduce autonomic dysfunction and muscle spasm:

Use:

magnesium sulfate 5 g (child: 75 mg/kg up to 5 g) IV, as a loading dose, then 2 to 3 g IV infusion, hourly until spasm controlled. Monitor patellar reflexes, and if areflexia occurs decrease the dose.

The anxiolytic activity of diazepam is useful in this very distressing disease, but its antispasmodic activity is even more important.

Only use magnesium sulfate IV and diazepam IV in a controlled hospital environment with access to respiratory support if required.

Duration: Treat with antibiotics for 7 to 10 days.

Melioidosis

This infection is caused by the bacteria *Burkholderia pseudomallei.* Disease occurs via inhalation and percutaneous inoculation. Patients can present with pneumonia that sometimes mimics tuberculosis, sepsis with abscesses in multiple organs, or cutaneous ulcers. Risk factors include diabetes, hazardous alcohol use, renal disease, chronic lung disease and other forms of immunocompromise (although HIV does not seem to be a risk factor).

Seek infectious diseases review where available.

Treatment of melioidosis

Send specimens of blood, urine, sputum, pus and/or wound swab for culture. All patients should have a chest X-ray and CT or ultrasound of their abdomen and pelvis to detect any abscesses. Treatment consists of an initial phase of intravenous (with or without oral) therapy, followed by oral eradication therapy to prevent relapse.

Intensive therapy	Use: ***meropenem*** *1 g (child: 25 mg/kg up to 1 g) IV, 8-hourly.* If there is neurological involvement, use: ***meropenem*** *2 g (child: 40 mg/kg up to 2 g) IV, 8-hourly.* If meropenem is not available, and the patient is not critically ill and does not have neurological involvement, use: ***ceftazidime*** *50 mg/kg up to 2 g IV, 6-hourly.* In neurological disease, osteomyelitis, septic arthritis, genitourinary infection, or skin and soft tissue infection, **add** to either meropenem or ceftazidime: ***trimethoprim+sulfamethoxazole*** *orally, 12-hourly* *adults 40 to 60 kg: 240+1200 mg* *adults > 60 kg 320+1600 mg* *child: 6+30 mg/kg* *PLUS* *folic acid 5 mg (child: 0.1 mg/kg up to 5 mg) orally, daily.* If neither meropenem nor ceftazidime are available, seek expert advice.
Eradication therapy	Once the course of initial therapy is completed, immediately follow with: ***trimethoprim+sulfamethoxazole*** *orally, 12-hourly* *adults 40 to 60 kg: 240+1200 mg* *adults > 60 kg: 320+1600 mg* *child: 6+30 mg/kg* *PLUS* *folic acid 5 mg (child: 0.1 mg/kg up to 5 mg) orally, daily.* Monitor electrolytes and creatinine regularly while on trimethoprim+sulfamethoxazole.

Duration:

Skin abscess, bacteraemia without focus: intensive phase 2 weeks; eradication phase 3 months.

Pneumonia: intensive phase 3 to 4 weeks, eradication phase 3 months.

Deep collection, septic arthritis: intensive phase 4 weeks from most recent drainage; eradication phase 3 months.

Osteomyelitis: intensive phase 6 weeks; eradication phase 6 months.

CNS infection, mycotic aneurysms: intensive phase 8 weeks; eradication phase 6 months.

Key additional references

European AIDS Clinical Society. Guidelines: Version 10.0: November 2019. Brussels: EACS; 2019. Available from: https://www.eacsociety.org/media/2019_guidelines-10.0_final.pdf.

Lipsitz R, Garges S, Aurigemma R, Baccam P, Blaney DD, Cheng AC, Currie BJ, Dance D, Gee JE, Larsen J, Limmathurotsakul D, Morrow MG, Norton R, O'Mara E, Peacock SJ, Pesik N, Rogers LP, Schweizer HP, Steinmetz I, Tan G, Tan P, Wiersinga WJ, Wuthiekanun V, Smith TL. Workshop on treatment of and postexposure prophylaxis for Burkholderia pseudomallei and B. mallei Infection, 2010. Emerg Infect Dis. 2012 Dec;18(12):e2.

RHDAustralia (ARF/RHD writing group). The 2020 Australian guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease (3.2 edition, March 2022); 2020.

Sullivan RP, Marshall CS, Anstey NM, Ward L, Currie BJ. 2020 Review and revision of the 2015 Darwin melioidosis treatment guideline; paradigm drift not shift. PLoS Negl Trop Dis. 2020 Sep 28;14(9):e0008659.

Antibiotic prophylaxis in surgical procedures

This topic includes information on the following topics:

The following topic is not included in this section:

Introduction to surgical antibiotic prophylaxis

The aim of surgical prophylaxis is to reduce rates of surgical site and healthcare-associated infections, and so reduce surgical morbidity and mortality. However, there is growing evidence that aspects of prescribing practice may themselves be associated with healthcare-associated infections and antimicrobial resistance.

Preoperative antibiotics are given for the purpose of reducing the risk of surgical site infection due to bacterial contamination of the wound that may occur during surgery. Extending antibiotic use into the postoperative period has a minimal impact on wound infection rates. It does not compensate for unhygienic postoperative care. Instead, such use increases the risk of a patient becoming colonised by bacteria that are resistant to the antibiotic given. Therefore, if an infection develops later, it can be more difficult to treat.

Principles of surgical antibiotic prophylaxis

The **indication for prophylaxis** should comply with these guidelines – see indications for surgical antibiotic prophylaxis and the recommendations for specific procedures in Table 11: Surgical antibiotic prophylaxis for specific procedures, page 355.

Timing of antibiotic(s):

- surgical antibiotic prophylaxis must be administered before surgical incision to achieve effective plasma and tissue concentrations at the time of incision
- short-acting antibiotics, such as cefazolin, should be administered ≤60 minutes prior to skin incision
- for antibiotics that are not short acting, the dose should be administered ≤120 minutes before surgical incision. For antibiotic-specific advice, see Table 10: Administration and timing of antibiotics for surgical prophylaxis, page 354.

Record the antibiotic prescription in the 'once only' section of medicine chart to avoid multiple doses being administered.

A **single preoperative dose of antibiotic(s)** is sufficient for the significant majority of procedures, unless:

- more than 1.5 L of blood loss intraoperatively, re-dose following fluid replacement (see administration guidance table)
- the operation prolonged (see administration guidance table)
- it is specifically stated in the guidelines.

Do not extend the duration of antibiotic prophylaxis because the patient has a urinary or intravascular catheter, or surgical drain, in situ.

Document any reason for antibiotic administration beyond a single dose or state the intention for antibiotic treatment course in medical notes.

The principles for appropriate prescribing of surgical antibiotic prophylaxis are as follows:

- the choice of agent should be directed against the organism(s) most likely to cause postoperative infection; most postoperative infections are caused by organisms that already colonise the patient.

- cefazolin is the preferred drug for the majority of procedures that require prophylaxis.
- antibiotic choice may need to be modified according to patient factors, including the presence of infection, recent antimicrobial use, colonisation with multidrug-resistant bacteria, prolonged hospitalisation or the presence of prostheses.
- cefazolin is not effective against methicillin-resistant *Staphylococcus aureus* (MRSA). For patients colonised or infected with MRSA, add vancomycin to cefazolin.
- avoid broad-spectrum cephalosporins (e.g. cefotaxime, ceftriaxone), clindamycin, quinolones and amoxicillin+clavulanate wherever possible.
- if the patient is being treated with antibiotic therapy for established infection, it is not necessary to give additional antibiotic prophylaxis, provided the treatment regimen has activity against the organism(s) most likely to cause postoperative infection. However, adjust the timing of the treatment dose to achieve adequate plasma and tissue concentrations at the time of surgical incision and for the duration of the procedure.

Complex individual prophylaxis issues should be discussed with a medical microbiologist or infectious disease physician preoperatively and recorded in the medical notes.

Surgical antibiotic prophylaxis for patients with specific cardiac conditions

Antibiotics for the prevention of endocarditis may be needed for patients with specific cardiac conditions who are undergoing a surgical procedure, even if surgical antibiotic prophylaxis is not indicated (e.g. tonsillectomy, adenoidectomy). See **infective endocarditis prophylaxis**, page 369 in 'Infections for medical conditions.'

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 **cross-reactivity between beta-lactams**, page 32 in 'Antimicrobial hypersensitivity'), and is often tolerated in patients with a penicillin or cephalosporin allergy.

For patients with immediate nonsevere or delayed nonsevere hypersensitivity to penicillins, cefazolin can be used.

For patients with immediate severe 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 11, page 355.

Administration and timing of antibiotics for surgical prophylaxis

Table 10: Administration and timing of antibiotics for surgical prophylaxis

Antibiotic	Dose [Note 1]	Administration and timing	Redosing interval [Note 2]
cefazolin	adult: 2 g in adults with body weight ≥120 kg use 3 g child: 30 mg/kg up to 2 g	slow IV bolus over 5 minutes or IV infusion; started within 60 minutes before incision	4 hours
clindamycin	adult: 600 mg child: 15 mg/kg up to 600 mg	IV infusion over at least 20 minutes; started within 120 minutes before incision	6 hours
gentamicin	2 mg/kg maximum dose 500 mg	slow IV bolus over 3 to 5 minutes or infusion over 30 minutes; started within 120 minutes before incision	redosing not required [Note 3]
metronidazole	adult: 500 mg child: 12.5 mg/kg up to 500 mg	IV infusion over 20 minutes; started within 120 minutes before incision	12 hours
vancomycin	15 mg/kg (**actual** body weight) to a maximum of 1.5 g	IV infusion at 10 mg/minute; started within 120 minutes before incision	12 hours

Note 1: This table includes the standard doses used for surgical prophylaxis. For specific procedures where a different dose is required, the dose is included in the recommendation for the procedure in Table 11.

Note 2: 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.

Note 3: Despite gentamicin's short half-life, redosing is not required because of its 'postantibiotic effect,' whereby bacterial killing continues for many hours after plasma concentration is undetectable.

Surgical antibiotic prophylaxis for specific procedures

Table 11: Surgical antibiotic prophylaxis for specific procedures

Procedure	Antibiotic	Alternative if immediate severe or delayed severe hypersensitivity to penicillins
Appendicectomy		
appendicectomy (including laparoscopic procedures, exploratory laparotomy, division of adhesions, resection)	**cefazolin** plus **metronidazole**	**gentamicin** plus **metronidazole**
	if patient is being treated with antibiotics for appendicitis, additional prophylaxis may not be required	
Biliary tract surgery		
open cholecystectomy OR laparoscopic surgery where the patient has risk factors for postoperative infection (e.g. older than 70 years, diabetes, obstructive jaundice, common bile duct stones, acute cholecystitis, nonfunctioning gallbladder)	**cefazolin**	**gentamicin** plus **vancomycin**
	if patient is being treated with antibiotics for acute cholecystitis, additional prophylaxis may not be required	
pancreatic surgery (Whipple's procedure, pancreatic necrosectomy, pancreatectomy)	**cefazolin** plus **metronidazole**	**gentamicin** plus **metronidazole**
liver resection	**cefazolin** plus **metronidazole**	**gentamicin** plus **metronidazole**
hernia repair with or without mesh insertion	**cefazolin** add **metronidazole** if entry into the bowel lumen is expected	**vancomycin** OR if entry into the bowel lumen is expected, use **gentamicin** plus **metronidazole**

cont...

Breast surgery		
uncomplicated clean procedures (diagnostic excisional biopsy, stand-alone sentinel node biopsy, excision of scar tissue, lumpectomy (with or without needle or wire localisation)	prophylaxis **not** recommended	
clean-contaminated procedures (reduction mammoplasty, simple mastectomy, wide local excision, axillary lymph node clearance, nipple surgery, all repeat or revision procedures)	**cefazolin**	**vancomycin**
complicated clean-contaminated procedures (prosthetic breast reconstruction surgery, prosthetic implant or acellular dermal matrix, autologous breast reconstruction surgery, breast augmentation surgery)	**cefazolin**	**vancomycin**
	postoperative doses can be considered but prophylaxis (IV or oral) should not continue beyond 24 hours, even in the presence of surgical drains adjacent to the implant	
clean-contaminated skin procedures (diagnostic excisional biopsy, stand-alone biopsy)	prophylaxis **not** recommended	
Cardiac surgery		
• coronary artery bypass surgery (CABG) • cardiac valve surgery	**cefazolin**	**vancomycin** plus **gentamicin 5 mg/kg**
	postoperative doses can be considered but prophylaxis (IV or oral) should not continue beyond 24 hours, even in the presence of chest drains	
patent ductus arteriosus (PDA) repair	**cefazolin**	**vancomycin** plus **gentamicin 5 mg/kg**
Colorectal surgery		
Colorectal surgery (nonendoscopic procedures e.g. colon resection, revision of anastomosis)	**cefazolin** plus **metronidazole**	**gentamicin** plus **metronidazole**

cont...

Ear, nose and throat surgery		
• uncomplicated nose or sinus surgery (including endoscopic procedures) • uncomplicated ear surgery • otoplasty • stapedectomy • tonsillectomy • adenoidectomy	prophylaxis **not** recommended	
• major ear surgery • complex septorhinoplasty • revision sinus surgery • laryngectomy (primary or salvage) • tympanomastoid surgery • hearing implant procedures, including cochlear implant procedures	**cefazolin** plus **metronidazole**	**clindamycin** add **gentamicin** for laryngectomy or tympanomastoid surgery
Gastrointestinal endoscopic procedures		
endoscopic retrograde cholangiopancreatography (ERCP) • involving transpapillary or transmural drainage of pseudocysts • with evidence of biliary tract obstruction and only if complete biliary drainage may not be achieved • if the patient has communicating pancreatic cysts or pseudocysts	**gentamicin** OR **cefazolin** consider adding **metronidazole**	**gentamicin** consider adding **metronidazole**
endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) of cystic lesions	**metronidazole** plus either **cefazolin** OR **gentamicin**	**gentamicin** plus **metronidazole**

cont...

• gastrostomy or jejunostomy tube insertion • insertion of PEG = percutaneous endoscopic gastrostomy; PEJ = percutaneous endoscopic jejunostomy.	**cefazolin**	**vancomycin**
all other procedures (with or without biopsy), e.g.: • endoscopic ultrasound-guided fine-needle aspiration of solid lesions along the GI tract • diagnostic endoscopic ultrasound • endoscopy • colonoscopy • sigmoidoscopy • sclerotherapy • oesophageal stricture dilatation	prophylaxis **not** recommended	
Gastrointestinal surgery		
gastroduodenal or oesophageal procedure that enters gastrointestinal tract lumen OR nonendoscopic procedures that do not enter the gastrointestinal lumen but only if the patient has risk factors for postoperative infection (morbid obesity, gastric outlet obstruction, reduced gastric acidity/motility, gastrointestinal bleeding, malignancy or perforation), i.e. gastric bypass, resection, ulcer oversew, oesophagectomy.	**cefazolin**	**gentamicin** plus **vancomycin**
small intestinal surgery (nonendoscopic procedures only)	**cefazolin** add **metronidazole** if the small intestine is obstructed, where the bowel may be injured or if there are concerns of other complications	**gentamicin** plus **metronidazole**

cont...

Gynaecological procedures		
medical termination of pregnancy (TOP)	Prophylaxis **not** recommended	
surgical termination of pregnancy (TOP)	**metronidazole** plus **azithromycin** 1 g orally, within the 120 minutes before the procedure	n/a
abdominal and vaginal hysterectomy, other pelvic surgery done via laparotomy and vaginal repair	**cefazolin** plus **metronidazole**	**gentamicin** plus **clindamycin**
Head & neck surgery		
• thyroidectomy • simple lymph node excision (including submandibular lymph node excision) • parotidectomy	prophylaxis **not** recommended	
• extensive neck dissection for malignancy • debulking or reconstructive surgery for malignancy	**cefazolin** plus **metronidazole**	**gentamicin** plus **clindamycin**
	postoperative doses can be considered but prophylaxis (IV or oral) should not continue beyond 24 hours. Do **not** extend the duration of antibiotic prophylaxis because the patient has a surgical drain in situ.	
Neurosurgery		
craniotomy procedures including • trans-sphenoidal procedures • external ventricular drain insertion • microsurgery • pressure monitors insertion • procedures involving insertion of prosthetic material • re-exploration procedures • brain biopsy • intracranial shunt insertion	**cefazolin**	**vancomycin**

cont...

<table>
<tr><th colspan="3">Obstetric procedures</th></tr>
<tr><td>caesarean section (CS)</td><td>cefazolin</td><td>gentamicin plus
clindamycin</td></tr>
<tr><td>operative vaginal delivery (vacuum delivery)</td><td>amoxicillin+clavulanate 1+0.2 g IV, as a single dose as soon as possible after delivery.</td><td>For patients with nonsevere hypersensitivity to penicillins, use a single dose of both:
cefazolin plus
metronidazole as soon as possible after delivery.
For patients with severe hypersensitivity to penicillins, use:
chloramphenicol 1 g IV, as a single dose as soon as possible after delivery.</td></tr>
<tr><td rowspan="2">• prophylaxis for repair of obstetric anal sphincter injuries
• 3rd and 4th degree vaginal tears</td><td>cefazolin plus
metronidazole</td><td>clindamycin</td></tr>
<tr><td colspan="2">the role of postoperative antibiotic therapy following anal sphincter repair is unclear but is recommended because infection in this setting carries a high risk of anal incontinence and fistula formation. Use:
trimethoprim+sulfamethoxazole 160+800 mg orally, 12-hourly for 5 days
PLUS
metronidazole 400 mg orally, 12-hourly for 5 days.
Alternatively, use (as a single agent):
amoxicillin+clavulanate 500+125 mg (child: 25+5 mg/kg up to 500+125 mg) orally, 8-hourly for 5 days</td></tr>
</table>

cont...

<table>
<tr><td colspan="3">Ophthalmic surgery
Active conjunctivitis, dacryocystitis or blepharitis must be treated and resolved before surgery.</td></tr>
<tr><td rowspan="2">cataract surgery</td><td>cefazolin 1 mg/0.1 mL intracamerally (into the anterior chamber of the eye), as a single dose at the end of surgery[23]</td><td>Seek appropriate advice for patients with cefazolin hypersensitivity</td></tr>
<tr><td colspan="2">The use of preoperative topical antibiotics does not provide additional benefit to the above interventions. Postoperative topical antibiotics, though widely prescribed, lack evidence; the rate of endophthalmitis was not increased in large cohort studies using intracameral antibiotics alone (without postoperative topical antibiotics).

If postoperative topical antibiotics are considered necessary, chloramphenicol is recommended. Use:

chloramphenicol 0.5% eye drops, 1 drop into the operated eye, four times a day for up to 7 days.</td></tr>
<tr><td colspan="3">Orthopaedic surgery</td></tr>
<tr><td>routine arthroscopic procedures not involving insertion of prosthetic material (e.g. pins, plates) or avascular tissue</td><td colspan="2">prophylaxis not recommended</td></tr>
<tr><td>• internal fixation of fractures of large bones
• procedures involving insertion of prosthetic or allograft material
• other (closed) internal fixation</td><td>cefazolin</td><td>vancomycin</td></tr>
</table>

cont...

23 In these guidelines, intracameral cefazolin is recommended for the prevention of endophthalmitis after cataract surgery because a parenteral formulation of cefuroxime (which was used in the key randomised controlled trial) is not on the Medical and Dental Catalogue. There is extensive clinical experience with intracameral cefazolin for this indication in Australia (where parenteral cefuroxime is not marketed). Cefuroxime 1 mg/0.1 mL can be used if available.

lower limb amputations	**cefazolin** if limb is ischaemic **add** **metronidazole**	**vancomycin** plus **gentamicin** 2 mg/kg IV (for procedures likely to continue for longer than 6 hours, consider using a 5 mg/kg dose) If limb is ischaemic **add** **metronidazole**
	If the patient is being treated with antibiotic therapy for an infected limb, additional antibiotic prophylaxis may not be required	
Plastic & reconstructive surgery		
clean bone or soft tissue injury: • open fractures of the distal phalanx (provided prompt irrigation/debridement of the fracture within 8 hours of injury) • noninfected lesions and minor excisions blepharoplasty / ptosis repair rhytidectomy • other clean or clean-contaminated skin and soft tissue procedures, including those that breach the oral mucosa	prophylaxis **not** recommended	
• groin/axilla dissection • abdominoplasty • insertion of implants, mesh, prostheses, screws, plates, etc. • traumatic wounds (nonsevere injuries) • open fractures (nonsevere injuries)	**cefazolin**	**clindamycin**
• open fractures (severe injury) • traumatic wounds (severe injuries)	see **open fractures** (page 56) in 'Bone and joint infections' or **traumatic wound infections** (page 333) in 'Wound infections'	

cont...

Spinal procedures		
spinal procedures including laminectomy, discectomy	**cefazolin**	**vancomycin**
Splenectomy		
splenectomy (emergency or elective)	**cefazolin**	**vancomycin**
Thoracic surgery		
• intercostal catheter insertion • brachiocephalic procedures (e.g. carotid endarterectomy, brachial artery repair) not involving prosthetic material	prophylaxis **not** recommended	
• procedures involving insertion of prosthetic material • procedures associated with an increased risk of infection, including video-assisted thoracoscopic surgery (VATS), aneurysm repair, thromboendarterectomy, vein bypass, mediastinoscopy	**cefazolin**	**vancomycin**
• decortication/pleurectomy • if infection present, continue with current antibiotic therapy.	**cefazolin** if anaerobic cover required (empyema or abscess) then **add metronidazole**	**vancomycin** if anaerobic cover required (empyema or abscess) then **add metronidazole**
Urological surgery • For elective urological procedures that enter the urinary tract (other than uncomplicated cystoscopic diagnostic procedures), perform preoperative urine culture. If bacteriuria is confirmed, treat with a short course of antibiotics even if the patient is asymptomatic • If an immediate operation is required and there is clinical evidence of a urinary tract infection, and the results of culture and susceptibility testing are unavailable, treat with gentamicin **3 mg/kg IV**, as a single preoperative dose.		
circumcision, orchidopexy or hydrocele repair, hypospadias repair	prophylaxis **not** recommended	

cont...

• endoscopic intrarenal and ureteric stone procedures (e.g. percutaneous nephrolithotomy, pyeloscopy for ureteric or kidney stones) • ureteroscopy/instrumentation of upper tract (including retrograde pyelogram) • other endoscopic procedures only if there are risk factors for postoperative infection (e.g. urinary tract obstruction or abnormalities, urinary stones, indwelling or externalised catheters)	**gentamicin** if gentamicin is contraindicated use **cefazolin**	**gentamicin**
open prostatectomy	**cefazolin** PLUS **gentamicin** if risk of entry into bowel lumen, then **add** **metronidazole**	**vancomycin** PLUS **gentamicin** if risk of entry into bowel lumen, then **add** **metronidazole**
• transurethral resection of prostate (TURP) • endoscopic prostatectomy *Consider the results of culture and susceptibility testing if available.*	**gentamicin** if gentamicin is contraindicated use **cefazolin**	**gentamicin**

Key additional references

Allegranzi B, Bischoff P, de Jonge S, Kubilay NZ, Zayed B, Gomes SM, Abbas M, Atema JJ, Gans S, van Rijen M, Boermeester MA, Egger M, Kluytmans J, Pittet D, Solomkin JS; WHO Guidelines Development Group. New WHO recommendations on preoperative measures for surgical site infection prevention: an evidence-based global perspective. Lancet Infect Dis. 2016 Dec;16(12):e276-e287.

Anderson DJ., Sexton DJ. (2021). "Control measures to prevent surgical site infection following gastrointestinal procedure in adults". South Australian expert Advisory Group on Antimicrobial Resistance (SAAGAR). Available from: https://www.sahealth.sa.gov.au/wps/wcm/connect/3207d478-65c9-4dc2-ac77-b8a4b50f8255/Appendix+1+-+Gastro_v3.0_Mar_2022_.pdf?MOD=AJPERES.

Bayston R, de Louvois J, Brown EM, Johnston RA, Lees P, Pople IK. Use of antibiotics in penetrating craniocerebral injuries. "Infection in Neurosurgery" Working Party of British Society for Antimicrobial Chemotherapy. Lancet. 2000 May 20;355(9217):1813-7.

Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, Fish DN, Napolitano LM, Sawyer RG, Slain D, Steinberg JP, Weinstein RA; American Society of Health-System Pharmacists; Infectious Disease Society of America; Surgical Infection Society; Society for Healthcare Epidemiology of America. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health Syst Pharm. 2013 Feb 1;70(3):195-283.Brook I, Frazier EH. Aerobic and anaerobic microbiology in intra-abdominal infections associated with diverticulitis. J Med Microbiol 2000; 49:827.

Brook I, Frazier EH. Aerobic and anaerobic microbiology in intra-abdominal infections associated with diverticulitis. J Med Microbiol 2000; 49:827.

SIGN 104 Antibiotic Prophylaxis in Surgery. July 2008. https://docslib.org/doc/4867816/sign-104-antibiotic-prophylaxis-in-surgery

South Australian expert Advisory Group on Antimicrobial Resistance (SAAGAR). Surgical Antimicrobial Prophylaxis Guideline. December 2021. Available from: https://www.sahealth.sa.gov.au/wps/wcm/connect/6bb523804358edbd883b9ef2cadc00ab/Surgical+Antimicrobial+Prophylaxis+Clinical+Guideline_v2.0_14112017.pdf?MOD=AJPERES

Swenson RM, Lorber B, Michaelson TC, Spaulding EH. The bacteriology of intra-abdominal infections. Arch Surg 1974; 109:398.

Tunkel AR, Hasbun R, Bhimraj A, Byers K, Kaplan SL, Scheld WM, van de Beek D, Bleck TP, Garton HJL, Zunt JR. 2017 Infectious Diseases Society of America's Clinical Practice Guidelines for Healthcare-Associated Ventriculitis and Meningitis. Clin Infect Dis. 2017 Mar 15;64(6):e34-e65.

Prevention of infection for medical conditions

This topic includes advice on the following topics in adults and children older than 3 months:

- **secondary prevention of rheumatic fever**, page 367
- **prophylaxis for infective endocarditis prevention**, page 369
- **antibiotic prophylaxis in patients with liver cirrhosis**, page 372
- **prophylaxis for patients with asplenia** (no spleen) **or hyposplenia** (impaired splenic function), page 372
- overview of **malaria prophylaxis in pregnancy** and **prophylaxis in patients with neutropenia**, page 375
- **prophylaxis for opportunistic infections in immunocompromised people** including *Pneumocystis jirovecii* pneumonia (PJP) prophylaxis; cryptococcal invasive disease prophylaxis, page 375
- **prophylaxis following exposure to infectious conditions:** meningococcal disease, page 377
- **tetanus prophylaxis following traumatic wounds**, page 378.

Other relevant guidelines:

- *Guidelines for the Diagnosis, Treatment and Prevention of Leprosy* (WHO)
- *National Guidelines for HIV Care and Treatment*
- *National Malaria Treatment Protocol*
- *National Tuberculosis Management Protocol*
- *The Guidelines of Cancer Management in Papua New Guinea.*

Secondary prevention of rheumatic fever

For diagnosis and management of acute rheumatic fever (ARF), see page 341 in 'Miscellaneous infections.'

Continuous antimicrobial prophylaxis against *Streptococcus pyogenes* is recommended for patients after a first episode of ARF or following a new diagnosis of rheumatic heart disease (RHD) to prevent recurrence of ARF and the development or progression of RHD.

Penicillin is the drug class of choice. Assess patients reporting penicillins allergy to confirm immune-mediated hypersensitivity, so that they are not incorrectly denied optimal therapy.

Intramuscular benzathine benzylpenicillin is the most effective prevention of *S. pyogenes* infections and subsequent recurrences of ARF as it results in more predictable serum penicillin concentrations, and long-term adherence is higher

than with twice-daily oral regimens. In patients who consistently decline benzathine penicillin, oral penicillin may be given instead (ensure adequate attempts to identify and address the barriers to injections).

However, in patients with severe valvular heart disease, there is a growing body of evidence that pain or fear associated with benzathine benzylpenicillin administration may cause a vasovagal response that, due to the reduced cardiovascular reserve in these patients, can lead to severe cardiovascular compromise and sudden cardiac death. Therefore, for patients with severe valve disease, oral prophylaxis is now recommended.

The minimum duration of secondary prophylaxis depends on the presence and severity of cardiac involvement. Definitions of cardiac involvement are:

- **Mild cardiac valve involvement:** involvement of single or multiple left-sided heart valves in mild form. Echocardiographic confirmation is required.
- **Moderate cardiac valve involvement:** at least mitral or aortic moderate valve disease (regurgitation or stenosis). Clinically, murmurs will be present. Undertake echocardiogram if available.
- **Severe cardiac valve involvement:** severe regurgitation or stenosis of either mitral or aortic valve. Murmurs and clinical features of dominant valve lesion present.

The decision to stop secondary prophylaxis should be based on clinical and echocardiographic assessment.

Secondary prevention of rheumatic fever

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

benzathine benzylpenicillin *(BPG) IM, every 21 or 28 days*

adult and child ≥ 20 kg: 1,200,00 units

child < 20 kg 600,000 units.

Administer every 28 days for most patients. Administer every 21 days for those who have had valve surgery or previous breakthrough of ARF in a 28-day regimen.

The ventrogluteal site is the preferred site for intramuscular injection.

Patients with severe valvular heart disease or heart failure may be at increased risk of cardiovascular compromise after injection with benzathine penicillin. If patients have severe aortic insufficiency, severe mitral stenosis, severe aortic stenosis, ventricular dysfunction (EF < 50%) or severe symptoms of heart failure, use oral phenoxymethylpenicillin as for the second-line regimen.

Second-line regimen

Oral penicillin is not as effective as intramuscular benzathine benzylpenicillin because oral administration achieves less predictable serum concentrations and

cont...

the twice-daily oral regimen is more difficult to adhere to over many years of prescribed therapy. Reserve oral penicillin for patients who experience bleeding problems following injection, those who consistently decline intramuscular benzathine benzylpenicillin or those with severe disease as described above. Use:

phenoxymethylpenicillin *(adult or child) 250 mg orally, 12-hourly.*

For patients with confirmed hypersensitivity to penicillins, use:

erythromycin *(adult or child more than 20 kg) 250 mg orally, 12-hourly.*

Duration

The purpose of prophylaxis is to prevent progression to more severe disease. Prolong prophylaxis in patients who have experienced an episode of ARF (or signs or symptoms suggestive of ARF) while on prophylaxis or with high risk factors for relapse e.g. abnormal echocardiogram or unstable echocardiographic features in patients who already have severe cardiac involvement.

No cardiac valve involvement: Treat for a minimum of 5 years or until age 21 (whichever is longer).

Mild cardiac valve involvement: Treat for a minimum of 10 years or until age 21 (whichever is longer).

Moderate cardiac valve involvement: Treat for a minimum of 10 years or until age 35 (whichever is longer)

Severe cardiac valve involvement: Treat for a minimum of 10 years or until age 40 (whichever is longer). Consider patient or family preference to cease due to advancing age and/or end of life care in this group.

Infective endocarditis prophylaxis

Antibiotic prophylaxis against infective endocarditis is only recommended for individuals that have a cardiac condition associated with an increased risk of developing infective endocarditis and are at a high risk of adverse outcomes from endocarditis.

High-risk cardiac conditions:

- rheumatic heart disease
- previous infective endocarditis
- unrepaired congenital cyanotic defects, including palliative shunts and defects
- prosthetic cardiac valve or prosthetic material used for cardiac valve repair.

Procedures for which endocarditis prophylaxis is recommended for patients with a cardiac condition listed above include:

- **dental procedures:** only those involving manipulation of gingival or periapical tissue or perforation of the oral mucosa (e.g. extraction, implant placement, biopsy, removal of soft tissue or bone, subgingival scaling, and root planning, replanting avulsed teeth), abscess or necrotic tissue damage
- **skin and musculoskeletal procedures:** only those involving infected skin, skin structures or musculoskeletal tissue
- **respiratory tract and ENT procedures:** only for tonsillectomy or adenoidectomy, or invasive respiratory tract or ENT procedures to treat an established infection (e.g. abscess drainage)
- **genitourinary and gastrointestinal procedures:** only if surgical antibiotic prophylaxis is required or for patients with an established infection.

There is insufficient evidence to recommend extra antibiotic prophylaxis against endocarditis during vaginal delivery or caesarean section in addition to the standard antibiotics recommended[24] in 'Antibiotic prophylaxis for surgical procedures' (see page 360 for specific recommendations).

Infective endocarditis prophylaxis for dental procedures

Use:

amoxicillin *2 g (child: 50 mg/kg up to 2 g) orally, 60 minutes before, or IM 30 minutes before the procedure.*

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

cefalexin *2 g (child: 50 mg/kg up to 2 g) orally, 60 minutes before the procedure.*

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

clindamycin *600 mg (child: 20 mg/kg up to 600 mg) orally, 60 to 120 minutes before the procedure.*

Infective endocarditis prophylaxis for skin, musculoskeletal, respiratory and ENT procedures

Use:

amoxicillin *2 g (child: 50 mg/kg up to 2 g) orally, 60 minutes before the procedure.*

OR

cont...

24 RHD Australia (ARF/RHD writing group). The 2020 Australian guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease (3rd edition); 2020

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

For patients with **immediate nonsevere** or **delayed nonsevere** hypersensitivity to penicillins:

cefalexin *2 g (child: 50 mg/kg up to 2 g) orally, 60 minutes before the procedure.*

OR

cefazolin *2 g (child: 30 mg/kg up to 2 g) IV, within the 60 minutes before the procedure*

OR

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

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

clindamycin *600 mg (child: 20 mg/kg up to 600 mg) orally, 60 to 120 minutes before the procedure*

OR

clindamycin *600 mg (child: 20 mg/kg up to 600 mg) IV, within the 120 minutes before the procedure.*

Infective endocarditis prophylaxis for genitourinary and gastrointestinal procedures

Use:

amoxicillin *2 g (child: 50 mg/kg up to 2 g) orally, 60 minutes or IM 30 minutes before the procedure*

OR

amoxicillin *2 g (child: 50 mg/kg up to 2 g) IM, 30 minutes before the procedure or IV within the 60 minutes before the procedure.*

For patients with hypersensitivity to penicillins, use:

vancomycin *15 mg/kg IV, started within the 15 to 120 minutes before the procedure (recommended infusion rate 10 mg/minute).*

Antibiotic prophylaxis in patients with liver cirrhosis

Patients with liver cirrhosis have an increased susceptibility to infection due to disease-related immune-dysfunction – see also 'Intraabdominal infections,' page 179.

Evaluate all patients with liver cirrhosis for hepatitis B and C. If positive, these patients should be targeted for viral hepatitis management – see **viral hepatitis**, page 155 in 'Gastrointestinal infections.'

Variceal bleeding

Antibiotic prophylaxis is recommended for all patients who have cirrhosis with acute upper gastrointestinal bleeding (variceal or nonvariceal) because it reduces the risk of infection, recurrent haemorrhage and mortality.

Use:

ceftriaxone *1 g IV, once daily for 3 days, or until bleeding has stopped (maximum 7 days).*

Alternatively, use:

ciprofloxacin *500 mg orally, 12-hourly for 3 days, or until bleeding has stopped (maximum 7 days).*

Patients with asplenia or hyposplenism (impaired splenic function)

Individuals with asplenia (absent spleen) or hyposplenism (impaired splenic function) are at increased risk of severe infection, particularly from encapsulated organisms (e.g. *Streptococcus pneumoniae)*. Other bacteria (including those acquired from animal bites) and parasites (e.g. malaria) may also cause sepsis. Conditions associated with hyposplenism include massive hyperreactive malarias, hyperreactive malarial splenomegaly syndrome (HMS), leukaemias (chronic myeloid leukaemia [CML)/lymphocytic leukaemia [CLL])] myelofibrosis, sickle cell disease, active chronic graft-versus-host disease, and patients who have received therapeutic irradiation.

Measures to prevent infection in patients with asplenia or hyposplenism are education, immunisation, antibiotic prophylaxis and malaria prophylaxis.

Education includes advice about the risk of sepsis, infection risks associated with travel and animal bites, and the provision of a fever action plan.

If available, all patients should also receive immunisations against *S. pneumoniae* (pneumococcal vaccine), *Neisseria meningitidis* (meningococcal vaccine) and *Haemophilus influenzae* type b (Hib).

Vaccinations for people with asplenia or hyposplenia

Table 12: Vaccinations for people undergoing splenectomy

Indication	Vaccines [Note 1]	Administration
Elective splenectomy	• pentavalent vaccine (diphtheria, tetanus, pertussis, hepatitis B and *Haemophilus influenzae*) 0.5 mL IM, preferably into the deltoid muscle • 13-valent pneumococcal conjugate vaccine (13vPCV) 0.5 mL IM	single dose, two weeks prior to splenectomy
Emergency splenectomy	• pentavalent vaccine (diphtheria, tetanus, pertussis, hepatitis B and *Haemophilus influenzae*) 0.5 mL IM, preferably into the deltoid muscle • 13-valent pneumococcal conjugate vaccine (13vPCV) 0.5 mL IM	single dose, 7 days after splenectomy
Note 1: Vaccines can be administered safely at the same time (administer into different sites).		

For children under 5 years, give the recommended course of Hib-containing vaccine (pentavalent vaccine) and pneumococcal vaccine or catch-up vaccination. Those who have completed their vaccinations as per the Papua New Guinea immunisation schedule do not need extra or repeat doses.

For children 5 years or older who have not been given routine pneumococcal or pentavalent vaccine, or if the course is incomplete, give a single dose of pentavalent and/or PCV-13. If they have received all vaccines as per the schedule, there is no need for extra or repeat doses.

Antibiotic prophylaxis for patients with asplenia or hyposplenism

For prevention of pneumococcal infection in patients with asplenia or hyposplenism, 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; 5 years or older: 250 mg) orally, 12-hourly.*

In patients with hypersensitivity to penicillins, use:

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

All people with asplenia or hyposplenism should also receive malaria prophylaxis – see advice in the next section.

cont...

Instruct patients with asplenia or hyposplenism to seek urgent medical attention in the event of a sudden onset of unexplained fever. Ensure they have an emergency supply of antibiotics in case medical review is not immediately available:

For adults, use:

amoxicillin *3 g orally, as a single dose, then 1 g orally, 8-hourly until review.*

For children, use:

amoxicillin+clavulanate *25+5 mg/kg (max 500+125 mg) orally, 8-hourly until review.*

Duration

Children with sickle cell disease or other haemoglobinopathy should remain on prophylaxis until (whichever is longer):

- the age of 5 years
- at least 3 years after splenectomy.

For adults, continue prophylaxis for at least 3 years and then review.

Consider lifelong prophylaxis for patients who:

- are significantly immunocompromised (e.g. hypogammaglobulinaemia or solid organ transplants)
- have had a splenectomy for haematological malignancy, who are receiving immunosuppressive therapy or who have survived overwhelming postsplenectomy infection (particularly with *S. pneumoniae*).

Malaria prophylaxis in asplenia or hyposplenism

For adults, use:

chloroquine 300 mg (2 x 150 mg tablets) orally, once weekly.

For patients who are known to have hypersensitivity to chloroquine and for children, seek advice from an infectious diseases physician and/or paediatrician.

Duration

Adults and children with hyperreactive malarial splenomegaly (HMS) should receive malaria prophylaxis for 3 months, then review or until spleen size regressed.

Patients without a spleen require lifelong malaria prophylaxis.

Malaria prophylaxis in pregnancy

Malaria prophylaxis is recommended for pregnant people in malarious areas. See the *National Malaria Treatment Protocol* and *Manual of Standard Managements in Obstetrics and Gynaecology* ('Red Book') for information on recommended prophylaxis and other prevention strategies.

Prophylaxis in patients with neutropenia

Antimicrobial prophylaxis is recommended for patients who have, or are expected to have, severe neutropenia (neutrophils < 0.5 X 10^9/L) for 7 days or more.

Consider prophylaxis in the following patient groups:

- hypersplenism with pancytopenia
- bone marrow failure with neutropenia.

Refer to local protocols and/or seek advice from an oncologist for the appropriate regimen.

Prophylaxis for opportunistic infections in immunocompromised people

Many opportunistic infections in people living with human immunodeficiency virus (HIV) can be prevented by using trimethoprim+sulfamethoxazole (cotrimoxazole) prophylaxis therapy. The diseases include bacterial pneumonias, *Pneumocystis jirovecii* pneumonia (PJP), toxoplasmosis and severe bacterial infections. See the *National Guidelines for HIV Care and Treatment* for more information.

Opportunistic infections may also occur in patients with healthcare-associated immune compromise (e.g. immunosuppressive therapy).

PJP prophylaxis

These recommendations apply to all people living with HIV and in those with reduced immunity due to special circumstances as follows:

- prescribed ≥20 mg prednisone (or equivalent corticosteroid dose) for more than 4 weeks
- acute lymphocytic leukaemia (ALL).

See also *National Guidelines for HIV Care and Treatment.*

In adults, use:

trimethoprim+sulfamethoxazole *160+800 mg orally, daily.*

In children, use:

trimethoprim+sulfamethoxazole *orally, daily or 3 times weekly*

child 3 to 5 kg: 20+100 mg

child 6 to 13 kg: 40+200 mg

child 14 to 30 kg: 80+400 mg.

Monitor complete blood count, folate status (if available) and renal function regularly in patients on long-term trimethoprim+sulfamethoxazole. Consider folic acid supplementation, particularly if folate status cannot be monitored.

Duration

For people living with HIV, see the *National Guidelines for HIV Care and Treatment* for recommended duration.

For patients on high dose corticosteroids, continue for at least 6 weeks after stopping steroids.

For people with ALL, see special sections in *The Guidelines of Cancer Management in Papua New Guinea*.

Cryptococcal invasive disease prophylaxis

Give prophylaxis to all people living with HIV with a negative cryptococcal antigen.

See **cryptococcal meningitis**, page 81 in 'CNS infections' for advice on secondary prophylaxis maintenance therapy following cryptococcal infection.

For primary prophylaxis in adults and children 2 years or older, use:

fluconazole 200 mg (child: 6 to 12 mg/kg) orally, 3 times weekly.

Screening and prophylaxis for children less than 2 years is not recommended.

Duration

Continue for 1 year and until the following are criteria met:

- minimum of 3 months (12 weeks) with undetectable viral load (if viral load monitoring is available)
- the person is stable and adherent on antiretroviral therapy.

Prophylaxis for other opportunistic infections

Detailed recommendations for the following conditions are available in other guidelines:

- for prophylaxis of ***Toxoplasma gondii*** in people living with HIV, see the *National Guidelines for HIV Care and Treatment*.
- for ***Mycobacterium avium* complex** (MAC) prophylaxis for people living with HIV, see the *National Guidelines for HIV Care and Treatment*.
- for **tuberculosis**-preventative treatment and isoniazid-preventative therapy, see the *National Guidelines for HIV Care and Treatmen*t and the *National Tuberculosis Management Protocol*.

Prophylaxis for exposure to infectious conditions

Invasive meningococcal disease

Clearance antibiotics are recommended for some patients ('index cases') and close contacts after an episode of *Neisseria meningitidis* (meningococcal) meningitis or other invasive meningococcal disease (e.g. sepsis).

'Close contacts' generally refers to individuals who have had prolonged (>8 hours) contact while in close proximity to the patient or who have been directly exposed to the patient's oral secretions during the 7 days before the onset of the patient's symptoms and until 24 hours after initiation of appropriate antibiotic therapy. These include:

- **household contacts**: including 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), and roommates in a 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/daycare contacts**: only children and staff at the childcare/daycare 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, e.g. boarding schools 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, e.g. the person who intubated the case.

For chemoprophylaxis against *Neisseria meningitidis* (meningococcal) meningitis or other invasive meningococcal disease (e.g. sepsis), use:

ciprofloxacin *500 mg (child younger than 5 years: 30 mg/kg up to 125 mg; child 5 to 12 years: 250 mg) orally, as a* ***single dose***

OR

ceftriaxone *250 mg (child ≥1 month: 125 mg) IM, as a* ***single dose****.*

Ceftriaxone is the preferred option for pregnant people.

Other conditions

Detailed recommendations for the following conditions are available in other guidelines:

- for **leprosy** postexposure prophylaxis, refer to the *Guidelines for the Diagnosis, Treatment and Prevention of Leprosy, 2018 (WHO)* for further information on contact definitions and management.
- for **HIV postexposure prophylaxis**, see the *Papua New Guinea National Guidelines for HIV Care and Treatment.*

Tetanus prophylaxis following traumatic wounds

Tetanus immunoglobulin is recommended for babies born before arrival (BBA) – see **tetanus in neonates**, page 218 in 'Infections in neonates and young infants.'

Tetanus prophylaxis needs to be considered in all patients presenting with wounds of any type.

For patients with traumatic wounds, ensure that tetanus immunisation is up-to-date. See table below for prophylaxis requirements.

Table 13: Guide to tetanus prophylaxis in wound management

	Type of wound	Is tetanus-toxoid-containing vaccine indicated? [Note 1]	Is tetanus immunoglobulin indicated?
Patient has received less than 3 doses of tetanus-toxoid-containing vaccine OR vaccination history is unknown [Note 3]			
	clean and minor wound	yes	no
	all other wounds	yes	yes

cont...

Patient has received 3 or more doses of tetanus-toxoid-containing vaccine			
less than 5 years since last dose of tetanus-toxoid-containing vaccine	clean and minor wound	no	no
	all other wounds	no	no, unless the person has immunodeficiency, [Note 2]
5 to 10 years since last dose of tetanus-toxoid-containing vaccine	clean and minor wound	no	no
	all other wounds	yes	no, unless the person has immunodeficiency [Note 2]
more than 10 years since last dose of tetanus-toxoid-containing vaccine	clean and minor wound	yes	no
	all other wounds	yes	no, unless the person has immunodeficiency [Note 2]

Note 1: Tetanus toxoid is only available in combination with other antigens.

Note 2: People with HIV infection or severe humoral immune deficiency should receive tetanus immunoglobulin, regardless of their tetanus immunisation history.

Note 3: People who have no documented history of a complete primary vaccination course (3 doses) with a tetanus-toxoid vaccine should receive all missing doses and must receive tetanus immunoglobulin for tetanus-prone wounds.

If tetanus immunoglobulin is indicated, use:

tetanus immunoglobulin

within 24 hours of exposure: 250 units IM as a single dose

more than 24 hours since exposure: 500 units IM as a single dose.

Key additional references

Ak G, Baines SL, Ferguson J, Kangapu S. The Port Moresby General Hospital's 2019 Antibiogram, Papua New Guinea.

Australian Immunisation Handbook. https://immunisationhandbook.health.gov.au/. Commonwealth of Australia 2023.

Ferrarese A, Passigato N, Cusumano C, Gemini S, Tonon A, Dajti E, Marasco G, Ravaioli F, Colecchia A. Antibiotic prophylaxis in patients with cirrhosis: Current evidence for clinical practice. World J Hepatol 2021; 13(8): 840-852 DOI: https://dx.doi.org/10.4254/wjh.v13.i8.840

Guidelines on the diagnosis, prevention and management of cryptococcal disease in HIV-infected adults, adolescents and children: supplement to the 2016 consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Geneva: World Health Organization; 2018.

Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta J-P, Del Zotti F, et al., ESC Scientific Document Group, 2015 ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC) Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM), Eur Heart J 2015; 36 (44): 3075–3128.

Kanhutu K, Jones P, Cheng AC, Grannell L, Best E, Spelman D. Spleen Australia guidelines for the prevention of sepsis in patients with asplenia and hyposplenism in Australia and New Zealand. Intern Med J 2017;47(8):848–55.

Liang JL, Tiwari T, Moro P, et al. Prevention of Pertussis, Tetanus, and Diphtheria with Vaccines in the United States: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2018; 67:1.

National Department of Health. Papua New Guinea Guidelines for HIV care and Treatment. Port Moresby: Government of Papua New Guinea; 2019.

National Department of Health/PNG Sexual Health Society. Papua New Guinea Standard management of Sexually Transmitted infections & Genital conditions. Port Moresby: Government of Papua New Guinea; 2019.

Parkes-Ratanshi R, Wakeham K, Levin J, Namusoke D, Whitworth J, Coutinho A, Mugisha NK, Grosskurth H, Kamali A, Lalloo DG; Cryptococcal Trial Team. Primary prophylaxis of cryptococcal disease with fluconazole in HIV-positive Ugandan adults: a double-blind, randomised, placebo-controlled trial. Lancet Infect Dis. 2011 Dec;11(12):933-41.

RHD Australia (ARF/RHD writing group). The 2020 Australian guideline for prevention diagnosis and management of acute rheumatic fever and rheumatic heart disease (3rd edition); 2020.

Sanyahumbi A, Ali S, Benjamin IJ, Karthikeyan G, Okello E, Sable CA, Taubert K, Wyber R, Zuhlke L, Carapetis JR, Beaton AZ; American Heart Association. Penicillin Reactions in Patients with Severe Rheumatic Heart Disease: A Presidential Advisory From the American Heart Association. J Am Heart Assoc. 2022 Mar;11(5): e024517. doi: 10.1161/JAHA.121.024517. Epub 2022 Jan 20. PMID: 35049336; PMCID: PMC9075066.

Taplitz R, Kennedy E, Bow E, Crews J, Gleason C, Hawley D, et al. Antimicrobial prophylaxis for adult patients with cancer-related immunosuppression: ASCO and IDSA clinical practice guideline update. J Clin Oncol 2018; 36 (30): 3043-3054.

The European Association for the Study of the Liver. EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis. J Hepatol 2018; 69 (2):406-460.

Appendix 1: Gentamicin dosing

Contraindications and precautions	These apply to all indications for gentamicin. **Contraindications** Do **not** use aminoglycosides in patients with: • a history of aminoglycoside-induced vestibular or auditory impairment • a history of a serious hypersensitivity reaction/allergy to an aminoglycoside • myasthenia gravis. **Precautions** • for intravenous or intramuscular administration only (not absorbed orally) • use a slow push for intravenous administration (over 3 to 5 minutes) – no need for infusion.

The dosing information in this topic only applies to short-term empirical treatment of serious infections. Dosing advice includes

- **empirical gentamicin dosing**
  - gentamicin dosing in adults 18 years and older, page 384
  - gentamicin dosing in neonates, infants and children, page 385.

For dosing information for other indications, see:

- **infective endocarditis:** see Box 1: Synergistic gentamicin therapy (page 65) in 'Cardiovascular infections,' for dosing information
- **surgical prophylaxis:** see Table 10: Administration and timing of antibiotics for surgical prophylaxis (page 354) in 'Antibiotic prophylaxis for surgical procedures'
- **serious infections due to susceptible organisms that are resistant to other antibacterials:** seek advice from a clinical microbiologist or infectious disease physician.

Empirical gentamicin dosing

Indications for empirical gentamicin use	Gentamicin is used for short-term empirical treatment of serious infections (sepsis or septic shock) potentially caused by Gram-negative bacilli (rods) such as *Escherichia coli*, *Proteus* species*, Klebsiella* species, *Brucella* species and most *Pseudomonas* species. Frequent and reliable monitoring of both renal function and plasma levels is not regularly available in Papua New Guinea. As a result, **gentamicin dosing in adults should not continue beyond 48 hours (i.e. a maximum of 3 empirical doses at 0, 24 and 48 hours)**. Given the postantibiotic effect of aminoglycosides, whereby bacterial killing continues for many hours after plasma concentration is undetectable, this effectively provides **72 hours of therapy**. In infants and children, gentamicin can be continued for up to a **maximum of 7 days**. If ongoing empirical intravenous therapy is required (i.e. a causative organism is not identified), therapy should be changed to an alternative drug likely to cover the suspected Gram-negative organism, such as ceftriaxone. If a pathogen is isolated by the laboratory, choose a directed treatment antibiotic based on the results of culture and susceptibility testing. If no alternative to gentamicin is reported, seek advice from a clinical microbiologist or infectious disease physician about appropriate ongoing therapy.

Dosage (see tables below)	**Adults from 18 years**: Use 5 mg/kg based on actual body weight (7 mg/kg in critical illness). The dosing interval and total number of doses are based on estimated baseline renal function (serum creatinine value), see Table 14 on the next page. **Dosing in pregnancy**: gentamicin pharmacokinetics may be altered in pregnancy but, in the absence of gentamicin plasma level monitoring, it is recommended that prescribers take the same dosing approach in pregnant people as for other patients i.e. use actual body weight for calculating doses. **Neonates, infants and children**: See Table 15 (page 385) for dosing in neonates (0 to 30 days) and Table 16 (page 385) for dosing in infants and children.
Monitoring	It is essential to obtain creatinine results within 24 hours of starting gentamicin to determine the correct dosing interval. If this is not possible, see Table 14 for advice. Observe/question the patient about hearing or balance problems and do not administer any further doses if problems are occurring.
Adverse effects	• **Renal function may be affected by aminoglycosides**: this is usually reversible with cessation of therapy. There is an increased risk with prolonged therapy and when administered with other nephrotoxic agents (e.g. piperacillin+tazobactam, frusemide, radiographic contrast media). • **Balance or hearing (ototoxicity) may be affected by aminoglycosides**: this may become apparent early in the treatment course or weeks after therapy has stopped, and may persist after stopping aminoglycoside therapy. Instruct patients to report any problems with balance or hearing, and question them daily while on treatment. If a significant problem occurs, then aminoglycoside treatment should cease. • **Allergy**, including rash, may occasionally occur.

Gentamicin dosing in adults 18 years and older

Table 14: Gentamicin dosing in adults 18 years or older

Serum creatinine value [Note 1] [Note 2]	Dose	Dosing interval	Maximum number of doses
Males Creatinine < 140 micromol/L	**5 mg/kg** up to 520 mg In critically ill patients, use **7 mg/kg** up to 680 mg	24-hourly	3 (0, 24, 48 hours)
Females Creatinine < 120 micromol/L	**5 mg/kg** up to 420 mg In critically ill patients, use **7 mg/kg** up to 580 mg		
Males Creatinine 140 to 200 micromol/L	**5 mg/kg** up to 520 mg	36-hourly	2 (0, 36 hours)
Females Creatinine 120 to 160 micromol/L	**5 mg/kg** up to 420 mg		
Males Creatinine > 200 micromol/L	**5 mg/kg** up to 520 mg	Single dose only	1 (0 hours)
Females Creatinine > 160 micromol/L	**5 mg/kg** up to 420 mg		

Note 1: It is essential to obtain creatinine results within 24 hours of starting gentamicin. If this is not possible, treat patients as for normal renal function unless they have known chronic renal impairment, or a strong suspicion of chronic renal impairment (such as diabetes with complications), in which case treat as for moderate renal impairment (i.e. use 2 doses, 36 hours apart).

Note 2: In other guidelines, dosage adjustment for patients with renal impairment is often calculated from the estimated creatinine clearance (CrCl) using the Cockcroft–Gault formula. However, in these guidelines, although it is less accurate, serum creatinine is used as an estimation of renal function, as it is much less complex.

Gentamicin dosing in neonates, infants and children

Table 15: Gentamicin dosing in neonates (0 to 30 days)

Gestational age at birth	Postnatal age (days)	Dose [Note 1, Note 2, Note 3]	Dosing frequency	Maximum duration
Younger than 30 weeks	0 to 14	5 mg/kg	48-hourly	7 days
	15 or more	5 mg/kg	36-hourly	7 days
30 to 34 weeks	0 to 10	5 mg/kg	36-hourly	7 days
	11 or more	5 mg/kg	24-hourly	7 days
35 weeks or older	from day 0	5 mg/kg	24-hourly	7 days

Note 1: There are few data on aminoglycoside dosing in children. The dosages recommended in this table are based on the available data and the consensus view of the Australian Therapeutic Guidelines Antibiotic Expert Groups.

Note 2: For neonates with impaired kidney function (estimated glomerular filtration rate less than 50 mL/minute/1.73 m^2), give a single dose, then seek appropriate advice for subsequent dosing or selection of an alternative antibiotic.

Note 3: Round dose down to the nearest multiple of 20 mg.

Table 16: Gentamicin dosing for infants and children 1 month and older

Age	Dose [Note 1, Note 2, Note 3]	Dosing frequency	Maximum duration
Children 1 month and older	7 mg/kg up to 560 mg [Note 4]	24-hourly	7 days

Note 1: There are few data on aminoglycoside dosing in children. The dosages recommended in this table are based on the available data and the consensus view of the Australian Therapeutic Guidelines Antibiotic Expert Groups.

Note 2: 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 appropriate advice for subsequent dosing or selection of an alternative antibiotic.

Note 3: For children who are obese, using actual body weight to calculate gentamicin dose may lead to overdosing and potential toxicity. Give a single dose, then seek appropriate advice for subsequent dosing in these patients.

Note 4: Round dose down to the nearest multiple of 20 mg.

Clinical monitoring and dose adjustment in children

Measure serum creatinine at baseline and repeat after 3 days of gentamicin therapy. If creatinine has risen more than 1.5 times from baseline or exceeds the upper limit of normal, switch to an alternative agent e.g. cefotaxime or ceftriaxone. If there is no suitable alternative agent available, seek appropriate advice for ongoing therapy.

Undertake clinical monitoring for vestibular and auditory toxicity in all patients being treated with gentamicin.

Appendix 2: Vancomycin dosing

Precautions	Administer vancomycin by **slow** intravenous infusion (maximum 10 mg/min), **not** by intramuscular administration or intravenous injection (push). See Table 20 (page 393) for minimum infusion times. Do **not** use vancomycin if the patient has a history of vancomycin allergy or vancomycin-induced thrombocytopenia. Note that vancomycin flushing syndrome is not an allergy and a history of vancomycin flushing syndrome does **not** contraindicate future use, see section on adverse effects later in this topic.

The dosing information in this section only applies to short-term empirical treatment of serious infections. Advice for dosing includes:

- **intravenous vancomycin dosing in adults**
  - starting and maintenance dosing, page 389
  - adult loading dose (when required), page 390
- **intravenous vancomycin dosing in infants and children**
  - vancomycin dosing in young infants (0 to 90 days), page 391
  - vancomycin dosing in children 3 months or older, page 392
  - vancomycin dosing for infants and children with kidney impairment, page 392
- **vancomycin infusion times (adults and children)**, page 393.

For dosing information for other indications:

- **oral vancomycin for treatment of *Clostridioides difficile* infection**, see antibiotic-associated diarrhoea (page 147) in 'Gastrointestinal infections'
- **endocarditis prophylaxis in patients with penicillin allergy**, see infective endocarditis prophylaxis (page 369) in 'Prophylaxis of infection for medical conditions'
- **surgical prophylaxis in patients with penicillin allergy**, see Table 10: Administration and timing of antibiotics for surgical prophylaxis (page 354) and Surgical antibiotic prophylaxis in specific procedures (page 355) in 'Antibiotic prophylaxis in surgical procedures.'

Empirical and directed vancomycin dosing

Indications	Vancomycin is used for directed treatment of methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-resistant coagulase-negative staphylococcal species (e.g. *Staphylococcus epidermidis*) or vancomycin-susceptible *Enterococcus faecium* isolated from sterile sites (i.e. blood, CSF, pleural fluid, joint, bone). It can also be used for treatment and prophylaxis of Gram-positive infections in the presence of immediate severe or delayed severe hypersensitivity to beta-lactams antibiotics (i.e. penicillins and cephalosporins).
Dosage (see tables below)	<u>Adults</u> Calculate vancomycin dose using **age** and **actual body weight**; the **dosing interval** is based on baseline estimated renal function (using serum creatinine). See **Table 17** (page 389) for recommended doses in adults < 40 years and **Table 18** (page 390)for doses in adults ≥40 years. For patients on haemodialysis and peritoneal dialysis use local protocols. <u>Infants and children</u> Calculate vancomycin dose using **age** and **actual body weight**. See **Vancomycin dosing in young infants (0 to 90 days** (page 391) and **Vancomycin dosing in children 3 months or older** (page 392).
Loading dose	A loading dose of vancomycin achieves a therapeutic concentration more quickly, however, clear evidence that this improves clinical or microbiological outcomes is lacking. These guidelines recommend that a loading dose should be considered for critically ill adults or children, e.g. those requiring ICU admission, because these patients are at a high risk of poor outcomes and may have reduced vancomycin exposure.

cont...

	These guidelines also recommend a loading dose for all adults and children for some specific conditions; **omit** the loading dose if the patient has significant renal failure (creatinine male > 380 micromol/L, female > 280 micromol/L). See **loading dose for adults** (page 390) and **loading dose for children** (page 392) for recommended doses. **Do not give loading doses to infants younger than 90 days.**
Monitoring	**Measure serum creatinine at baseline and then twice weekly**; if creatinine rising, withhold dose(s) and seek advice (potentially restart later with a longer dose interval or substitute different antibiotic). Weekly full blood count.
Adverse effects	• **Nephrotoxicity**: this is usually reversible with cessation of therapy. There is an increased risk with prolonged therapy and when administered with other nephrotoxic agents (e.g. aminoglycosides such as gentamicin, piperacillin+tazobactam, frusemide, contrast media). In these situations, monitor creatinine more frequently, if possible. • **Vancomycin flushing syndrome**: this is an infusion-related histamine release reaction, causing flushing (usually involving the face and upper body) with or without pruritus, dyspnoea or hypotension. It is **not** an allergic reaction. If it occurs, pause the infusion for at least 30 minutes and then restart at half the previous infusion rate. Antihistamines can also be used as premedication. • **Allergy** including rash (occasionally severe) and anaphylaxis. • **Thrombocytopaenia:** this occurs in over 5% of recipients (it is reversible, but may recur – cease vancomycin and avoid future use).

Intravenous vancomycin dosing in adults

Starting and maintenance dosing

Dosing and frequency of administration depends on the patient's age, weight and renal function (see Tables 17 and 18 below). The maximum usual dose is 2 grams. For loading dose when indicated, see the next section.

Table 17: Vancomycin dosing for adults less than 40 years age

Actual body weight (kg)	**Dose**	**Dosing frequency based on initial serum creatinine value [Note 1]**			**Minimum infusion duration**
		Serum creatinine value			
		Male < 140 µmol/L Female < 120 µmol/L	Male 140 to 380 µmol/L Female 120 to 280 µmol/L	Male > 380 µmol/L Female > 280 µmol/L	See instructions above if reactions occur during infusion
< 45	20 mg/kg	12-hourly	24-hourly	In general, a single dose only is recommended (unless the patient is on dialysis, use local protocols)	10 mg/minute
45 to 55	1 g	12-hourly	24-hourly		100 minutes
56 to 70	1.25 g	12-hourly	24-hourly		125 minutes
71 to 82	1.5 g	12-hourly	24-hourly		150 minutes
83 to 94	1.75 g	12-hourly	24-hourly		175 minutes
≥ 95	2 g	12-hourly	24-hourly		200 minutes

µmol/L = micromol/L

Note 1: In other guidelines, dosage adjustment for patients with renal impairment is often calculated from the estimated creatinine clearance (CrCl) using the Cockcroft–Gault formula. However, in these guidelines, although it is less accurate, serum creatinine is used as an estimation of renal function, as it is much less complex.

Table 18: Vancomycin dosing for adults more than 40 years age

Actual body weight (kg)	Dose	Dosing frequency based on initial serum creatinine value [Note 1]			Minimum infusion duration (maximum 10 mg/minute)
		Serum creatinine value			
		Male < 140 µmol/L Female < 120 µmol/L	Male 140 to 380 µmol/L Female 120 to 280 µmol/L	Male > 380 µmol/L Female > 280 µmol/L	See instructions above if reactions occur during infusion
< 49	15 mg/kg	12-hourly	24-hourly	In general, a single dose only is recommended (unless the patient is on dialysis, use local protocols)	10 mg/minute
50 to 58	750 mg	12-hourly	24-hourly		75 minutes
59 to 75	1 g	12-hourly	24-hourly		100 minutes
76 to 92	1.25 g	12-hourly	24-hourly		125 minutes
93 to 108	1.5 g	12-hourly	24-hourly		150 minutes
109 to 125	1.75 g	12-hourly	24-hourly		175 minutes
≥ 125	2 g	12-hourly	24-hourly		200 minutes

µmol/L = micromol/L

Note 1: In other guidelines, dosage adjustment for patients with renal impairment is often calculated from the estimated creatinine clearance (CrCl) using the Cockcroft–Gault formula. However, in these guidelines, although it is less accurate, serum creatinine is used as an estimation of renal function, as it is much less complex.

Adult loading dose (when required)

A loading dose (i.e. the first dose is larger than subsequent doses) of vancomycin may be considered for critically ill patients (e.g. those requiring ICU admission) or if recommended for specific indications within these guidelines. **Do not** use a loading dose if the patient has significant renal failure (creatinine male > 380 micromol/L, female > 280 micromol/L).

If a loading dose is considered necessary, use:

> *vancomycin 25 mg/kg (actual body weight) up to a maximum of 3 g by IV infusion. The infusion time should be no faster than 10 mg/minute (see Table 20, page 393, for minimum infusion durations).*

If a loading dose is administered, the size and timing of the next dose should be determined from Table 17 (for adults < 40 years) or Table 18 (for adults ≥ 40 years).

Intravenous vancomycin dosing in infants and children

Vancomycin dosing in young infants (0 to 90 days)

For young infants aged 0 to 90 days without kidney impairment, attaining the target serum concentration depends upon postmenstrual age, weight and serum creatinine concentration.

Use the **Vancomycin intermittent dosing calculator for infants aged 0-90 days** online app to calculate the dose and frequency:

www.kidscalc.org/van-dose-calc/

If baseline serum creatinine is not available, give an initial dose of 15 mg/kg and calculate subsequent doses with the app when serum creatinine is available.

If serum creatinine increases during vancomycin treatment but is still within the normal reference range, is not more than twice the baseline value and urine output is normal, use the calculator to recalculate the dose using the updated creatinine value.

If the calculator cannot be used (e.g. if internet access is not available), a less preferred option is to dose based on age and weight as outlined in Table 19 below.

Table 19: Vancomycin dosing in young infants if the Vancomycin intermittent dosing calculator for infants aged 0-90 days cannot be used

Age [Note 1]		Dose	Dosing frequency
neonates younger than 30 weeks postmenstrual age	postnatal age 0 to 2 days	15 mg/kg	18-hourly
	postnatal age 3 days or older	15 mg/kg	12-hourly
neonates 30 to 36 weeks postmenstrual age	postnatal age 0 to 14 days	15 mg/kg	12-hourly
	postnatal age 15 days or older	15 mg/kg	8-hourly
neonates 37 to 44 weeks postmenstrual age	postnatal age 0 to 7 days	15 mg/kg	12-hourly
	postnatal age 8 days or older	15 mg/kg	8-hourly
neonates 45 weeks postmenstrual age or older		15 mg/kg	6-hourly

Note 1: 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).

Vancomycin dosing in children 3 months or older

For children aged 3 months to 18 years of age **without** impaired kidney function, use:

vancomycin 15 mg/kg (actual body weight) up to 1 g IV, 6-hourly. The infusion time should be no faster than 10 mg/minute (see Table 20 on the next page for minimum infusion durations).

Vancomycin loading dose for critically ill infants and children

A loading dose is **not recommended** in young infants (0 to 90 days).

A loading dose of vancomycin may be considered for infants and children older than 3 months if they are critically ill or if recommended for a specific indication. If a loading dose is considered necessary, use:

vancomycin 25 mg/kg (actual body weight) up to a maximum of 3 g by IV infusion. The infusion time should be no faster than 10 mg/minute (see Table 20 for minimum infusion durations).

Vancomycin dosing for infants and children with kidney impairment

For infants or children with kidney impairment, give a single dose of 15 mg/kg and seek appropriate advice for subsequent doses.

Vancomycin infusion times (adults and children)

Infuse vancomycin at a rate not exceeding 10 mg/minute to reduce the risk of infusion-related reactions.

Table 20: Minimum infusion times for vancomycin administration

Dose [Note 1]	Minimum infusion duration [Note 2]
0.25 g	25 minutes
0.5 g	50 minutes
0.75 g	75 minutes
1 g	100 minutes
1.25 g	125 minutes
1.5 g	150 minutes
1.75 g	175 minutes
2 g	200 minutes
2.25 g	225 minutes
2.5 g	250 minutes
2.75 g	275 minutes
3 g	300 minutes

Note 1: For infusion through peripheral lines, dilute to 5 mg/mL or weaker.

Note 2: Vancomycin flushing syndrome is a histamine-mediated, nonallergic response to rapid vancomycin administration that is characterised by rash, muscle spasms of the chest and back, and sometimes hypotension. If any of these occur, slow the infusion rate.

Key additional references

Gwee A, Cranswick N, McMullan B, Bolisetty S, Hunt RW, Curtis N, Duffull SB. Defining Target Vancomycin Trough Concentrations for Treating Staphylococcus aureus Infection in Infants Aged 0 to 90 Days. JAMA Pediatr. 2019 Aug 1;173(8):791-793

Appendix 3: Prevention of intravascular device-associated infections

Intravascular devices (peripheral or central) may cause serious or fatal infection. Infection may occur through one or more of five different routes – see Table 21 below. Avoid using intravascular devices whenever possible and remove unnecessary devices as soon as possible.

Many intravascular device-associated infections are preventable.

Regularly assess catheter site(s) for signs of infection, such as redness, swelling, warmth, pain or discharge, and monitor for signs of sepsis. The diagnosis may not be obvious as the line entry site often appears normal.

Always remove or replace an existing device when there is either evidence of entry site infection, inflammation or when sepsis is present and no other infective source is apparent.

Table 21: Measures to prevent intravascular device-associated infections

Route of infection	Essential preventative measures
insertion site infection is usually caused by contamination of the device during insertion.	• ensure proper hand hygiene (alcohol hand rub application) and use of gloves and eye protection by insertor • avoid insertion sites overlying joints – e.g. cubital fossa • thoroughly clean the insertion site and then apply antiseptic solution; allow the antiseptic to dry before placement • establish a large sterile field around the insertion site – this is especially important for central line insertion • use a nontouch technique for insertion – do not re-palpate the insertion site after disinfection and never touch the device tip • use a sterile transparent dressing that remains intact and provides adequate fixation to prevent movement of the catheter.

cont...

contamination of catheter hub neglect of hub disinfection is a major factor.	• perform hand hygiene prior to any procedure, gloves may be required if direct exposure to blood is possible. • disinfect the hub and access ports with an appropriate antiseptic (alcohol or alcohol+chlorhexidine) before any manipulation or administration of medication; allow time for the agent to dry. • avoid unnecessary disconnections or entries into the catheter system. • do **not** use an existing catheter for blood sample collection unless authorised.
infusate contamination (fluid or IV medication) many pathogens grow well within IV fluids; even scanty contamination may be responsible for sepsis.	• use single-use vials and syringes whenever possible. • perform hand hygiene prior to preparation and connection of intravenous set. • replace intravenous administration set according to established guidelines. • avoid using the same syringe to draw medication from multiple vials, as this can lead to cross-contamination. • prepare all intravenous medication in a separate clean area with appropriate aseptic measures. • clearly label all prepared syringes and bags with medication name, dose, concentration and expiration date.
haematogenous contamination from distant infection	• avoid central line insertion until after bloodstream infection has been successfully managed. • collect a clearance blood culture set for patients with *Staphylococcus aureus* bloodstream infection after 72 hours of treatment to show clearance of bacteraemia.
contaminated device from manufacturer or due to damage	• do not use a device where the sterile wrapping has been damaged. • only use quality-assured device manufacturers (ISO 9001 accredited). • look for evidence of patient bloodstream infection outbreaks due to similar environmental pathogens – e.g. *Burkholderia cepacia* complex.

Appendix 4: Antimicrobials in pregnancy and breastfeeding

Australian categorisation system for prescribing medicines in pregnancy

The categories for prescribing antimicrobials in pregnancy in these guidelines are taken from the Australian Therapeutic Goods Administration (TGA).

The categorisation is a risk stratification based on evidence of harm or the potential for harm to the fetus for taking particular medicines while pregnant. The categorisation assumes treatment at recommended therapeutic doses.

The Australian TGA categorisation system is not hierarchical. Different categorisation systems are used internationally and are not equivalent.

This information is for clinical prescribers rather than patients, and should be interpreted within the clinical context of each patient.

TGA pregnancy 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 fetus having been observed.

TGA pregnancy 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 fetus having been observed.

Studies in animals have not shown evidence of an increased occurrence of fetal damage.

TGA pregnancy 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 fetus having been observed.

Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of fetal damage.

TGA pregnancy 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 fetus having been observed.

Studies in animals have shown evidence of an increased occurrence of fetal damage, the significance of which is considered uncertain in humans.

TGA pregnancy category C

Drugs which, owing to their pharmacological effects, have caused or may be suspected of causing harmful effects on the human fetus or neonate without causing malformations. These effects may be reversible. Specialised texts should be consulted for further details.

TGA pregnancy category D

Drugs which have caused, are suspected to have caused or may be expected to cause an increased incidence of human fetal malformations or irreversible damage. These drugs may also have adverse pharmacological effects. Specialised texts should be consulted for further details.

TGA pregnancy category X

Drugs which have such a high risk of causing permanent damage to the fetus that they should not be used in pregnancy or when there is a possibility of pregnancy.

Definitions for compatibility with breastfeeding

The Papua New Guinea guidelines for antimicrobial use while breastfeeding have been adapted from the Australian *Therapeutic Guidelines*.

These guidelines include the following categories:

Compatible

There are sufficient data to demonstrate:

- an acceptably low relative infant dose and/or
- no significant plasma concentration in breastfed infants 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 to demonstrate:

- an acceptably low relative infant dose and/or
- no significant plasma concentration in breastfed infants and/or
- no adverse effects in breastfed infants.

However, the characteristics of the drug suggest significant adverse effects are unlikely. Consider monitoring the infant for adverse effects.

Avoid, insufficient data

the characteristics of the drug suggest significant adverse effects are possible and there are insufficient data to demonstrate:

- an acceptably low relative infant dose and/or
- no significant plasma concentration in breastfed infants and/or
- no adverse effects in breastfed infants.

Avoid

there are sufficient data to demonstrate:

- an unacceptably high relative infant dose and/or
- significant plasma concentration in breastfed infants and/or
- significant adverse effects in breastfed infants.

Table 22: Antimicrobials in pregnancy and breastfeeding

Antimicrobial	TGA pregnancy category	Compatibility with breastfeeding
aciclovir	B3	compatible
albendazole	D	compatible
amikacin	D	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
amoxicillin	A	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
amoxicillin+clavulanate	B1	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
amphotericin B (all formulations)	B3	compatible; absorption by infant unlikely
azithromycin	B1	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)

cont...

benzathine benzylpenicillin (benzathine penicillin)	A	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
benzylpenicillin (penicillin G, crystalline penicillin)	A	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
benzyl benzoate	B2	topical use: use with caution; prefer permethrin
cefalexin	A	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
cefazolin	B1	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
cefaclor	B1	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
cefepime	B1	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
cefixime	B2	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
cefotaxime	B1	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
ceftazidime	B1	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
ceftriaxone	B1	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
cefuroxime	B1	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
chlorhexidine (topical)	A	compatible
chloramphenicol (topical)	A	compatible
chloramphenicol (oral or parenteral)	limited data for systemic use. consider alternative agent in 3rd trimester as may increase the risk of 'grey syndrome' in the neonate	consider an alternative where possible
ciprofloxacin	B3	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
clarithromycin	B3	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
clindamycin	A	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)

cont...

clotrimazole (topical)	A	compatible
colistin (colistimethate sodium)	B2	caution, insufficient data; may cause diarrhoea in infants
diethylcarbamazine	B2	avoid, insufficient data
doxycycline	D safe for use during the first 18 weeks of pregnancy (16 weeks postconception) after which it may affect the formation of the baby's teeth and cause discolouration.	compatible for short courses (e.g. 10 days) if alternative drug not appropriate; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
entecavir	B3	avoid, insufficient data
erythromycin	A	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
flucloxacillin	B1	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
fluconazole	D	compatible; may cause diarrhoea in infant
flucytosine	B3	avoid, insufficient data
fusidic acid (sodium fusidate)	C	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
gentamicin	D (but used for serious infections in pregnancy)	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
griseofulvin	D	avoid, insufficient data
ivermectin	B3	compatible
levofloxacin	unlisted	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
linezolid	B3	use with caution; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
meropenem	B3	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)

cont...

metronidazole	B2	systemic use: compatible; may cause some bitterness in breast milk. monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush). consider withholding breastfeeding for 12 to 24 hours after high single-dose (2 g) treatment topical use: compatible
moxifloxacin	B3	use with caution; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
nitrofurantoin	A (short-term therapy only)	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 monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
nystatin	A	compatible
permethrin (topical)	B2	compatible
phenoxymethylpenicillin	A	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
piperacillin + tazobactam	B1	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
rifampicin	C	compatible; monitor infant for jaundice, diarrhoea, vomiting, rash and candidiasis (thrush). breast milk may appear a red-orange colour.
roxithromycin	B1	no data
terbinafine	systemic use: B1 topical use: unlisted	systemic use: avoid, insufficient data topical use: use with caution; avoid use in breast area
tinidazole	B3	use with caution; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)

cont...

trimethoprim+ sulfamethoxazole (cotrimoxazole)	unlisted (see product information)	avoid if infant has glucose-6-phosphate dehydrogenase (G6PD) deficiency use with caution if infant is less than 1 month old, or is premature, ill or jaundiced—may increase risk of haemolysis, bilirubin displacement and kernicterus. monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush) compatible if infant is older than 1 month and healthy—monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)
vancomycin	B2	compatible; monitor infant for diarrhoea, vomiting, rash and candidiasis (thrush)

Appendix 5: Renal impairment and antimicrobial dosing

These tables have been adapted from the Australian *Therapeutic Guidelines* and simplified to only encompass three categories of serum creatinine level, and haemodialysis and peritoneal dialysis. Please note these guidelines are for the management of **adult patients**. For antibiotic dosing in children with renal impairment, consult alternative references or seek appropriate advice.

Introduction

Renal impairment can contribute to supratherapeutic doses of antimicrobials or accumulation of toxic metabolites with standard dosing, and dosage reduction may be required. These tables were developed to guide dose adjustment of antimicrobials that may cause harm to patients with renal impairment.

Note that many commonly used antimicrobials that are principally renally excreted do not have prominent concentration related toxicity. Therefore, even if an antimicrobial is listed in the following tables as requiring dose adjustment if renal function is significantly impaired, it does not necessarily follow that renal function must always be measured before it can be prescribed. This is particularly the case if obtaining an urgent creatinine level is difficult or impossible (as may be the case in Papua New Guinea) and if there is no clinical reason for suspecting the patient is likely to have impaired renal function (e.g. longstanding diabetes).

Dosage adjustment for patients with renal impairment is guided by an assessment of glomerular filtration rate (GFR), which is usually proportional to renal drug clearance. In these guidelines, categories are based on serum creatinine levels as an estimate of renal function. These estimates have inherent limitations. They can also be inaccurate in patients who are critically unwell and have changing renal function; in these patients, please seek appropriate advice.

This topic provides dosage guidance for adults undergoing peritoneal dialysis and intermittent haemodialysis. However, the recommendations only apply to high-flux haemodialysis and peritoneal dialysis that is continuous or regular (performed regularly within each 24-hour cycle). If the patient is receiving dialysis that is operated differently to this, expert guidance is required for antimicrobial dosing.

Where possible, avoid nephrotoxic drugs in people with severe renal impairment.

Commonly used antimicrobial agents in Papua New Guinea which do **not** require dose adjustment in adults with renal impairment include:

- antibacterials: amoxicillin+clavulanate (**oral** formulations), azithromycin, benzathine benzylpenicillin, ceftriaxone, chloramphenicol, doxycycline, metronidazole, phenoxymethylpenicillin, tinidazole
- antivirals: entecavir
- anthelminthics: albendazole, ivermectin, mebendazole.

Agents for which dose adjustment is recommended in adults with impaired renal function

This section includes antimicrobials which are recommended throughout these guidelines but is not a comprehensive list of all antimicrobial agents for which dose adjustment in renal impairment may be recommended.

Table 23: Antibacterial dosages for adults with impaired renal function [Note 1]

antibacterial					
	creatinine (males)	**less than 190 micromol/L**	**191 to 400 micromol/L**	**more than 400 micromol/L**	**dialysis (HD and PD)**
	creatinine (females)	**less than 135 micromol/L**	**136 to 350 micromol/L**	**more than 350 micromol/L**	
amikacin		seek expert advice			
amoxicillin		no change	no change	100% 12-hourly	100% 12-hourly
amoxicillin+ clavulanate IV		no change	1000+200 mg 8- to 12-hourly	1000+200 mg 12-hourly	1000+200 mg 12-hourly
benzylpenicillin		no change	75% at normal dosing interval	25 to 50% at normal dosing interval (maximum 6 g per day)	25 to 50% at normal dosing interval (maximum 6 g per day)
cefalexin		no change	no change	50 to 100% 8- to 12-hourly	50 to 100% 8- to 12-hourly

cont...

cefazolin	no change	50% 8-hourly OR 100% 12-hourly	25% 12-hourly OR 50% 24-hourly	HD: 100% on dialysis days only [Note 2] PD: 25% 12-hourly OR 50% 24-hourly
cefixime	no change	no change	single dose ok	single dose ok
ceftazidime	no change	50% 8-hourly	25-50% 12-hourly	HD: 1-2 g three times a week on dialysis days; dose after dialysis. PD: 25-50% 12-hourly
cefuroxime	no change	no change	100% 24-hourly	100% 24-hourly [Note 2]
ciprofloxacin oral [Note 3]	no change	no change	500 mg 24-hourly	500 mg 24-hourly [Note 2]
ciprofloxacin IV [Note 3]	no change	no change	100% 24-hourly	100% 24-hourly [Note 2]
clarithromycin	no change	no change	50% 12-hourly	50% 12-hourly
erythromycin	no change	no change	50 to 75% at normal dosing interval	50 to 75% at normal dosing interval
flucloxacillin oral	no change	no change	100% 8-hourly	100% 8-hourly
flucloxacillin IV	no change	no change	50% 6- to 8-hourly	50% 6- to 8-hourly
gentamicin	See 'Appendix 1: Gentamicin dosing,' page 381			
meropenem	no change	100% to 12-hourly	50% to 100% 24-hourly	50% to 100% 24-hourly [Note 2]
nitrofurantoin	no change	avoid [Note 4]	avoid [Note 4]	avoid [Note 4]
piperacillin+ tazobactam	no change	100% 8-hourly	100% 12-hourly	100% 12-hourly

cont...

trimethoprim+ sulfamethoxazole [Note 5]	no change	no change for 3 days, then 100% 24-hourly	avoid	avoid
vancomycin	See 'Appendix 2: Vancomycin dosing,' page 386			

HD = haemodialysis; IV = intravenous; PD = peritoneal dialysis

Note 1: 'No change' indicates that the standard dosage regimen for the specific indication in these guidelines should be used. Percentage dosage adjustments are calculated using the intermittent dose rather than the total daily dose (e.g. 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).

Note 2: In haemodialysis, dose after dialysis.

Note 3: For dose adjustments in patients with infections caused by *Pseudomonas aeruginosa*, seek appropriate advice.

Note 4: Nitrofurantoin should be avoided because of an increased risk of treatment failure due to inadequate urine concentration and adverse effects.

Note 5: Seek appropriate advice for dosing for treatment or prophylaxis of *Pneumocystis jirovecii* pneumonia.

Table 24: Antifungal dosages for adults with impaired renal function [Note 1]

antifungal					
	creatinine (males)	**less than 190 micromol/L**	**191 to 400 micromol/L**	**more than 400 micromol/L**	**dialysis (HD and PD)**
	creatinine (females)	**less than 135 micromol/L**	**136 to 350 micromol/L**	**more than 350 micromol/L**	
amphotericin B deoxycholate		no change	no change	no change	no change
			amphotericin is highly nephrotoxic and can accumulate in patients with renal impairment; seek appropriate advice		
fluconazole		no change	50% 24-hourly	25 to 50% 24-hourly	25 to 50% 24-hourly [Note 2]
flucytosine [Note 3]		no change	100% 12- to 24-hourly	100% 24- to 48-hourly	100% 24- to 48-hourly [Note 2]

HD = haemodialysis; PD = peritoneal dialysis

Note 1: 'No change' indicates that the standard dosage regimen for the specific indication in these guidelines should be used. Percentage dosage adjustments are calculated using the intermittent dose rather than the total daily dose (e.g. 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).

Note 2: In haemodialysis, dose after dialysis.

Note 3: Treatment in combination with nephrotoxic drugs, such as amphotericin B, may reduce renal excretion of flucytosine and increase the risk of toxicity; seek appropriate advice.

Table 25: Antiviral dosages for adults with impaired renal function [Note 1]

antiviral (including anti-hepatitis antiviral agents)					
	creatinine (males)	**less than 190 micromol/L**	**191 to 400 micromol/L**	**more than 400 micromol/L**	**dialysis (HD and PD)**
	creatinine (females)	**less than 135 micromol/L**	**136 to 350 micromol/L**	**more than 350 micromol/L**	
aciclovir oral		no change	dosage depends on the indication and patient's immune status – see product information		
aciclovir IV		no change	100% 12- to 24-hourly	50% 24-hourly	50% 24-hourly [Note 2]
tenofovir alafenamide		no change	no change	avoid	avoid
tenofovir disoproxil fumarate		no change	SCr males 191–280 micromol/L; females 136–220 micromol/L: 100% 48-hourly	100% weekly	100% weekly [Note 2]
			SCr males 281–400 micromol/L, females 221–350 micromol/L: 100% 72-hourly		

HD = haemodialysis; IV = intravenous; PD = peritoneal dialysis; SCr = serum creatinine

Note 1: 'No change' indicates that the standard dosage regimen for the specific indication in these guidelines should be used. Percentage dosage adjustments are calculated using the intermittent dose rather than the total daily dose (e.g. 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).

Note 2: In haemodialysis, dose after dialysis.

Appendix 6: Administration of parenteral antimicrobials

Table 26: Administration of injectable antimicrobial drugs in adults [Note 1] [Note 2][Note 3]

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 with a compatible fluid; 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 do **not** refrigerate aciclovir solutions as crystals may form
amoxicillin	
250 mg vial, 500 mg vial	
reconstitution	reconstitute with WFI (or with lignocaine [lidocaine] for IM injection only)
compatible fluids	glucose 5%, Hartmann's, sodium chloride 0.9%, sodium chloride and glucose solutions
IV injection	inject **slowly** over at least 3-5 minutes; faster administration may cause seizures
IV infusion	dilute with 50-100 mL of a compatible fluid and infuse over 30-60 minutes
IM injection	IM injection is painful, reconstitute with 1% lignocaine (lidocaine); doses larger than 500 mg should be divided between multiple sites
notes	rapid IV administration may cause seizures use reconstituted and diluted solutions immediately
amoxicillin+clavulanate	
1000+200mg vial	
reconstitution	reconstitute with 20 mL of WFI
compatible fluids	sodium chloride 0.9%, Hartmann's

cont...

IV injection	inject **slowly** over 3-5 minutes
IV infusion	dilute with 50-100 mL of a compatible fluid and infuse over 30-40 minutes
IM injection	not recommended
notes	the reconstituted solution is stable for 20 minutes at 25 °C; any residue should be discarded after this time. diluted solutions made with sodium chloride 0.9% are stable if refrigerated at 2-8 °C for up to 8 hours.
amphotericin B desoxycholate	
50 mg vial (keep refrigerated at 2-8 °C)	
reconstitution	reconstitute with 10 mL WFI to make a concentration of 5 mg/mL; shake well to dissolve.
compatible fluids	glucose 5%
IV injection	not recommended
IV infusion	dilute the dose to a concentration of 0.1 mg/mL with glucose 5% (50 mg in 500 mL) infuse over at least 2 to 6 hours; flush the line with glucose 5% before and after the infusion
IM injection	not recommended
notes	the diluted solution is stable for 8 hours at 25 °C or 24 hours if refrigerated; protect from light (there is no need to protect from light during the infusion). Infusion reactions are common (e.g. phlebitis, fever, nausea and vomiting, headache and myalgia). These reactions may be reduced by: • prehydration with sodium chloride 0.9% (0.5 to 1 L intravenously) prior to infusion (recommended) • pretreatment with hydrocortisone, an antihistamine, an antiemetic and an analgestic or antipyretic • slowing the infusion rate. Note that the information provided here is for the deoxycholate (conventional) formulation; infusion rates (and dosing) are different for other formulations of amphotericin B (lipid complex or liposomal).
azithromycin	
500 mg vial	
reconstitution	reconstitute with WFI and shake until dissolved
compatible fluids	glucose 5%, Hartmann's, sodium chloride 0.9%, sodium chloride and glucose solutions
IV injection	not recommended

cont...

IV infusion	dilute with 250-500 mL of a compatible fluid and infuse over at least 1 hour; maximum concentration 2 mg/mL
IM injection	not recommended
notes	protect the vial from light reconstituted and diluted solutions are stable for 24 hours at 30°C
benzathine benzylpenicillin (benzathine penicillin)	
2.4 million units in 5 mL	
compatible fluids	may be given with lignocaine (lidocaine) 1% or 2% to reduce the pain of the injection
IV injection	contraindicated
IV infusion	contraindicated
IM injection	The ventrogluteal site is the preferred site for IM injection. Apply firm pressure to the injection site with a thumb for at least 10 seconds before inserting the needle. Use a 21 gauge needle and inject slowly, at a steady rate, over at least 2 to 3 minutes
notes	IM benzathine injections are painful; use non-pharmacological strategies such as firm pressure to the injection site for at least 10 seconds before injecting, an ice pack applied to the site before injecting and refrigerating the needle prior to injection. Consider pharmacological strategies such as injecting lignocaine (lidocaine) with benzathine benzylpenicillin and providing oral paracetamol before injection and afterwards as required.
benzylpenicillin	
600 mg (1 million units) vial	
compatible fluids	glucose 5%, sodium chloride 0.9%
IV injection	suitable for doses 1.2 g or less; dilute to a concentration of 60 mg/mL because it is isotonic (reconstitute with 5 mL of WFI then dilute with a further 5 mL of WFI); inject **slowly** over 5 to 10 minutes
IV infusion	reconstitute with 5-10 mL of WFI, dilute with 100 mL of a compatible fluid and infuse over 30-60 minutes
IM injection	dilute with 3.2 mL WFI to a concentration of 300 mg/mL and inject the appropriate volume deep into a large muscle
notes	rapid IV administration of large doses may cause seizures. use reconstituted and diluted solutions **immediately**
cefazolin	
1 g vial, 2 g vial	
reconstitution	reconstitute with WFI (or lignocaine [lidocaine] for IM injection)

cont...

compatible fluids	glucose 5%, Hartmann's, sodium chloride 0.9%, sodium chloride and glucose solutions
IV injection	doses < 2 g; inject **slowly** over at least 3 to 5 minutes
IV infusion	dilute with 50-100 mL of a compatible fluid and infuse over 10-60 minutes
IM injection	reconstitute with 1% lignocaine (lidocaine) or WFI; inject deep into a large muscle
notes	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.
cefepime	
1 g vial, 2 g vial	
compatible fluids	glucose 5%, sodium chloride 0.9%, sodium chloride and glucose solutions
IV injection	reconstitute with glucose 5% or sodium chloride 0.9% and inject **slowly** over 3 to 5 minutes
IV infusion	dilute with 50-100 mL of a compatible fluid and infuse over 30 minutes
IM injection	dilute to a concentration of 230 mg/mL with WFI, lignocaine (lidocaine) or a compatible fluid and inject deep into a large muscle; not usually painful
notes	reconstituted solutions made with sodium chloride, glucose 5% or WFI are stable for 24 hours if refrigerated at 2 to 8°C
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 with 50 mL of a compatible fluid 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.

cont...

chloramphenicol	
1 g vial	
reconstitution	reconstitute with WFI, sodium chloride 0.9% or glucose 5%, shake the vial gently to dissolve
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 of a compatible fluid and infuse over 30-40 minutes
IM injection	not recommended - absorption can be slow and unpredictable; if required, inject slowly into a large muscle
notes	reconstituted solution is stable for 24 hours if refrigerated at 2 to 8 °C do not use solutions that are cloudy
ciprofloxacin	
2 mg/mL / 50 mL bag (100 mg)	
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.
clindamycin	
various products available; some brands must be stored at 2-8 °C, check product information	
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	rapid administration may cause hypotension and cardiac arrest.

cont...

flucloxacillin	
500 mg vial	
reconstitution	reconstitute with WFI
compatible fluids	glucose 5%, sodium chloride 0.9%, Hartmann's, sodium chloride and glucose solutions
IV injection	only suitable for doses **less than** 2 g; inject **slowly** over 3-4 minutes
IV infusion	dilute in 50-100 mL and infuse over 30-60 minutes
IM injection	IM injection is painful. Reconstitute with 2 mL WFI or lignocaine (lidocaine) 1% and 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 IV injection use reconstituted and diluted solutions immediately.
fluconazole	
2 mg/mL / 50 mL bag (100 mg)	
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
flucytosine	
2.5 g in 250 mL	
compatible fluids	glucose 5%, glucose 4% and sodium chloride 0.18%, sodium chloride 0.9%
IV injection	not recommended
IV infusion	infuse over 20 to 40 minutes
IM injection	not recommended
notes	exposure to temperatures above 25°C may result in formation of 5-fluorouracil (cytotoxic), which cannot be detected visually may precipitate if stored below 15°C
gentamicin	
20 mg / 2 mL (paediatric), 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 (may be diluted to 20 mL with sodium chloride 0.9% to allow slow injection if required)
IV infusion	dilute with 50-100 mL and infuse over 15-30 minutes

cont...

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	
reconstitution	reconstitute with WFI or sodium chloride 0.9%; shake well
compatible fluids	sodium chloride 0.9% (preferred), glucose 5%, sodium chloride and glucose solutions
IV injection	≤ 500 mg; inject **slowly** 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 stability is temperature and concentration dependent: vials reconstituted with WFI and solutions (concentration 1-20 mg/mL) prepared with sodium chloride 0.9% are stable for up to 24 hours at 2-8°C
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	
reconstitution	reconstitute with WFI or sodium chloride 0.9%; shake well to dissolve
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

cont...

IM injection	not recommended
notes	reconstituted solution for some brands is stable for 24 hours when refrigerated at 2-8 °C (check product information for each brand); infusion solution is stable for 24 hours when refrigerated at 2-8 °C
vancomycin	
500 mg in 10 mL	
reconstitution	n/a
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. also see Table 20: Minimum infusion times for vancomycin administration, page 393 in 'Vancomycin dosing.' 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.

WFI = water for injection

Note 1: this table gives the maximum (fastest) safe administration rates; slower rates may be required.

Note 2: check the product information as different brands may have different dilution or storage requirements.

Note 3: IM route should only be used where IV route is not available for the medicines included in this table.