EMPIRICAL AND PROPHYLACTIC USE OF ANTIMICROBIALS

NATIONAL GUIDELINES – SRI LANKA

Second Edition -2024

The Sri Lanka College of Microbiologists
in collaboration with
Other Professional Colleges in Healthcare and
The Ministry of Health, Sri Lanka

Empirical and Prophylactic Use of Antimicrobials
National Guidelines – Sri Lanka

Sri Lanka College of Microbiologists

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Declaration:

The Sri Lanka College of Microbiologists is committed to provide guidance on prudent and evidence-based prescribing of antimicrobials. The 'National Guidelines on Empirical and Prophylactic Use of Antimicrobials' was first published in 2016, aiming to optimize the use of antimicrobials, minimize the risk of antimicrobial resistance and to ensure patient safety by reducing adverse effects. This second edition of the guidelines is prepared according to the evidence available at the time of revision. All reasonable precautions have been taken to verify the information contained in the guidelines. However, the responsibility of interpretation and appropriate application of information lies with the prescriber. All members involved in the development of the guidelines declare that they have no conflicts of interest, financial or otherwise that could compromise the impartiality, integrity, or evidence-based nature of the recommendations and affirm that this is a no-cost activity intended solely for the improvement of antimicrobial prescribing and patient care.

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- Association of Sri Lankan Neurologists
- Ceylon College of Critical Care Specialists
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Purpose

These guidelines are developed with the intention of improving the outcome of infectious diseases through early and appropriate antimicrobial therapy while minimizing the emergence of antimicrobial resistance. It is intended to be used by house officers, medical officers, postgraduate trainee doctors, specialist clinicians who are working in public and private healthcare settings and general practitioners.

Scope

Antimicrobial regimes given here are intended to be used for empiric or prophylactic therapy. Antimicrobial therapy should be reviewed whenever a microbiological diagnosis and antibiotic susceptibility results are available. Investigations done for diagnosis of infections are not described in the guidelines. The results of basic non-specific investigations may support the empiric treatment decision. Appropriate specimens for microbiological investigations should be collected before starting empirical antimicrobials. Treatment options in the guidelines have been selected for the optimal use of antimicrobials in the country and may not include all therapeutic options available globally for a given infection. These guidelines are not intended to serve as complete management guidelines for infectious diseases since other aspects of management of infections are not covered here. It is mentioned to seek specialist opinion in the guidelines for some infections, since individualized assessment and management is essential in most infectious diseases. The main focus of these guidelines has been the common bacterial, fungal and viral infections and the scope does not include a comprehensive range of infections caused by uncommon bacteria, viruses, parasitic and fungal agents. Best practices in antimicrobial therapy will continue to change with improving evidence on management of infections and the guidelines will be revised accordingly.

Message from the Secretary of Health

The profound impact of antibiotics on bringing down human morbidity and mortality was evident in the 20th century when antibiotics were considered a panacea for infectious diseases. Despite the advances in medical management and access to a multitude of antimicrobial agents, infectious diseases remain a threat to global health. Bacteria, viruses, fungi and parasites resistant to antimicrobial agents continue to pose the challenge of difficult-to-treat infections.

The spread of resistant microorganisms in healthcare facilities and in the community threatens the enormous gains achieved through antimicrobial therapy. Development of new antimicrobials is hindered due to the complexity of resistance mechanisms and the high costs involved in the process. Therefore, optimising the use of currently available antimicrobials is the best recommended strategy. The World Health Organization has identified antimicrobial resistance (AMR) as one of the ten global public health threats and advocates on the judicious use of antimicrobials by all nations.

Guidelines on the use of antimicrobials are essential to promote appropriate prescribing to improve patient outcomes as well as to minimize the emergence of AMR.

The National Guidelines on Empirical and Prophylactic Use of Antimicrobials in Sri Lanka was first issued in 2016, as a collaborative effort lead by the Sri Lanka College of Microbiologists.

It is my pleasure to endorse the second edition of the 'National Guidelines on Empirical and Prophylactic Use of Antimicrobials' developed by the Sri Lanka College of Microbiologists in collaboration with other Professional Colleges involved in providing healthcare and the Ministry of Health, Sri Lanka. I extend my thanks to all those who contributed to this revised edition.

I earnestly request all medical professionals to make the maximum use of these guidelines when prescribing antimicrobials, to ensure the best care for patients with infectious diseases.

Dr. P. G. Mahipala
Secretary of Health
Ministry of Health, Sri Lanka

Message from the Director General of Health Services

Antimicrobials, one of the cornerstones of modern medicine, play a pivotal role in the treatment of infections. However, their overuse or misuse poses a significant threat to global health, contributing to the emergence of antimicrobial resistance (AMR). It has been identified as one of the most pressing public health threats by WHO. The world is heading towards a "post-antibiotic era" with an end to the golden age of antibiotics, putting humans and animals once again at risk of death due to infections, as a result of non-availability of effective antimicrobials.

The burden and impact of antimicrobial resistance falls disproportionately on low and middle-income countries with an immense burden on healthcare services by increasing morbidity, mortality and healthcare cost. Infections due to resistant organisms have escalated in both healthcare settings and the community in Sri Lanka during the past two decades. The most effective and practical approach to minimize this problem is through a national scale consensus on the use of antimicrobials in the country. Identifying this vital need, the Sri Lanka College of Microbiologists developed the National Guidelines on Empirical and Prophylactic Use of Antimicrobials, which was first published in 2016. I am pleased to write this message for the second edition of the guidelines developed through a collaborative effort of experts in many medical and surgical professional colleges and associations. With the endorsement of the Ministry of Health, this document will serve as an invaluable tool to empower healthcare professionals with evidence-based practices for prescribing antimicrobials rationally.

I would request the healthcare providers to give priority and the fullest support in implementing these guidelines and facilitate antimicrobial stewardship programmes in all healthcare institutions to optimize patient care outcomes while mitigating the risk of antimicrobial resistance. I wish to thank all stakeholders involved in the development of these guidelines.

Dr. Asela Gunawardena
Director General of Health Services
Ministry of Health, Sri Lanka

Message from the National AMR-Focal Point

I am pleased that the second edition of the "National Guidelines on Empirical and Prophylactic Use of Antimicrobials" is now launched. This remarkable accomplishment is the result of collaborative efforts of the Sri Lanka College of Microbiologists and other professional colleges with the Ministry of Health.

The updated guidelines are becoming more and more obligatory as the spectrum of infectious diseases continues to evolve and the misuse of antibiotics increases. The development of these guidelines highlights our joint commitment on addressing the antimicrobial resistance (AMR), a serious threat to global health.

This revised edition integrates the latest research and insights into antimicrobial stewardship, offering evidence-based recommendations for both empirical and prophylactic use of Antimicrobials. Our goal is to protect the efficacy of antimicrobial treatment options while reducing the threat posed by AMR by giving healthcare professionals clear guidelines.

I would want to express my heartfelt gratitude to everyone who contributed to developing and polish these guidelines. Your knowledge and commitment have been crucial in creating this valuable guideline for medical practitioners all throughout Sri Lanka.

Let's not compromise in our dedication to practicing appropriate antimicrobial stewardship as we set out to put these suggestions into practice. By working together, we can significantly lessen the threat posed by AMR and guarantee the continued use of antimicrobial medicines for future generations.

Dr. Sudath K Dharmaratne
Deputy Director General of Laboratory Services
Ministry of Health, Sri Lanka

Abbreviations

ABST	Antibiotic sensitivity test
AMR	Antimicrobial resistance
AUC	Area under the curve
BMI	Body mass index
BNF	British National Formulary
CA-MRSA	Community acquired methicillin resistant *Staphylococcus aureus*
CAPD	Continuous ambulatory peritoneal dialysis
CIED	Cardiovascular implantable electronic devices
CMV	Cytomegalovirus
CNS	Central nervous system
COPD	Chronic obstructive pulmonary disease
CRF	Chronic renal failure
CRRT	Continuous renal replacement therapy
CSF	Cerebro-spinal fluid
DM	Diabetes mellitus
DRESS	Drug reaction with eosinophilia and systemic symptoms
EBV	Epstein-Barr virus
ECMO	Extracorporeal membrane oxygenation
eGFR	Estimated glomerular filtration rate
ENT	Ear, nose and throat
GBS	Group B Streptococci
HHV	Human herpesvirus
HSV	Herpes simplex virus
ICU	Intensive care unit
I & D	Incision and drainage
IUD	Intra-uterine devices
IV	Intravenous
MASCC	Multinational association for supportive care in cancer
MDRO	Multi-drug resistant organisms
MIC	Minimum inhibitory concentration
NA	Not applicable
NPTCCD	National Programme for Tuberculosis Control and Chest Diseases
NSACP	National STD and AIDS Control Programme
OPAT	Outpatient parenteral antibiotic therapy
PCR	Polymerase chain reaction
PO	Per-oral
SBP	Subacute bacterial peritonitis
STI	Sexually transmitted infections
UTI	Urinary tract infections
TB	Tuberculosis
TDM	Therapeutic drug monitoring
TRUS	Transurethral ultrasound
TURP	Transurethral resection of the prostate
TURBT	Transurethral resection of bladder tumour
VZV	Varicella Zoster virus
WHO	World Health Organization

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SECTION A

Chapter 1: General Principles of Antimicrobial Therapy

Antimicrobial resistance (AMR) is a global public health threat. Current evidence clearly demonstrates that inappropriate use of broad-spectrum antimicrobials is associated with the selection of resistant microorganisms and a higher risk of *Clostridioides difficile* infection, and causes harmful effects to the body's protective microbial flora. Therefore, rational prescribing of antimicrobials is essential to minimize negative consequences while ensuring the best outcome for the patient. Rational use of antimicrobials requires that patients receive medications appropriate to their clinical needs, in correct doses that meet their own individual requirements, for an adequate period, and at the lowest cost to them and their community.

1.1 General principles to be adhered to when prescribing antimicrobials

- Do not prescribe antibacterials for viral or self-limiting bacterial infections. Start antimicrobials empirically only if there is a clinical indication.
- Before commencing empirical antimicrobial therapy, obtain appropriate samples for cultures and other relevant microbiological investigations. However, in critically ill patients, initiate empirical antimicrobial treatment as soon as possible, at least within one hour of diagnosis of probable/definite sepsis or septic shock.
- Choose the correct empirical antimicrobial therapy i.e. the 'best guess' therapy and directed against an anticipated and likely cause of infectious disease. Single-agent antimicrobial therapy is generally preferred, however, a combination of two or more antimicrobial agents is recommended in certain situations (e.g. for synergistic activity against a microorganism, critically ill patients, treatment of polymicrobial infections, and prevention of emergence of resistance).
- Choose the correct dose, dosing interval and appropriate route of antimicrobial therapy according to the site, severity of infection and pharmacodynamics/kinetics of the antimicrobial.
- Document the dose, route, duration, and the review date on the drug chart and in the clinical notes, for all antimicrobials prescribed.
- Review the clinical diagnosis, response to therapy and the continuing need for antimicrobials by 48-72 hours and make a clear plan of action.
- If cultures are positive, the empirical therapy should be de-escalated to pathogen specific targeted therapy according to antibiotic sensitivity test results (ABST results). Avoid continuation of broad-spectrum antimicrobials unnecessarily.

- Review the patients on intravenous antimicrobials every 48 hours and consider the possibility of switching to an oral therapy if they are improving.
- Use antimicrobials for the shortest duration according to the nature/site of the infection and the causative agent. Prolonged courses may be needed in the treatment for some specific organisms (e.g. *Burkholderia pseudomallei*), specific infections (e.g. infective endocarditis) and in immune-compromised patients.
- Enhance timely and adequate source control by surgical interventions (e.g. draining of pus, removal of foreign material, debridement of necrotic tissue) and avoid using antimicrobials as the sole management option in such situations.
- Refer to the latest version of the British National Formulary (BNF) to check the contraindications, cautions and drug interactions before initiating antimicrobial therapy.
- Monitor for adverse effects during antimicrobial therapy.

1.2 Optimizing the use of antimicrobials

1.2.1 Antimicrobial stewardship

- Antimicrobial stewardship involves a coherent set of actions which promote and monitor the responsible use of antimicrobials.
- Stewardship is achieved by selection of the right antimicrobial for the right patient, administered at the right time with the correct dose via the right route for adequate duration causing least harm to the patients.
- Stewardship programmes coupled with infection prevention and control programmes, optimize the use of antimicrobials by promoting behaviour change in antimicrobial prescribing and dispensing practices, improve patient outcomes, reduce further emergence, selection and spread of AMR, prolong the lifespan of existing antimicrobials, reduce healthcare-associated infections, and minimize healthcare costs.

1.2.2 WHO AWaRe classification (Refer Annex 1)

- To improve antibiotic prescription practices globally, a pragmatic approach was taken by WHO to develop actionable guidance for empiric antibiotic use. In this regard, the AWaRe classification of antibiotics was developed in 2017 (and revised in 2019, 2021 and 2023) by a WHO Expert Committee as a tool to support antibiotic stewardship efforts at local, national and global levels.
- Antibiotics are classified into three groups; “Access”, “Watch” and “Reserve”, considering the impact of different antibiotics and antibiotic classes on antimicrobial resistance, to emphasize the importance of their appropriate use.
- It is a useful tool for monitoring antibiotic consumption, defining targets and

monitoring the effects of stewardship policies that aim to optimize antibiotic use and curb antimicrobial resistance.

- WHO has set a target to achieve at least 60% of total antibiotic consumption to be with "Access" group antibiotics by 2023.
- Access, Watch and Reserve antibiotics definitions:
  - *"Access"* antibiotics are antibiotics with a narrow spectrum of activity, generally with less side-effects, a lower potential for the selection of antimicrobial resistance and of lower cost. They are recommended for the empiric treatment of most common infections and should be widely available.
  - *"Watch"* antibiotics generally have a higher potential for the selection of antimicrobial resistance and are more commonly used in sicker patients in the hospital facility setting. Their use should be carefully monitored to avoid overuse.
  - *"Reserve"* antibiotics are last-resort antibiotics that should only be used to treat severe infections caused by multidrug-resistant pathogens.

1.2.3 Red Light antimicrobials

- Currently, prescription of some antimicrobials has been restricted in state sector hospitals of Sri Lanka according to the circular released by Ministry of Health in 2016 on "Red Light" antimicrobials. These are antimicrobials that need authorization by the consultant microbiologist of the hospital prior to prescribing.
- The red-light antimicrobials are aztreonam, cefixime, colistin, daptomycin, fusidic acid, linezolid, moxifloxacin, levofloxacin, tigecycline, anidulafungin, liposomal amphotericin B, posaconazole, voriconazole, cefoperazone-sulbactam and rifampicin (for indications other than TB).
- Ministry of Health, Sri Lanka is in the process of adopting the AWaRe classification of antibiotics replacing the circular on "Red Light Antimicrobials".

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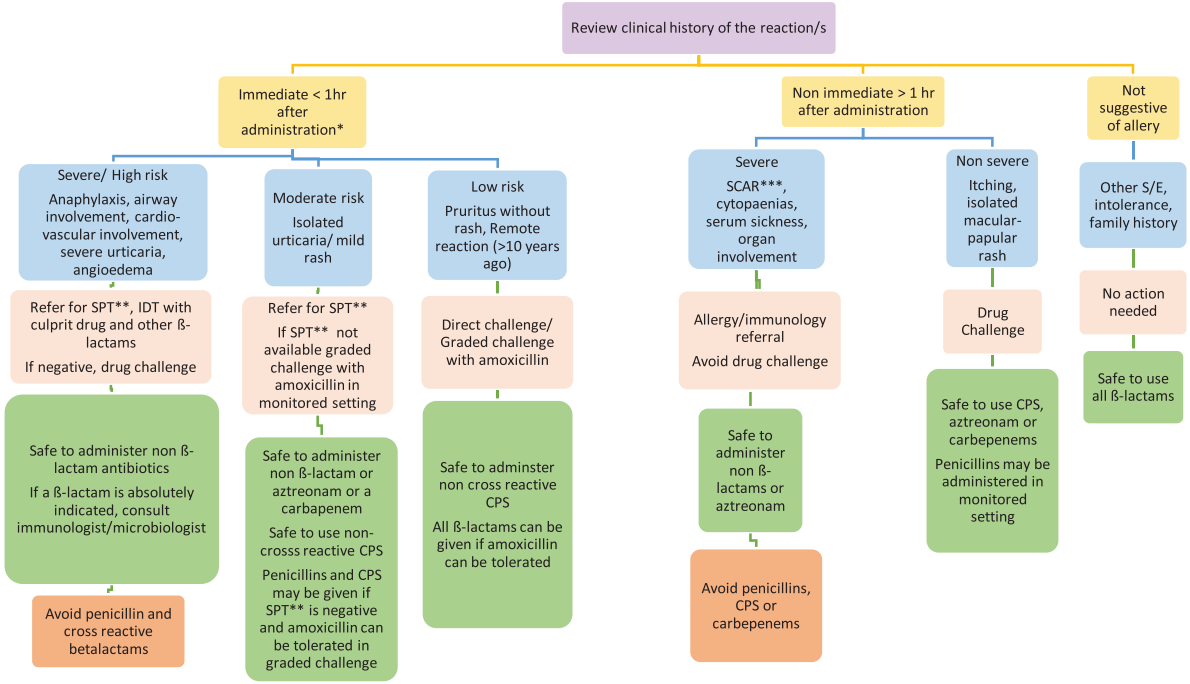
Chapter 2: Prescribing in Patients with a History of Antimicrobial Allergy

- Allergic reactions to antimicrobials are considered off-target, previously classified as type B adverse drug reactions. Antibiotics are reported to be the most common cause for drug induced anaphylaxis, particularly beta-lactams.
- However, allergies to antimicrobials are commonly over-reported; thus, it is important to verify "allergy labels" through proper evaluation of the patient clinically, and/or via immunology referral. Most patients appear erroneously labelled when stratified for risk, tested, and re-challenged**.** Confirmed IgE-mediated penicillin and cephalosporin allergy wanes over time, with 80% of patients being tolerant after a decade.
- Allergy labels result in displacement of first-line therapies for antimicrobial prophylaxis and treatment. They are associated with increased use of broad-spectrum antimicrobials, adverse events, AMR, and increased healthcare costs.
- The underlying mechanisms vary from immunologically mediated hypersensitivities with a memory response which are either immediate IgE mediated (<1 hour) or non-immediate (>1 hour) reactions. Some reactions are non-immunologically mediated due to direct mast cell activation (without IgE), therefore not associated with memory, but have immunological phenotype.
- True IgE mediated and immunological mediated reactions are uncommon with non-beta lactam antibiotics, e.g. anaphylactoid reactions with fluoroquinolones and red man syndrome with vancomycin are due to direct mast cell activation.
- Intravenous administration results in higher risk of immunologically and non-immunologically mediated allergic reactions.
- Estimated cross-reactivity between penicillins and cephalosporins is around 2%. Cross-reactivity could occur amongst cephalosporins with similar side chains; therefore, avoiding re-exposure to the same cephalosporin as well as other cephalosporins and beta-lactams that share similar side chains is important. Cross-reactivity between penicillins and carbapenems is <1%. Monobactams show negligible cross-reactivity with beta-lactams, except ceftazidime that has a similar side chain to aztreonam (refer table 1).
- In a patient with a history of antimicrobial induced anaphylaxis or severe cutaneous adverse reactions (SCAR) (i.e. Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction eosinophilia and systemic symptoms (DRESS) syndrome and acute generalized pustulosis), avoid the use of implicated drug and structurally similar potentially cross-reactive drugs.
- Evaluation of a patient with a history of antimicrobial allergy includes a thorough history, skin prick test (SPT), intradermal test and graded challenge. SPT should be done only in patients with a history of beta-lactam allergy, by an expert, in an appropriate setting, using non-irritant concentrations and interpreted carefully with positive and negative controls.

Figure 1: Risk stratification, recommended action, and treatment options for patients with a history of penicillin allergy



SPT (Skin prick test), IDT (Intra-dermal test), CPS (Cephalosporins)
*Could be delayed up to 6 hours due to slow absorption, metabolism etc
**SPT (Skin prick test)- see the description in the introduction
***SCAR- Severe cutaneous adverse reactions – see the description in introduction

Table 1: Antibacterials with a structurally similar side chain which are potentially cross-reactive

Type	Antibiotic	Cross-reactive antibiotics
penicillin	penicillin	amoxicillin, ampicillin, flucloxacillin, piperacillin, ticarcillin, cephalothin, cefoxitin
	amoxicillin/ ampicillin	penicillin, ampicillin, flucloxacillin, piperacillin, ticarcillin, cefadroxil, cephalexin, cefaclor, cefprozil
	flucloxacillin	penicillin, amoxicillin, ampicillin, piperacillin, ticarcillin
	piperacillin	penicillin, amoxicillin, ampicillin, flucloxacillin, ticarcillin
	ticarcillin	penicillin, amoxicillin, ampicillin, flucloxacillin, piperacillin
1st generation cephalosporins	cefadroxil	amoxicillin, ampicillin, cephalexin, cefaclor, cefprozil
	cephalexin	amoxicillin, ampicillin, cefadroxil, cefaclor, cefprozil
	cephalothin	penicillin, cefoxitin, cefotaxime
2nd generation cephalosporins	cefaclor	amoxicillin, ampicillin, cefadroxil, cephalexin, cefprozil
	cefuroxime	cefoxitin
	cefoxitin	penicillin, cephalothin, cefuroxime
3rd generation cephalosporins	cefotaxime	cephalothin, ceftriaxone, cefepime
	ceftazidime	aztreonam
	ceftriaxone	cefixime, cefotaxime
4th generation cephalosporins	cefepime	cefotaxime, ceftriaxone
carbapenems	meropenem	imipenem, ertapenem
	imipenem	meropenem, ertapenem
	ertapenem	meropenem, imipenem
monobactam	aztreonam	ceftazidime

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Chapter 3: Prescribing in Renal Impairment

- Certain antimicrobials and their metabolites are primarily eliminated by the kidneys. In renal impairment, the pharmacokinetics of these antimicrobials can be significantly altered.
- Reduced renal excretion of an antimicrobial and its metabolites may lead to adverse effects. Antimicrobial doses and dosing intervals need to be adjusted according to the renal function to prevent these adverse effects while maintaining therapeutic efficacy and reducing emergence of antimicrobial resistance.
- Creatinine clearance and eGFR should be used to determine the dose of antimicrobials in renal impairment and electronic calculators are available online for this purpose.

$$CrCl(mL/min) = \frac{(140-age)x\ Ideal\ body\ weight(kg)}{Serum\ Creatinine(mg/dl)x72}$$ x (0.85 if female)

  - **Use actual body weight if less than ideal body weight.**
  - **Use adjusted body weight if actual body weight is >120% of ideal body weight.**
  - **Adjusted body weight = ideal body weight + 0.4 * (actual body weight – ideal body weight).**

- Therapeutic drug monitoring may be necessary to optimize antimicrobial dosing in these patients.
- Some antimicrobials are eliminated during haemodialysis, peritoneal dialysis, and continuous renal replacement therapy (CRRT) etc. Additional dosing may be needed in such situations.
- Antibacterials given in table 2 **do not require** dose adjustment as no significant pharmacokinetic changes have been observed in renal insufficiency.

Table 2: Antibacterials that <u>do not need</u> adjustment in renal impairment

• azithromycin • ceftriaxone • chloramphenicol • clindamycin	• doxycycline • erythromycin • isoniazid • linezolid	• moxifloxacin • pivmecillinam • phenoxymethyl penicillin • rifampicin	• sodium fusidate • quinupristin/ dalfopristin • tigecycline

- For dosages of antimicrobials in adult patients with renal impairment, refer Chapter 7- Table 6.
- For dosage of antimicrobials in children with renal impairment, refer to the latest version of BNF for children.

This chapter has been prepared in collaboration with Sri Lanka Association of Clinical Pharmacology and Therapeutics.

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1. Gilbert DN, Chambers HF, Saag MS, Pavia AT, Boucher HW, editors. The Sanford Guide to Antimicrobial Therapy.52nd ed. Sperryville, Virginia: Antimicrobial Therapy, Inc;2022.
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Chapter 4: Prescribing in Hepatic Impairment

- Liver is responsible for metabolism of some important antimicrobial agents. Therefore, liver disease may influence pharmacokinetics of these antimicrobials.
- Due to its wide array of functions, liver impairment has the potential to affect bioavailability, enterohepatic circulation, distribution, metabolism, clearance, and biliary elimination of medicines.
- Antimicrobials that are highly protein bound, and those cleared via hepatic elimination or biliary excretion require dose adjustments in hepatic impairment. In addition, some antimicrobials can cause significant hepatic toxicity.
- Table 3 lists the antimicrobials in alphabetical order which are excreted/ metabolized by the liver and, therefore, to **be used with caution or avoided if possible or dose adjustment** considered. Please note that the list is dynamic and therefore refer to the latest BNF.

Table 3: Examples of antimicrobials which may need caution in hepatic impairment.

Antibacterials		Antifungals
• clindamycin • chloramphenicol • quinupristin-dalfopristin • rifabutin • rifampicin • nafcillin	• fusidic acid • isoniazid • metronidazole • telithromycin • tigecycline • tinidazole	• anidulafungin • fluconazole • itraconazole • voriconazole

This chapter has been prepared in collaboration with Sri Lanka Association of Clinical Pharmacology and Therapeutics.

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Chapter 5: Prescribing in Pregnancy and Lactation

- Antimicrobials should be prescribed to women during pregnancy only if the expected benefit to the mother is assessed to be greater than the risk to the fetus. It should be avoided, if possible, during the first trimester. Antimicrobials which have been extensively used during pregnancy and appear to be safe should be prescribed in preference to new or untried ones.

Table 4: Safety information on prescribing during pregnancy and lactation for commonly used antimicrobials (BNF; 2022)

Antimicrobial	Pregnancy considerations	Lactation considerations
aciclovir	Not known to be harmful. Manufacturers advise to use only when potential benefit outweighs risk.	Present in milk after systemic administration. Not known to be harmful. Manufacturer advises caution.
amikacin	Avoid - No information available.	Avoid - No information available.
amoxicillin/ ampicillin	Not known to be harmful.	Trace amounts in milk, but appropriate to use.
amoxicillin-clavulanate (co-amoxiclav)	Avoid unless essential. Shown to be associated with an increased risk of necrotising enterocolitis in neonates when given prophylactically to women with premature rupture of membranes.	Trace amounts in milk, but appropriate to use.
ampicillin-sulbactam	Safety is not established. Use only if the potential benefits outweigh the potential risks.	Use only if the potential benefits outweigh the potential risks.

Antimicrobial	Pregnancy considerations	Lactation considerations
azithromycin	Use only if adequate alternatives are not available.	Present in milk, use only if no suitable alternatives.
aztreonam	No information available. Manufacturer advises to avoid.	Amount in milk probably too small to be harmful.
cefepime	Use with caution, no data available, but not known to be harmful in animal studies.	Use with caution, present in milk in very low quantities.
cefixime	Not known to be harmful.	Trace amounts in milk, but appropriate to use.
cefoperazone-sulbactam	Use only if clearly needed.	Use with caution.
cefotaxime	Not known to be harmful.	Trace amounts in milk, but appropriate to use.
cefoxitin	Not known to be harmful.	Trace amounts in milk, but appropriate to use.
ceftazidime	Not known to be harmful.	Present in milk in low concentration, but appropriate to use.
ceftriaxone	Use only if benefit outweighs risk, limited data available.	Trace amounts in milk, but appropriate to use.
cefuroxime	Not known to be harmful.	Trace amounts in milk, but appropriate to use.
cephalexin	Not known to be harmful.	Trace amounts in milk, but appropriate to use.
chloramphenicol	Avoid; neonatal ‘grey baby’ syndrome’ if used in T3.	Avoid; may cause bone-marrow toxicity in infant.

Antimicrobial	Pregnancy considerations	Lactation considerations
ciprofloxacin	A single dose of ciprofloxacin may be used for the prevention of a secondary case of meningococcal meningitis.	Amount too small to be harmful, but manufacturer advises to avoid.
clarithromycin	Avoid; particularly in T1, unless potential benefit outweighs risk.	Avoid unless potential benefit outweighs risk. Present in milk.
clindamycin	Not known to be harmful in T2 and T3; use with caution in T1; limited data.	Present in milk, use with caution. Monitor infant for effects on the GI flora.
flucloxacillin	Not known to be harmful.	Trace amounts in milk, but appropriate to use.
colistin	IV- use only if potential benefit outweighs risk. Inhalation- probably safe.	Avoid or use only if potential benefit outweighs risk.
co-trimoxazole	Teratogenic risk in T1. Neonatal haemolysis and methaemoglobinaemia in T3; fear of increased risk of kernicterus in neonates appears to be unfounded.	Small risk of kernicterus in jaundiced infants and haemolysis in G6PD-deficient infants.
doxycycline	Can be used for malaria prophylaxis when travel to malarious areas is unavoidable if other regimens are unsuitable; and if the entire course can be completed before 15 weeks' gestation.	Present in human milk; insufficient data; compatible for short courses (e.g.10 days). Long-term therapy is not recommended.

Antimicrobial	Pregnancy considerations	Lactation considerations
ertapenem	Avoid unless potential benefit outweighs risk.	Avoid; present in milk.
erythromycin	Not known to be harmful.	Trace amounts in milk, but appropriate to use.
fusidic acid	Use only if potential benefit outweighs risk of using systemically.	Use with caution if using systemically.
fluconazole	Avoid; multiple congenital abnormalities reported with long-term high doses.	Present in milk but amount probably too small to be harmful.
gentamicin	See advise under amikacin.	Present in human milk; compatible.
imipenem-cilastatin	Avoid unless potential benefit outweighs risk (toxicity in animal studies).	Present in milk but unlikely to be absorbed.
levofloxacin	Avoid	Avoid
linezolid	Use only if potential benefit outweighs risk.	Avoid; present in milk in animal studies.
meropenem	Use only if potential benefit outweighs risk, no information available.	Unlikely to be absorbed (however, manufacturer advises to avoid).
metronidazole	Avoid high dose regimens systemically; use only if potential benefit outweighs risk.	With systemic use significant amount in milk; the manufacturer advises avoiding large single doses though otherwise compatible; may give the milk a bitter taste.
nalidixic acid	No controlled studies in humans; use only if potential benefit outweighs risk.	Avoid; haemolytic anaemia has been reported in an infant with G6PD deficiency.
netilmicin	See advise under amikacin.	Insufficient data.

Antimicrobial	Pregnancy considerations	Lactation considerations
nitrofurantoin	Avoid at term; may produce neonatal haemolysis.	Avoid; only small amounts in milk but enough to produce haemolysis in G6PD-deficient infants.
oseltamivir	Although safety data are limited, can be used when the potential benefit outweighs the risk (during a pandemic).	Use if the potential benefit outweighs the risk (during a pandemic).
piperacillin-tazobactam	Use only if potential benefit outweighs risk.	Trace amount in milk, but appropriate to use.
penicillin	Not known to be harmful	Trace amounts in milk, but appropriate to use.
tetracycline	Avoid; effects on skeletal development documented in T1 in animal studies. If used during T2 and T3 may cause discoloration of the child's teeth.	Avoid
teicoplanin	Use only if potential benefit outweighs risk.	No information available.
ticarcillin-clavulanic acid	Not known to be harmful.	Trace amounts in milk, but appropriate to use.
vancomycin	Use only if potential benefit outweighs risk. Vancomycin level monitoring is essential to reduce risk of fetal toxicity.	Present in milk; significant absorption following oral administration is unlikely.

T1/T2/T3 – 1st /2nd /3rd trimester

This chapter has been prepared in collaboration with Sri Lanka Association of Clinical Pharmacology and Therapeutics.

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Chapter 6: Therapeutic Drug Monitoring

- Therapeutic drug monitoring (TDM) is the clinical practice of measuring drug concentrations in plasma at designated intervals to maintain a relatively constant concentration in the blood and site of action thereby optimizing a safe and effective dosing regimen. This is done in special indications.

- Indications for TDM:
    1. When antimicrobials with narrow therapeutic indices are used for treatment e.g. vancomycin, gentamicin
    2. Critically ill patients
    3. Patients with infective endocarditis or bacterial meningitis
    4. During increased volume of distribution e.g. hypoalbuminaemia leading to unbound drug, capillary leakage, fluid resuscitation, third space loss
    5. Decreased clearance e.g. renal and hepatic dysfunction
    6. Increased clearance e.g. augmented renal clearance
    7. Variable changes in volume of distribution and /or clearance e.g. extra corporal interventions (RRT/ ECMO)
    8. When optimal serum levels are important to treat certain infections effectively e.g. MRSA bacteraemia, prosthetic joint infections with MRSA

- Benefits of TDM
    1. To minimize toxicity of antimicrobials that have narrow therapeutic indices
    2. To optimize clinical efficacy of antimicrobials
    3. To reduce antimicrobial resistance
    4. To reduce the cost associated with antimicrobial use

- Limitations
    1. Cost of testing
    2. Non-availability

Table 5: Therapeutic drug monitoring of commonly used antibacterials

Antibacterial	Recommendations
amikacin	For multiple daily dose regimen - Collect peak serum level (PSL) exactly 1 hour after the start of infusion of the 3rd dose. In critically ill patients, PSL after the first dose. Target peak: 15 -30 µg/mL Collect trough 30 minutes prior to 4th dose. Target trough: 5-10 µg/mL. For once daily dose regimen contact microbiologist.
chloramphenicol	Monitor levels in patients who are elderly or with renal and hepatic impairment.
colistimethate/ colistin	Monitoring the trough and peak levels may be useful.
daptomycin	Monitor creatine phosphokinase levels, muscle pain or weakness. Stop concomitant statin therapy. Therapeutic drug monitoring (TDM) may be beneficial.
gentamicin	For multiple daily dose regimen- Collect PSL exactly 1 hour after the start of infusion of the 3rd dose. In critically ill patients PSL after the first dose. Target peak: 4-10 µg/mL. Collect trough 30 minutes prior to the 4th dose. Target trough: 1-2 µg/mL. For once daily dose regimen contact microbiologist.
netilmicin	Collect PSL exactly 1 hour after the start of infusion of the 3rd dose. In critically ill patients PSL after the first dose. Target peak: 22-30 µg/mL Collect blood for trough level 30 minutes prior to the 4th dose. Target trough: <1µg/mL For once daily dose regimen contact microbiologist.
teicoplanin	Measure serum levels if treatment exceeds 14 days. The preferred method of monitoring is AUC24 which is calculated based on measured peak serum and trough levels. Target AUC24: 500-600ug/ml x hr
tobramycin	Collect PSL exactly 1 hour after the start of infusion of 3rd dose. In critically ill patients PSL after the first dose.
vancomycin	Measure the trough level on the second day of treatment just before the next dose. Target trough level 10-20mg/L which can vary depending on the site of infection and the susceptibility of the pathogen.

This chapter has been prepared in collaboration with Sri Lanka Association of Clinical Pharmacology and Therapeutics.

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Chapter 7: Administration of Antimicrobials

- Successful treatment of an infection depends on efficacious and safe antimicrobial agents reaching the site of action in adequate concentrations and maintaining a consistent steady state concentration.
- All antimicrobials should be administered according to the manufacturer's instructions (given in the product leaflet).
- Certain antimicrobials (e.g. vancomycin, amphotericin B) should be given as slow infusions to minimize adverse reactions.
- Prolonged infusion (continuous or extended) of beta-lactams is recommended to increase time above MIC (reduction of bacterial burden is best predicted by t > MIC) in order to improve patient outcome. However, stability of the antimicrobials based on the environmental temperature must be considered. (e.g. meropenem and piperacillin-tazobactam over 3-4 hour infusions in critically ill patients).
- Doses mentioned in this guideline are for immunocompetent adults with normal renal and liver functions unless otherwise specified.
- Doses should be calculated according to the patient's actual body weight, unless otherwise specified.
- Ideal body weight (BW) or adjusted body weight are used in patients at extremes of body weights.
- Ideal BW calculation:
    - For males- 50kg+0.9kg per each cm over 152cm (2.3kg per each inch over 5 feet)
    - For females- 45.5 kg+0.9kg per each cm over 152cm (2.3kg per each inch over 5 feet)
- Adjusted BW = Ideal BW + 0.4 * (Actual BW-Ideal BW)
- Refer the relevant chapters for specific doses as the doses may vary according to the site and severity of infection. (e.g. meningitis and endocarditis).
- Table 6,7 and 8 describe the important aspects of administration of commonly used antimicrobials in Sri Lanka.

Table 6: Administration of commonly used antibacterial agents

Antibacterial	Normal adult dose and frequency	Dose adjustment for renal failure (CrCl ml/min)			Dose and frequency in peritoneal dialysis (CAPD)	Dose and frequency in haemodialysis	Dose in CRRT
		>50	10-50	<10			
amikacin IV/IM	15mg/kg[a] q24h 30-60min infusion[b] (maximum 1.5g/day; maximum cumulative dose 15g)	7.5mg/kg q12h	7.5mg/kg q24h	7.5mg/kg q48h	No data	7.5mg/kg q48h + 3.75mg/kg AD	7.5mg/kg q24h
amoxicillin PO	500mg-1g q8h (maximum 6g/day)	No adjustment	250-500mg q12h	250-500mg q24h	250-500mg q12h	250-500mg q24h AD	250-500mg q8-12h
ampicillin IV	1-2g q4-6h 10-15 min infusion[b] (maximum 12g/day)	1-2g q4-6h	1-2g q6-12h	1-2g q12h	500mg-1g q12h	1-2g q12h AD	1-2g q8-12h

Antibacterial	Normal adult dose and frequency	Dose adjustment for renal failure (CrCl ml/min)			Dose and frequency in peritoneal dialysis (CAPD)	Dose and frequency in haemodialysis	Dose in CRRT
		>50	10-50	<10			
azithromycin PO	500mg q24h	No adjustment	No adjustment	No adjustment	No adjustment	No adjustment	No adjustment
benzylpenicillin IV/IM (1MU=600mg)	0.5-4MU q4h 15-30 min infusion[b]	No adjustment	0.5-4MU q8h	0.5- 4 MU q12h	0.5-4MU q12h	0.5-4MU q12h AD on dialysis days	No adjustment
cefalexin PO	500mg q8-12h In severe infections: 1-1.5g q6-8h	No adjustment	250-500mg q8-12h	250-500mg q24-48h	250-500mg q12-24h	250-500mg q12-24h AD on dialysis days	No data
cefoperazone-sulbactam IV	2g (1g/1g) q12h 15-60min infusion[b] In severe infections: 4g (2 g/2 g) q12h	1g q12h	1g q12h	500mg q12h	No data	No data	No data

Antibacterial	Normal adult dose and frequency	Dose adjustment for renal failure (CrCl ml/min)			Dose and frequency in peritoneal dialysis (CAPD)	Dose and frequency in haemodialysis	Dose in CRRT
		>50	10-50	<10			
cefotaxime IV/IM	1-2g q8h 20-60 min infusion[b]	1-2g q8-12h	2g q12-24h	2g q24h	0.5-1g q24h	2g q24h + extra 1g AD	2g q12-24h
ceftriaxone IV/IM	1-2g q24h 30 min infusion [b]	No adjustment	No adjustment	No adjustment	No adjustment	No adjustment	No adjustment
ceftazidime IV	1-2g q8-12h 15-30 min infusion [b]	1-2g q8-12h	1-2g q12-24h	1-2g q24h	1.5–2g intraperitoneal q24–48h	0.5–1g q24h AD	1-2g q8-12h
cefuroxime PO	250-500mg q12h	No adjustment	500mg q24h	500mg q48h	500mg q24h	500mg q48h	No data
cefuroxime IV/IM	750mg-1.5g q6-8h over 30 min infusion[b]	No adjustment	750mg-1.5g q8-12h	750mg-1.5g q24h	750mg-1.5g q24h	750mg-1.5g q24h AD on dialysis days	750mg-1.5g q8-12h

Antibacterial	Normal adult dose and frequency	Dose adjustment for renal failure (CrCl ml/min)			Dose and frequency in peritoneal dialysis (CAPD)	Dose and frequency in haemodialysis	Dose in CRRT
		>50	10-50	<10			
ciprofloxacin PO	500-750mg q12h	No adjustment	250-500mg q12h	500-750mg q24h	250-500mg q24h	250-500mg q24h AD on dialysis days	250-500mg q12h
ciprofloxacin IV	200-400mg q8-12h over 60 min infusion[b]	200-400mg q8-12h	200-400mg q8-12h	200- 400mg q8-12h	200- 400mg q24h	200- 400mg q24h AD	200- 400mg q12h
clarithromycin PO/IV	500mg q12h over 60 min infusion[b]	No adjustment	500mg q12-24h	500mg q24h	500mg q24h	500mg q24h AD on dialysis days	500mg q12-24h
clindamycin PO	150-450mg q6-8h	No adjustment	No adjustment	No adjustment	No adjustment	No adjustment	No adjustment
clindamycin IV/IM	300-900mg q6-8h 10-60 min infusion[b]	No adjustment	No adjustment	No adjustment	No adjustment	No adjustment	No Adjustment

Antibacterial	Normal adult dose and frequency	Dose adjustment for renal failure (CrCl ml/min)			Dose and frequency in peritoneal dialysis (CAPD)	Dose and frequency in haemodialysis	Dose in CRRT
		>50	10-50	<10			
co-trimoxazole PO	960mg q12h	960mg q12h	480mg q12h	Not recommended	Not recommended	Not recommended	480mg q8h
co-amoxiclav IV	1.2g q8h 30 - 40 min Infusion[b]	No adjustment	1.2g 1st dose then 0.6g q12h	1.2g 1st dose then 0.6g q24h	No data	1.2g 1st dose then 0.6g q24h AD	No data
co-amoxiclav PO	625mg q8h	No adjustment	250-500mg q12h	250-500mg q24h	No data	250-500mg q24h AD	No data
doxycycline PO	100mg q12h	No adjustment	No adjustment	No adjustment	No adjustment	No adjustment	No adjustment
ertapenem IV	1g q24h 30 min infusion [b]	1g q24h	500mg-1g q24h	500mg q24h	500mg q24h	500mg q24h + extra 150mg AD	0.5-1g Daily
erythromycin PO	500mg q6h or 500mg-1g q12h	No adjustment	No adjustment	No adjustment	No adjustment	No adjustment	No adjustment

Antibacterial	Normal adult dose and frequency	Dose adjustment for renal failure (CrCl ml/min)			Dose and frequency in peritoneal dialysis (CAPD)	Dose and frequency in haemodialysis	Dose in CRRT
		>50	10-50	<10			
flucloxacillin PO	500mg-1g q6h	No adjustment	No adjustment	250-500mg q6h	No adjustment	No adjustment	No adjustment
flucloxacillin IV/IM	IV: 500mg-1g q6h over 30 min infusion[b] up to 2g q6h in severe infections IM: 500mg q6h	No adjustment	No adjustment	250-500mg q6h	No adjustment	No adjustment	No adjustment
gentamicin IV	5mg/kg[a] q24h 30-120 min infusion[b] (maximum 500mg/dose)	3.5-5mg/kg q24h	3-4mg/kg q48h	2mg/kg q72h	No data	1.7-2mg/kg q24h +1mg/kg AD	1.7-2mg/kg q24h
imipenem/ cilastatin IV	500mg q6h or 1g q8h 20-60min infusion [2]	500mg q6h	500mg q8-12h	Not recommend-ed	125-250mg q12h	500mg q12h AD	500mg-1g q12h

Antibacterial	Normal adult dose and frequency	Dose adjustment for renal failure (CrCl ml/min)			Dose and frequency in peritoneal dialysis (CAPD)	Dose and frequency in haemodialysis	Dose in CRRT
		>50	10-50	<10			
meropenem IV	500mg–1g q8h 30 min infusion[b]	No adjustment	500mg-1g q12h	500mg q24h	500mg q24h	500mg q24h AD	1g q12h
metronidazole PO/IV	PO 400mg q8h IV 500mg q8h 30 min infusion	No adjustment	No adjustment	PO 400mg q12h IV 500mg q12h	PO 400mg q12h IV 500mg q12h	PO 400mg q12h IV 500mg q12h AD	PO 400mg q8h IV 500mg q8h
netilmicin IV	6.5mg/kg[a] q24h or 1.7-2mg/kg q8h	1.7-2 mg/kg q8h	1.7-2 mg/kg q12-24h	1.7-2 mg/kg q48h	No data	1.7-2mg/kg q48h + extra 1mg/kg AD	1.7-2mg/kg q12-24h
nitrofurantoin PO	100mg q6h	No adjustment	Not recommended	Not recommended	Not recommended	Not recommended	Not recommended
norfloxacin PO	400mg q12h	No adjustment	No adjustment till CrCl<30	CrCl<30: 400mg q24h	400mg q24h	400mg q24h	Not applicable

Antibacterial	Normal adult dose and frequency	Dose adjustment for renal failure (CrCl ml/min)			Dose and frequency in peritoneal dialysis (CAPD)	Dose and frequency in haemodialysis	Dose in CRRT
		>50	10-50	<10			
pivmecillinam PO	400mg q12h	No adjustment	No adjustment	No adjustment	No adjustment	No adjustment	No adjustment
phenoxymethyl penicillin (penicillin V) PO	500mg-1g q6h	No adjustment	No adjustment	No adjustment	No adjustment	No adjustment AD	No data
piperacillin-tazobactam IV	4.5g q6-8h 30-240 min infusion [b]	4.5g q6-8h	2.25g q6h	2.25g q6h	2.25g q8h	2.25g q8h + extra 0.75g AD	2.25g q6h
sodium fusidate PO	500mg-1g q8h	No adjustment	No adjustment	No adjustment	No adjustment	No adjustment	No adjustment
teicoplanin IV/IM	400mg q12h for 3 loading doses then 400mg q24h	CrCl 80-30 Load as usual then 400mg q48h		CrCl <30 Load as usual then 400mg q72h		Load as usual then 6mg/kg q72h	Load as usual then 6mg/kg q48h

Antibacterial	Normal adult dose and frequency	Dose adjustment for renal failure (CrCl ml/min)			Dose and frequency in peritoneal dialysis (CAPD)	Dose and frequency in haemodialysis	Dose in CRRT
		>50	10-50	<10			
vancomycin[c] IV	Loading dose to be infused at rate of 10-15mg/min (maximum 3g) <60kg:1g 60-85kg: 1.5g >85kg: 2g Maintenance dose 15mg/kg (max 2g per dose) q12h 60 min infusion[b]	No adjustment	CrCl: 20-49 15mg/kg q24h CrCl: <20 15mg/kg q48h		7.5mg/kg q48-96h	Contact microbiologist	7.5-10 mg/kg q12h with effluent rate 20-25 ml/kg/hr

[a] Use adjusted body weight in obesity; [b] refer the manufacturer's leaflet for specific instructions. Beta-lactams may be given as slow boluses or as extended/prolonged infusion in specific indications; [c] Use actual body weight including in obese patients;
AD – dose after dialysis; frequency: q24h – every 24 hours; q12h – every 12 hours; q6-8h – every 6-8 hours. q12-24h – every 12 to 24 hours.

Table 7: Administration of commonly used antifungal agents

Antifungal	Normal adult dose and frequency	Dose adjustment for renal failure (CrCl ml/min)			Dose and frequency in peritoneal dialysis (CAPD)	Dose and frequency in haemodialysis	Dose in CRRT
		>50	10-50	<10			
fluconazole PO	100-400mg q24h	100-400mg q24h	50-200mg q24h	50-200mg q24h	50-200mg q24h	50-200mg q24h on non-dialysis days 100-400mg q24h AD on dialysis days	200-400mg q24h
fluconazole IV	12mg/kg loading dose, followed by 6mg/kg q24h	200-400mg q24h	100-200mg q24h	100-200mg q24h	100-200mg q24h	100-200mg q24h	100-200mg q24h

Table 8: Administration of commonly used antiviral agents

Antiviral	Normal adult dose and frequency	Dose adjustment for renal failure (CrCl ml/min)			Dose and frequency in peritoneal dialysis (CAPD)	Dose and frequency in haemodialysis
acilovir PO Use adjusted body weight in obesity.	1. Varicella zoster and Herpes zoster **Treatment**: 800mg 5 times a day **Prophylaxis for Varicella zoster –** contact microbiologist/virologist 2. Genital Herpes Simplex (first episode) 400mg q8h	**CrCl >25:** 800mg 5 times a day 400mg q8h	**CrCl =10-25:** 800mg q8h 400mg q8h	**CrCl <10:** 800mg q12h 200mg q8h	800 mg q12h 200mg q8h	800 mg q12h Give extra dose AD 200mg q8h Give extra dose AD
aciclovir IV Use adjusted body weight in obesity.	10mg/kg q8h 60 min infusion[b]	**CrCl >50:** 10mg/kg q8h	**CrCl =25-50:** 10mg/kg q12h **CrCl =10-25:** 10mg/kg q24h	**CrCl <10:** 5mg/kg q24h	5mg/kg q24h	5mg/kg q24h give extra dose AD

Antiviral	Normal adult dose and frequency	Dose adjustment for renal failure (CrCl ml/min)			Dose and frequency in peritoneal dialysis (CAPD)	Dose and frequency in haemodialysis
ganciclovir IV	**Induction**: 5mg/kg q12h	**Induction:** **CrCl 70-90:** 5mg/kg q12h **CrCl 50-69:** 2.5mg/kg q12h	**Induction:** **CrCl 25-49:** 2.5mg/kg q24h **CrCl 10-24:** 1.25mg/kg q24h	**Induction:** **CrCl <10:** 1.25mg/kg 3 times per week	**Induction:** 1.25mg/kg 3 times per week	**Induction**: 1.25mg/kg 3 times per week following haemodialysis.
	Maintenance 5mg/kg q24h 60 min infusion[b]	**Maintenance** **Crcl 50-90:** 2.5mg/kg q24h	**Maintenance** **CrCl 25-49:** 1.25mg/kg q24h **CrCl 10-24:** 0.625mg/kg q24h	**Maintenance** **CrCl <10:** 0.625mg/kg 3 times per week	**Maintenance** 0.625mg/kg 3 times per week	**Maintenance:** 0.625mg/kg 3 times per week following haemodialysis

Antiviral	Normal adult dose and frequency	Dose adjustment for renal failure (CrCl ml/min)			Dose and frequency in peritoneal dialysis (CAPD)	Dose and frequency in haemodialysis
valganciclovir PO	**Treatment** 900mg q12h **Prophylaxis** 900mg q24h	**CrCl >40:** **Treatment** 900mg q12h **Prophylaxis** 900mg q24h	**CrCl =10-24:** **Treatment** 450mg once in 2 days **Prophylaxis** 450mg 2 times per week **CrCl 25-39:** **Treatment** 450mg q24h **Prophylaxis** 450mg once in 2 days	**CrCl <10:** Not recommended	No data	Not recommended

Antiviral	Normal adult dose and frequency	Dose adjustment for renal failure (CrCl ml/min)			Dose and frequency in peritoneal dialysis (CAPD)	Dose and frequency in haemodialysis
oseltamivir PO	**Treatment** 75mg q12h for 5days	**CrCl >60:** No dose adjustment necessary	**Treatment CrCl 30-60:** 30mg q12h **CrCl 11-30:** 30mg q24h	**Treatment** ESRD-see under haemodialysis, peritoneal dialysis.	**Treatment** An initial 30mg dose can be administered prior to the start of dialysis. A single 30mg dose administered immediately after a dialysis exchange.	**Treatment** 30mg immediately and then 30mg after every haemodialysis cycle; treatment not to exceed 5 days.

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Chapter 8: Outpatient Parenteral Antimicrobial Therapy (OPAT)

- Outpatient parenteral antimicrobial therapy (OPAT) is useful for carefully selected patients in whom other aspects of care can be addressed without hospitalization.
- It has been shown to be safe and effective for a wide range of infections in adults and children.
- Outpatient parenteral antimicrobial therapy is useful especially in infections where prolonged parenteral antimicrobial treatment is indicated (e.g. infective endocarditis, bone and joint infections).
- Potential benefits to the healthcare system include shorter or avoided hospital stays, reduction of hospital-associated infections and significant cost savings. It is a routine part of care in several countries around the world.
- Always discuss with the consultant microbiologist before implementation of OPAT.
- Proper monitoring of OPAT is essential to ensure the best clinical outcomes and reduce the chances of unintended complications.
- There are several issues to consider when selecting antimicrobials for OPAT. The regimen should be clinically effective, safe, relatively easy to administer, and affordable.

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Chapter 9: Spectrum of Commonly Used Antibacterials

- In vivo activity of antibacterial agents against bacterial pathogens is determined by several factors such as inherent or acquired resistance, poor drug penetration to the site of infection, etc.
- Table 9 lists selected antibacterials categorized according to the spectrum of activity as follows.
    1. Antipseudomonal antibacterials
    2. Antibacterials with anaerobic activity
    3. Antibacterials which act only against Gram negative bacteria
    4. Antibacterials which act only against Gram positive bacteria

Table 9: Examples of antibacterials with their effectiveness against selective groups of pathogenic bacteria.

Antipseudomonal antibacterials	Antibacterials which act only against Gram-negative bacteria	Antibacterials which act only against Gram-positive bacteria	Antibacterials which are effective against anaerobes
amikacin	aztreonam	clindamycin	amoxicillin/ampicillin
aztreonam	mecillinam	daptomycin	clindamycin
ceftazidime	nalidixic acid	flucloxacillin	co-amoxiclav
cefepime	polymyxin B	fusidic acid	doxycycline
ciprofloxacin	polymyxin E (colistin)	linezolid	imipenem
			meropenem
gentamicin		quinupristin-dalfopristin	metronidazole
imipenem		teicoplanin	penicillin
meropenem		vancomycin	piperacillin-tazobactam
piperacillin-tazobactam			ticarcillin-clavulanic acid
polymyxin B			teicoplanin
polymyxin E			tigecycline
ticarcillin-clavulanic acid			vancomycin

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SECTION B

Chapter 10: Bacterial Endocarditis

- For acutely ill patients, empirical therapy should be commenced after obtaining at least three blood cultures taken at 30-minute intervals from three different venipuncture sites, using an aseptic technique.
- In patients without acute symptoms, best to defer antimicrobial therapy, until blood cultures are taken or results available.
- Surgical specimens (vegetations, cardiac valves, cardiac implantable electronic devices, vegetations on leads, emboli, aspirated pus) should be sent for culture and ABST.
- When the cultures become positive, antibiotics and doses should be adjusted according to the minimum inhibitory concentration (MIC) of the antibiotic of the isolated organism.
- Defervescence might take 5-10 days despite appropriate antibiotic therapy.

Table 10: Empirical antimicrobial therapy for bacterial endocarditis

Condition	Primary therapy	Alternative therapy / Immediate beta-lactam hypersensitivity[1] / High risk for MRSA	Comment
Native valve endocarditis or late prosthetic valve (≥12 months post-surgery) endocarditis	ceftriaxone 2g IV q24h + gentamicin[2] 3mg/kg/day IV q24h or in 3 equally divided doses or ampicillin 2g IV q4h + gentamicin[2] 3mg/kg/day IV q24h or in 3 equally divided doses	vancomycin[3] 30mg/kg/day IV in 2 equally divided doses +/- gentamicin[2] 3mg/kg/day IV q24h or in 3 equally divided doses	Discuss with the microbiologist for organism-specific therapy and duration. If the patient is acutely ill, add flucloxacillin to ampicillin and gentamicin combination.
Native valve right sided endocarditis or endocarditis in IV illicit drug users	flucloxacillin 2g IV q4h	vancomycin[3] 30mg/kg/day IV in 2 equally divided doses	Contact microbiologist.

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]/ High risk for MRSA	Comment
Early prosthetic valve endocarditis (≤ 12 months post-surgery endocarditis) or healthcare-associated endocarditis	vancomycin[3] 30mg/kg/day IV in 2 equally divided doses + gentamicin[2] 3mg/kg/day IV q24h or in 3 equally divided doses	Contact microbiologist	Contact microbiologist. Early surgical consultation is required. If staphylococcal infection is suspected in prosthetic valves, rifampicin to be added after 3-5 days of starting vancomycin and gentamicin. **Rifampicin is a "Reserve Category" antibiotic** (Annex 01).
Cardiac Implantable Electronic Devices related endocarditis (CIED related Endocarditis) CIED endocarditis includes vegetation on leads and/or valves, embolism or systemic infection.	vancomycin[3] 30mg/kg/day IV in 2 equally divided doses + gentamicin[2] 3mg/kg/day IV q24h or in 3 equally divided doses	Contact microbiologist	Contact microbiologist. Definitive treatment of CIED infection is early and complete extraction of all parts of the system; antibiotic therapy is to be considered as a complement to treat associated systemic infection and to cure the remaining infection in native tissues. Device / tissue should be sent for culture in addition to blood culture.

Table 11: Antibacterials for endocarditis in children – doses, route, frequency

Antibiotic	Route, dose & frequency (refer BNF-C for details)
ampicillin	IV 200-300mg/kg/day q4-6h
ceftriaxone	IV 100mg/kg q24h
flucloxacillin	IV 200-300mg/kg/day q4-6h
gentamicin	IV 3mg/kg/day q8h
vancomycin	IV 40mg/kg/day q8-12h

Prepared in collaboration with Sri Lanka College of Cardiologists.

[1]Refer chapter 2.
[2]TDM is recommended (refer chapter 6). Monitor renal functions and adjust doses (refer chapter 7). Vestibular function should be assessed when continued for more than 5 days. Gentamicin when given in single daily dose, aim for a trough concentration of <1mg/L and peak levels of 10-12mg/L.
[3]TDM is recommended (refer chapter 6). Monitor renal functions and adjust doses (refer chapter 7).
Please note that serum vancomycin concentrations should achieve 10-15mg/L at pre dose (trough) level. Although some experts recommend to increase the dose of vancomycin to 45-60mg/kg/day intravenously in 2 or 3 divided doses to reach serum trough vancomycin levels (Cmin) of 15-20mg/L as in staphylococcal endocarditis, vancomycin dose should not exceed 2g/d unless serum levels are monitored and can be adjusted to obtain a peak plasma concentration of 30-45µg/ml 1 hour after completion of the intravenous infusion of the antibiotic.

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Chapter 11: Bone and Joint Infections

- In all cases of suspected acute bone and joint infections including acute septic arthritis and acute osteomyelitis, blood cultures should be obtained before commencing empirical antimicrobial therapy.
- In patients with bone and joint infections, joint aspirates and tissue/bone specimens should be collected for culture and ABST.
- In patients with chronic osteomyelitis and prosthetic joint infections without features of sepsis or acute skin and soft tissue infection (SSTI), empirical antibiotic therapy should be delayed until specimens are collected. Multiple intra-operative samples should be taken in suspected prosthetic joint infections.
- Empirical antimicrobial therapy should be reviewed according to susceptibility test results.
- Fungal and mycobacterial cultures should be arranged if clinical history, epidemiological factors, host risk factors or radiological clues suggest these organisms.

Table 12: Empirical antimicrobial therapy for bone and joint infections

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Acute septic arthritis in adults (native joints)	flucloxacillin 50mg/kg IV q6h (maximum 2g q6h) **If high risk of MRSA** vancomycin[3] 25–30 mg/kg IV loading dose followed by 15–20 mg/kg/dose IV q12h **If high risk of infection with a Gram-negative organism add** cefotaxime 2g IV q8h / ceftriaxone 2g IV q24h	clindamycin[4] 600mg IV q6h or vancomycin[3] 25–30 mg/kg IV loading dose followed by 15–20 mg/kg/dose IV q12h or teicoplanin 10mg/kg/dose IV q12h for 3 doses followed by 10mg/kg/dose IV q24h **Adults with high risk of infection with a Gram-negative organism and immediate beta lactam hypersensitivity[1] add** ciprofloxacin 400mg IV q12h	Septic joints should be aspirated to dryness / may require wash out in addition to antibiotics. Initial empirical therapy should ideally be guided by Gram stain results. Risk factors for Gram negative infection includes frailty and old age, recurrent UTI, end stage renal failure, recent abdominal surgery etc. Renal function should be monitored with vancomycin. Total 4 weeks of antibiotics with minimum 2 weeks of intravenous antibiotic is generally recommended. A shorter duration may be considered depending on the organism isolated and clinical response. Contact microbiologist.

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Acute osteomyelitis in adults	flucloxacillin 50mg/kg/dose IV q6h (max 2g q6h) **If high risk of MRSA** vancomycin[3] 25–30 mg/kg IV loading dose followed by 15–20 mg/kg/dose IV q12h **If an infection with a Gram-negative organism is suspected add** cefotaxime 2g IV q8h/ ceftriaxone 2g IV q24h	clindamycin[4] 600mg IV q6-8h or vancomycin[3] 25–30 mg/kg IV loading dose followed by 15–20 mg/kg/dose IV q12h or teicoplanin 10mg/kg/dose IV q12h for 3 doses followed by 10mg/kg/dose IV q24h	Monitor LFT with prolonged (> 2 weeks) flucloxacillin therapy. Haematogenous acute osteomyelitis usually needs empirical antibiotic coverage for MRSA. Acute vertebral osteomyelitis can be caused by *S. aureus* including MRSA, *Mycobacterium tuberculosis*, Gram-negative bacilli and streptococci. Risk factors for Gram negative infection include frailty and old age, recurrent UTI, end stage renal failure, recent abdominal surgery etc. For transition from intravenous to oral therapy and duration of therapy, contact microbiologist.

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Chronic osteomyelitis	See comments		**Empirical treatment is not indicated.** Obtain biopsy for culture before commencing antimicrobials. Antimicrobial therapy should be guided by susceptibility patterns of culture isolates. Antimicrobial therapy alone is not sufficient without surgical intervention. Contact microbiologist for duration of treatment.
Prosthetic joint infection	See comments		**Empirical treatment is not indicated.** Withholding antimicrobials for 2 weeks prior to aspiration/ biopsy improves isolation of the pathogen. In cases of acute infection or if the patient is systemically unwell, arrange a blood culture. Contact microbiologist. Multiple intraoperative samples taken using separate instruments for separate sites should be sent for microbiology and histology.

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Suspected Gonococcal or Meningococcal septic arthritis (peripheral joints)	ceftriaxone 2g IV q24h/ cefotaxime 1g IV q8h	ciprofloxacin 400mg IV q12h	Duration: 10-14 days
Diabetic foot infections complicated with osteomyelitis • Mild to moderate infections	clindamycin[4] 600mg IV q6h + ciprofloxacin 750mg PO q12h		Contact microbiologist if the patient is in sepsis, with a high risk for MRSA or with a history of beta-lactam allergy.
• Severe infection with osteomyelitis and systemic sepsis	ticarcillin-clavulanic acid 3.2g IV q8h or piperacillin-tazobactam 4.5g IV q6-8h or meropenem 1g IV q8h		

Prepared in collaboration with the Association of Orthopaedic Surgeons.

[1]Refer chapter 2.
[3]TDM is recommended (refer chapter 6). Monitor renal functions and adjust doses (refer chapter 7).
[4]For administration of clindamycin, refer chapter 7.

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- Blood cultures should be collected in suspected bacterial meningitis as early as possible before starting empirical antimicrobials.
- Cerebrospinal fluid (CSF) specimens should be sent for culture and other relevant investigations whenever possible prior to starting antimicrobials. However, antimicrobial therapy should not be delayed until CSF collection or availability of CSF investigation results.
- Neuroimaging is not mandatory before lumbar puncture unless there is low GCS, presence of focal neurological signs or features of raised intracranial pressure.
- Empirical antimicrobial therapy should be started according to age, clinical history and risk factors.
- Table 13 includes the empirical antibiotic choices for CNS infections. Antibiotics should be administered through intravenous route. Refer table 15 for doses and dosing frequency.
- Refer table 14 for antibiotic duration for specific pathogens. If no organism is isolated, a minimum of 10 days of antibiotics are required.

Table 13: Empirical antimicrobial therapy for central nervous system infections

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Community acquired acute bacterial meningitis	ceftriaxone/cefotaxime +/- vancomycin[3]	chloramphenicol +/- vancomycin[3]	Adjunctive dexamethasone therapy is recommended. (Dexamethasone IV 8-10mg (child:0.15mg/kg up to 10mg), starting before or with the first dose of antibiotic, then 6 hourly for 2-4 days). Antibiotic therapy should not be delayed if corticosteroids are not available. Ceftriaxone is preferred over cefotaxime due to lower frequency of administration. Vancomycin should be added when there is a high possibility of pneumococcal meningitis in a critically ill patient with poor response to ceftriaxone/ cefotaxime. Ampicillin should be considered when there is a risk of Listeria meningitis in elderly or immunocompromised patients.

Condition	Primary therapy	Alternative therapy / immediate beta-lactam hypersensitivity[1]	Comments
Immunocompromised patients e.g. severe neutropenia, chronic illnesses, HIV	ampicillin + cefotaxime /ceftriaxone + vancomycin[3]	chloramphenicol + vancomycin[3]	In HIV/AIDS patients, consider the possibility of Cryptococcal meningitis. Contact microbiologist.
Base of skull fracture with CSF leakage	cefotaxime /ceftriaxone +/- vancomycin[3]	chloramphenicol + vancomycin[3]	Routine antibiotic prophylaxis is not recommended for basilar skull fracture with CSF leakage. Consider pneumococcal vaccine.
Healthcare associated meningitis and ventriculitis e.g. penetrating trauma, post-neurosurgery, CSF shunt infections	vancomycin[3] + ceftazidime/ cefepime/ meropenem	vancomycin[3] + ciprofloxacin	Removal of infected shunt with appropriate antimicrobial therapy is the most effective treatment. Intrathecal/intraventricular therapy may be indicated in certain circumstances. Contact microbiologist.
Chronic meningitis	Treatment depends on the causative organism No urgent need for empirical therapy		Contact microbiologist for special investigations and treatment.

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Meningoencephalitis when there is evidence of focal or diffuse neuropsychological dysfunction with meningitis	aciclovir + antibiotic/s according to the age group and risk factors		Aciclovir should be withdrawn if there is: • Strong evidence for bacterial meningitis on CSF analysis • No evidence of HSV encephalitis in EEG/MRI • Negative CSF HSV PCR
Brain abscess **Subdural empyema** **Cranial epidural abscess** **Spinal epidural abscess**	vancomycin[3] + cefotaxime/ ceftriaxone/ ceftazidime/ cefepime + metronidazole	vancomycin[3] + ciprofloxacin + metronidazole	Adequate source control is necessary. It is mandatory to send specimens collected during surgery/ guided aspiration for culture & ABST. Contact microbiologist regarding sample collection and transport prior to intervention. The appropriate duration of antibiotic treatment depends on the susceptibility of the organism, size of the abscess, adequacy of surgical drainage and patient's response as determined clinically and by serial CT scans. • If surgical intervention is carried out – IV antibiotics for 3-4 weeks and if not carried out – IV antibiotics for 6-8 weeks • Longer durations recommended in immunocompromised/ accompanying osteomyelitis

Table 14: Duration of antibiotic treatment for specific pathogens in acute community acquired bacterial meningitis

Microorganism	Duration (days)
Streptococcus pneumoniae	10-14
Haemophilus influenzae	7-10
Neisseria meningitidis	7
Group B *Streptococcus*	14-21
Listeria monocytogenes, Escherichia coli and other coliforms	21 Longer duration in immunocompromised patients.
Staphylococcus aureus/ Staphylococcus epidermidis	14-28

(If no pathogen is isolated, continue the empirical regimen for a minimum of 10 days depending on the response)

Table 15: Doses, route, and frequency of antibiotics for central nervous system infections

Antibiotic	Dose
ampicillin	2g IV q4h
acyclovir	10mg/kg IV q8h
cefepime	2g IV q8h
cefotaxime	2g IV q4-6h
ceftazidime	2g IV q8h
ceftriaxone	2g IV q12h
chloramphenicol	12.5mg-25mg/kg IV q6h If a high dose is used, reduce the dose as soon as clinical improvement is noted
ciprofloxacin	400mg IV q8h
meropenem	2g IV q8h
metronidazole	500mg IV q8h
vancomycin	15mg/kg IV q8h

Prepared in collaboration with Ceylon College of Physicians, Sri Lanka College of Internal Medicine and Association of Sri Lankan Neurologists

[1]Refer chapter 2.
[3]TDM is recommended (refer chapter 6). Monitor renal functions and adjust doses (refer chapter 7).

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Chapter 13: Diarrhoea

- Diarrhoea is defined as passage of 3 or more loose or liquid stools per 24 hours, or more frequently than is normal for an individual person.
- Diarrhoea is commonly caused by viruses. Most bacterial diarrhoeal diseases are self-limiting and usually do not require antimicrobials.
- In immunocompromised people with severe illness and bloody diarrhoea empirical antimicrobial therapy should be considered.
- In immunocompetent children and adults, empirical antimicrobial therapy for bloody diarrhoea is recommended only for the following categories:
    - Clinically ill with fever, abdominal pain and bacillary dysentery (frequent scanty bloody stools, fever, abdominal cramps, tenesmus) presumptively due to *Shigella* spp.
    - People who have recently travelled internationally developing body temperatures ≥38.5°C and/or signs of sepsis.
    - Enteritis-associated sepsis or specific bacterial pathogens in selected cases in paediatric gastroenteritis (e.g. non-typhoidal salmonella in patients under 3 months, associated with sepsis) or with severe *Clostridioides difficile* infection.

  For others, rehydration is the primary therapy and antibiotics can be delayed until the results of investigations are available.
- Antimicrobial therapy should be avoided in people with infections attributed to Shiga Toxin-producing *Escherichia coli* (STEC O157:H7 and other STEC) that produce shiga toxin 2 (or if the toxin genotype is unknown).
- Whenever possible, a microbiological diagnosis should be attempted.

Table 16: Empirical antimicrobial therapy for diarrhoea in adults

Condition	Primary therapy	Alternative therapy	Comments
Mild diarrhoea (<6 unformed stools/day and no fever)	Rehydration Antibiotic therapy is not recommended		Treatment with co-trimoxazole or fluoroquinolones may increase the risk of haemolytic uraemic syndrome (HUS). Antibiotic therapy is recommended if cholera is suspected.
Severe diarrhoea (≥ 6 unformed stools per day and/or blood and mucus, fever)	ciprofloxacin 500mg PO q12h or ciprofloxacin 400mg IV q12h for 3-5 days	co-trimoxazole 960mg PO q12h for 3-5 days	IV therapy is required only when oral therapy is not tolerated.
Traveller's diarrhoea Mild	Antibiotic therapy is not recommended.		
Moderate to severe	ciprofloxacin 500mg PO q12h for 1-3 days or azithromycin 1g PO single dose or 500mg PO q24h for 2-3 days	co-trimoxazole 960mg PO q12h for 3 days	IV therapy is required when oral therapy is not tolerated.

Condition	Primary therapy	Alternative therapy	Comments
Antibiotic associated diarrhoea (*Clostridioides difficile* diarrhoea**)**			If possible, stop antibiotics likely to be causing symptoms. Stop antimotility drugs and laxatives.
• **First episode, non-severe disease** (WBC<15000/µL, <5 stools per day, creatinine normal)	metronidazole 400mg PO q8h for 10 days	vancomycin* 125mg PO q6h for 10 days	Before starting treatment, send a sample of faeces for detection of *C. difficile* toxin A & B.
• **Severe disease** (WBC>15000/µL, acute rise in serum creatinine, temperature >38.5^{0}C, severe colitis)	vancomycin* 125mg PO q6h for 10 days + metronidazole 500mg IV q8h for 10 days	fidaxomicin 200mg PO q12h for 10 days (contact microbiologist)	If not responding, severe/life threatening disease or recurrent disease, contact microbiologist. Fidaxomicin is not currently available in Sri Lanka.
• **Life threatening /fulminant** (Hypotension, partial/complete ileus or megacolon, CT evidence of fulminant colitis, lactate >5mmol/L)	vancomycin* 500mg PO q6h for 10 days + metronidazole 500mg IV q8h for 10 days		The maximum daily dose of PO vancomycin should not exceed 2g.

Condition	Primary therapy	Alternative therapy	Comments
Suspected cholera (adults including pregnant women)	doxycycline 300mg PO single dose	If resistance to doxycycline is documented ciprofloxacin 1g PO single dose or azithromycin 1g PO single dose or erythromycin 500mg PO q6h for 3 days	Antibiotic therapy will reduce the volume and duration of diarrhoea.

*Oral administration of vancomycin powder for intravenous use is recommended only for the treatment of antibiotic associated diarrhoea. Each dose (125mg or 500mg) may be reconstituted in 30 mL water and either given to the patient to drink or administered by nasogastric tube.

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- Relevant specimens should be sent for culture and antibiotic susceptibility before starting antibiotics whenever possible. Antimicrobial therapy should be guided by the sensitivity results.

Table 17: Empirical antimicrobial therapy for ear, nose and throat infections.

Condition	Primary therapy	Alternative therapy/ immediate beta - lactam hypersensitivity[1]	Comments
Otitis externa • Bacterial (Usually treated with topical preparations) **Indications for systemic antibiotics**: Fever/spread of inflammation to pinna/folliculitis/acute localized otitis externa/ infections not responding to topical treatment/ patients with other comorbidities/ immunocompromised	Ear drops: 3 drops q8h 0.5% neomycin + 0.1% betamethasone or 0.3% ofloxacin/ 0.3% ciprofloxacin/ 0.3% gentamicin/ +/- 0.1% betamethasone +/- If systemic antibiotics are indicated: ciprofloxacin 500mg PO q12h +/- cloxacillin/ flucloxacillin 500mg PO q6h	Ear drops + ciprofloxacin 500mg PO q12h +/- clindamycin 300-450mg PO q6-8h	Gentamicin ear drops should be considered only when there is no perforation of the ear drum. Avoid prolonged use. Local antibiotics can be combined with steroids when there is oedema. Review antibiotics according to culture results. Duration of antibiotics is 5 to 7 days. Patients with severe or recurrent otitis externa should be referred to ENT surgeon.

Condition	Primary therapy	Alternative therapy/ immediate beta - lactam hypersensitivity[1]	Comments
Otitis externa • Malignant	ciprofloxacin 400mg IV q12h or ticarcillin-clavulanate 3.2g IV q8h or piperacillin-tazobactam 4.5g IV q6-8h + topical therapy as in otitis externa	ceftazidime 2g IV q8h + topical therapy as in otitis externa **In immediate beta lactam hypersensitivity[1]** contact microbiologist for alternative options	Suspect malignant otitis externa in diabetic or immunocompromised patient with severe earache and refer to an ENT surgeon. Continue treatment for 4-6 weeks. Step down to oral ciprofloxacin with clinical improvement. The possibility of fungal aetiology should be considered when not responding to treatment and bacterial cultures are negative.
Otitis externa • Fungal	1% clotrimazole solution 3-4 drops q8h or 2% miconazole + 0.25 % betamethasone q8h for 10-14 days		Send relevant specimens for fungal cultures. Refer to an ENT surgeon.

Condition	Primary therapy	Alternative therapy/ immediate beta - lactam hypersensitivity[1]	Comments
Otitis media • Acute otitis media If no antibiotics were used within the last month	amoxicillin 1g PO q8h for 5-7 days or cefuroxime 500mg PO q12h	clarithromycin 500mg PO q12h for 5-7 days	Treat children < 2 years. For children > 2 years and adults, who do not have complications can be observed without antibiotics for 48h. There is no place for topical antibiotics. If complicated or immunocompromised, IV antibiotics should be used.
If antibiotics were used within last month or poor clinical response after 3 days of amoxicillin	co-amoxiclav 625mg PO q8h for 5-7 days		
Otitis media • Otitis media with effusion	Antibiotics are not required.		Often bilateral and without pain. Most commonly due to viruses or allergies. Refer to an ENT surgeon if persistent.

Condition	Primary therapy	Alternative therapy/ Immediate beta - lactam hypersensitivity[1]	Comments
Otitis media Chronic suppurative otitis media			Aural toilet is very important. In acute exacerbations, may have to use culture guided oral antibiotics. Intravenous antibiotics may be required if severe and not responding to oral antibiotics. Duration depends on severity and complications.
• Chronic mucoid type (Safe CSOM)	0.3% ciprofloxacin otic solution	5% chloramphenicol* ear drops 3-4 drops q12h for 1-2 weeks	
• Chronic squamous type (Cholesteatoma)	0.3% ciprofloxacin otic solution	5% chloramphenicol* ear drops 3-4 drops q12h until surgical intervention	Surgical intervention is essential. Refer to an ENT surgeon. *Chloramphenicol ear drops should be avoided unless essential due to irritant effects.

Condition	Primary therapy	Alternative therapy/ immediate beta - lactam hypersensitivity[1]	Comments
Mastoiditis • Uncomplicated acute	co-amoxiclav 1.2g IV q8h or ceftriaxone 1g IV q24h	vancomycin[3] 1g IV q12h + ciprofloxacin 500mg PO q12h	Patient should be referred to an ENT surgeon. Switch to oral treatment with clinical response.
• Complicated (e.g. mastoid abscess, intracranial extension, facial palsy)	Empirical therapy may depend on the extent/severity of the infection. Contact microbiologist for empirical antibiotic therapy. .		Refer to an ENT surgeon for surgical intervention. Antibiotic therapy should be reviewed with culture and ABST results.
Perichondritis of auricle	ciprofloxacin 400mg IV q12h/ ceftazidime 1g IV q8h +/- clindamycin[4] 900mg IV q8h		Total duration of therapy 7-10 days.

Condition	Primary therapy	Alternative therapy/ immediate beta - lactam hypersensitivity[1]	Comments
Acute bacterial sinusitis If no antibiotics were used within the last month	amoxicillin 500mg PO q8h	doxycycline 100mg PO q24h or clarithromycin 500mg PO q12h or erythromycin 250-500mg PO q6h (preferred in pregnancy)	Viruses are the most common causes of acute sinusitis. Antibiotic therapy is not indicated for acute allergic rhinosinusitis. Acute bacterial sinusitis should be considered when symptoms persisting for ≥10 days with no improvement/ systemically unwell/ have symptoms and signs of a more serious illness or condition/ those who are at high risk of complications. Parenteral antibiotic therapy is required only for severe/ complicated cases.
If antibiotics were used within last month or no response to amoxicillin in 48 hours	co-amoxiclav 625mg PO q8h Antibiotics are usually not effective. Topical steroids/ nasal drops/ sprays are the mainstay of treatment. Treat acute exacerbations as acute sinusitis.		
Chronic Sinusitis	Antibiotics are not effective. Steroid nasal sprays and surgery are mainstay of treatment.		Refer to an ENT surgeon for assessment/surgical intervention.

Condition	Primary therapy	Alternative therapy/ immediate beta - lactam hypersensitivity[1]	Comments
Fungal sinusitis • Allergic fungal rhinosinusitis	Antibiotics are not effective.		Refer to an ENT surgeon. Surgical treatment is indicated in all types of fungal sinusitis.
• Fungal ball • Invasive fungal sinusitis	Antibiotics are not effective.		Refer to an ENT surgeon. Contact mycologist/ microbiologist for antifungal therapy. Need appropriate sampling for fungal cultures.
Nasal vestibulitis • Mild	fusidic acid cream local application q12h-q8h		
• Severe	flucloxacillin 500mg IV q6h + fusidic acid cream local application q12h-q8h	clindamycin 300-450mg PO q6-8h or clindamycin[4] 900mg IV q8h + fusidic acid cream local application q12h-q8h	Commence treatment as early as possible. Refer to an ENT surgeon. Contact microbiologist, if not responding to initial therapy.

Condition	Primary therapy	Alternative therapy/ immediate beta - lactam hypersensitivity[1]	Comments
Nasal septal abscess	flucloxacillin 1g IV q6h	clindamycin[4] 900mg IVq8h	Surgical intervention is essential as early as possible. Refer to an ENT surgeon. Contact microbiologist, if not responding to initial therapy.
Acute bacterial tonsillitis/pharyngitis As most pharyngitis are of viral origin, antibiotic treatment is not usually indicated. Associated cough, rhinorrhoea, hoarseness and/oral ulcers suggest viral aetiology.	phenoxymethylpenicillin 500mg PO q6h or amoxicillin 500mg PO q8h or co-amoxiclav 625mg PO q8h for 5-10 days	cefalexin 500mg PO q8h for 5-10 days or **In immediate beta lactam hypersensitivity[1]** clarithromycin 500mg PO q12h	Five days may be enough for symptomatic cure; but a 10-day course may increase the chance of microbiological cure.

Condition	Primary therapy	Alternative therapy/ immediate beta - lactam hypersensitivity[1]	Comments
Acute bacterial tonsillitis/ pharyngitis not responding to oral therapy	benzylpenicillin 2MU IV q6h or cefuroxime 750mg IV q8h	clindamycin[4] 600mg IVq8h	Step down to oral therapy with clinical improvement. Total duration - 10 days
Peritonsillar abscess	benzylpenicillin 2MU IV q6h + metronidazole 500mg IV q8h or co-amoxiclav 1.2g IV q8h or cefuroxime 750mg IV q8h + metronidazole 500mg IV q8h	clindamycin[4] 900mg IV q8h	Surgical intervention is essential. Refer to an ENT surgeon. Step down to oral therapy after surgery with clinical improvement. Total duration -10 days. Contact microbiologist if not responding to initial therapy.

Condition	Primary therapy	Alternative therapy/ immediate beta - lactam hypersensitivity[1]	Comments
Retropharyngeal/ parapharyngeal abscess	ceftriaxone 1-2g IV q24h + metronidazole 500mg IV q8h or co-amoxiclav 1.2g IV q8h	clindamycin[4] 900mg IV q8h + ciprofloxacin 400mg IV q12h	Early surgical intervention and airway management are essential. Refer to an ENT surgeon. Step down to oral therapy after surgery with clinical improvement. Contact microbiologist, if not responding to initial therapy.
Acute Laryngitis	Antibiotic treatment is generally not indicated as most cases are of viral aetiology		Voice rest for 7-10 days. If symptoms persist for >48hrs (voice change and pain) treat as acute bacterial tonsillitis
Acute epiglottitis	cefotaxime 1g IV q8h/ ceftriaxone 1g IV q24h or co-amoxiclav 1.2g IV q8h start IV steroids with antibiotics	clindamycin[4] 900mg IV q8h + levofloxacin[*] 750mg IV q24h Start IV steroids with antibiotics	Contact ENT surgeon and microbiologist immediately. Urgent surgical intervention/intubation needed for paediatric patients. Step down to oral therapy after surgery with clinical improvement. [*]**Levofloxacin is a "Reserve Category" antibiotic** (Annex 01).

Condition	Primary therapy	Alternative therapy/ immediate beta - lactam hypersensitivity[1]	Comments
Suppurative jugular thrombophlebitis (Lemierre's syndrome)	ceftriaxone 2g IV q24h + metronidazole 500mg IV q8h	clindamycin[4] 900mg IVq8h	Refer to an ENT surgeon and microbiologist. Step down to oral therapy with clinical improvement Duration 3-6 weeks

Prepared in collaboration with College of Otorhinolaryngologists & Head and Neck Surgeons of Sri Lanka

[1]Refer chapter 2.
[4]For administration of clindamycin, refer chapter 7.

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- Individual containers of eye drops are recommended for each patient to minimize cross contamination.
- If multidose vials are used for more than one patient, infection prevention and control precautions should be practised during handling and administration of eye drops to avoid cross contamination.

Table 18: Empirical antimicrobial therapy for eye infections

Condition	Primary therapy	Alternative therapy/ immediate beta- lactam hypersensitivity[1]	Comments
Conjunctivitis Most cases are viral. Bacterial conjunctivitis is usually unilateral and self-limiting (suspect when the discharge is purulent or if there is associated naso lacrimal duct obstruction). Treat only if severe.	Bathe/clean eyelids regularly to remove crusting. chloramphenicol 0.5% eye drops q6h or chloramphenicol 1% eye ointment applied q6-8h Continue for 48 hours after resolution.	Allergic to chloramphenicol or poor compliance with frequent instillation: fusidic acid 1% eye drops q12h or ciprofloxacin 0.3% eye drops q6h Continue for 48h after resolution.	Send eye discharge swab for Gram stain and culture prior to treatment if a bacterial infection is suspected. Advise meticulous hand washing and avoid sharing of personal items. Do not wear contact lenses until 24 hours after treatment is completed and all symptoms resolved. Topical steroids are contraindicated.

Condition	Primary therapy	Alternative therapy/ immediate beta- lactam hypersensitivity[1]	Comments
Gonococcal ophthalmia neonatorum*	saline lavage hourly ceftriaxone 25-50mg/kg (maximum 125 mg) IV/IM single dose or cefotaxime 100 mg/kg IV/IM, single dose (which may be preferred, if available, due to the risk of increasing bilirubin levels associated with ceftriaxone)		Take conjunctival swabs for Gram staining and special culture for *Neisseria* species. Topical antimicrobials are not recommended. Treat mother and her sexual partner. Consider *Chlamydia trachomatis* infection. *Refer Sexually Transmitted Infections – Management Guidelines, National STD, AIDS Control Programme, Sri Lanka College of Sexual Health and HIV Medicine.
Chlamydial conjunctivitis	**For neonates:** erythromycin syrup 12.5mg/kg PO q6h for 14 days **For adults**: doxycycline 100mg PO q12h for 1-3 weeks	**For adults:** erythromycin 500mg PO q6h for 7 days / 500mg PO q12h for 14 days or azithromycin 1g PO single dose	If *Chlamydia trachomatis* is suspected send conjunctival scrapings for testing. Contact microbiologist.

Condition	Primary therapy	Alternative therapy/ Immediate beta- lactam hypersensitivity[1]	Comments
Endogenous Endophthalmitis • Results from bacteraemia or fungaemia seeding the eye	**Intravitreal therapy:** vancomycin** 1mg + ceftazidime** 2.25mg/ amikacin** 0.4mg with **Topical therapy** ciprofloxacin 0.3% eye drops hourly + teicoplanin 1% eye drops hourly with **Systemic therapy** ciprofloxacin 400mg IV q12h/ ceftazidime 2g IV q8h + teicoplanin 400mg IV q12h 3 doses followed by 400mg q24h (depend on renal function)	**Intravitreal therapy:** amikacin** 0.4 mg + clindamycin** 1.0 mg with **Systemic therapy:** vancomycin[3] 1g IV q12h + ciprofloxacin 400mg IV q12h	**Ophthalmic emergency**. An immediate ophthalmology referral is needed. Immediate vitrectomy may be needed. Vitreous tap/biopsy should be sent for microscopy and culture. Treatment of the underlying source of bacteraemia with systemic antibiotics is necessary and should be initiated after obtaining blood cultures and samples from the primary focus if identified. Contact microbiologist. **Each agent diluted in 0.1ml of sterile water or normal saline (may need to repeat in 2-3 days). Note the risk of retinal microvasculitis with intravitreal amikacin.

Condition	Primary therapy	Alternative therapy/ Immediate beta- lactam hypersensitivity[1]	Comments
Endogenous Endophthalmitis	**If suspected fungal infection intravitreal therapy:** amphotericin B*** 5µg/0.1ml sterile water stat and repeat after 48h or more if needed or voriconazole*** 100µg in 0.1ml sterile water + **Systemic therapy:** fluconazole 400-800mg IV q24h		Systemic antifungals should be continued for a minimum of 6 weeks based on antifungal susceptibility. Contact microbiologist /mycologist. *** Preparation of amphotericin B / voriconazole solutions for intravitreal use should be done under strict aseptic conditions under the guidance of consultant ophthalmologist to ensure the sterility and strength of the solution.

Condition	Primary therapy	Alternative therapy/ immediate beta- lactam hypersensitivity[1]	Comments
Exogenous Endophthalmitis • Post-operative endophthalmitis (post-cataract surgery) occurs within 1-7 days after intraocular surgery. • Post-intravitreal injection. Typically present within 5 days after the injection. • Bleb-related infection may occur immediately after or months to years following glaucoma surgery in which a "bleb" is created.	**Intravitreal therapy:** vancomycin** 1mg + ceftazidime** 2.25mg/ amikacin** 0.4mg with **Topical therapy** ciprofloxacin 0.3% eye drops hourly + teicoplanin 1% eye drops hourly with **Systemic therapy** ciprofloxacin 400mg IV q12h/ ceftazidime 2g IV q8h + teicoplanin 400mg IV q12h 3 doses followed by 400mg q24h; depend on renal function	**In immediate beta lactam hypersensitivity[1]** **Intravitreal therapy** vancomycin** 1mg + ciprofloxacin** 0.2mg with topical and systemic therapy as in primary therapy	**Each agent diluted in 0.1ml of sterile water or normal saline (may need to repeat in 2-3 days) Immediate ophthalmology referral is needed. Immediate vitrectomy may be needed. Vitreous tap/biopsy should be sent for microscopy and culture. If fungal endophthalmitis is suspected see endogenous endophthalmitis section above for antifungal therapy. Contact microbiologist/mycologist. Note the risk of retinal microvasculitis with intravitreal amikacin.

Condition	Primary therapy	Alternative therapy/ Immediate beta- lactam hypersensitivity[1]	Comments
Penetrating ocular trauma at risk of getting endophthalmitis	**Intravitreal therapy:** ceftazidime 2.25mg**/ amikacin 0.4mg** + moxifloxacin (preservative free) off label use with **Systemic therapy:** vancomycin[3] 1g IV q12h + ceftazidime 1-2g IV q8h (If high level of contamination can add vancomycin intravitreal therapy)	Severe cases, probable intraocular foreign body or anaerobic bacteria: clindamycin[4] 300mg IV q8h + gentamicin[2] 5mg/kg IV q24h	Immediate ophthalmology referral is needed. Systemic antifungal treatment is recommended for suspected fungal infections. Contact microbiologist/ mycologist. **Each agent diluted in 0.1ml of sterile water or normal saline (may need to repeat in 2-3 days).
Suspected viral keratitis Herpes simplex virus	aciclovir 400mg PO 5 times per day for 7 days + aciclovir 3% eye ointment topically 5 times per day for 14 days or for at least 3 days after healing	aciclovir 400mg PO 5 times per day for 7 days + ganciclovir 0.15% gel 1 drop 5 times per day until healing then q8h for 7 days	An immediate ophthalmology referral is needed.

Condition	Primary therapy	Alternative therapy/ Immediate beta- lactam hypersensitivity[1]	Comments
Herpes zoster ophthalmicus with or without keratitis	aciclovir 800mg PO 5 times per day for 7 days + topical aciclovir 3% 5 times per day for 14 days	aciclovir 800mg PO 5 times per day for 7 days + topical ganciclovir 0.15% gel 1 drop 5 times per day until healing then three times per day for 7 days	An immediate ophthalmology referral is needed.
Suspected bacterial keratitis	gatifloxacin 0.3% eye drops / moxifloxacin 0.5% eye drops hourly + tobramycin 0.3% eye drops intensive therapy hourly	gentamicin 0.3% eye drops hourly	An immediate ophthalmology referral is needed. Send scrapings of the ulcer base for bacterial and fungal culture before starting treatment.
Contact lens associated bacterial keratitis	gatifloxacin 0.3% eye drops/moxifloxacin 0.5% eye drops hourly + tobramycin 0.3% eye drops hourly intensive therapy	gentamicin 0.3% eye drops hourly	An immediate ophthalmology referral is needed. Contact lens and storage solution can be sent for microscopy and culture.

Condition	Primary therapy	Alternative therapy/ Immediate beta- lactam hypersensitivity[1]	Comments
Suspected fungal keratitis	natamycin 0.5% eye drops, 1 drop every 1-2 hourly for 3 to 5 days; then 1 drop 3-4 hourly for 6 weeks	amphotericin B 0.15% eye drops / voriconazole 1% eye drops, 1 drop 1-2 hourly; tail off according to response	An immediate ophthalmology referral is needed. Contact mycologist/ microbiologist. Send scrapings of the ulcer base for bacterial and fungal culture before starting treatment. *Acanthamoeba* infection must be excluded.
Blepharitis (inflammation of lid margins) If bacterial super-infection is suspected	Lid hygiene with gentle eyelid scrubs (e.g.: twice daily with warm water or diluted baby shampoo) 1% chloramphenicol topical ointment / fusidic acid ointment 2 times per day		
Meibomian abscess (internal hordeolum) **Stye (external hordeolum)**	Surgical treatment +/- flucloxacillin 500mg PO q6h for 5 days		Hot packs are adequate for external hordeolum. Role of topical antibiotics is unclear.

Condition	Primary therapy	Alternative therapy/ Immediate beta- lactam hypersensitivity[1]	Comments
Orbital (post-septal) cellulitis Infection of the tissues posterior to the orbital septum, including the fat and muscle within the bony orbit	flucloxacillin 2g IV q6h + cefotaxime 2g IV q8h/ ceftriaxone 2g IV q24h + metronidazole 500mg IV q8h Switch to co-amoxiclav 625mg PO q8h when clinically appropriate.	vancomycin[3] 1g IV q8-12h/ teicoplanin 400mg IV q12h 3doses followed by 400mg IV q24h + ciprofloxacin 400mg IV q12h + metronidazole 500mg IV q8h	An immediate ophthalmology referral is needed. If MRSA is suspected replace flucloxacillin with vancomycin/ teicoplanin. Contact microbiologist.

Condition	Primary therapy	Alternative therapy/ Immediate beta- lactam hypersensitivity[1]	Comments
Periorbital (pre-septal) cellulitis[****] Infection of skin and soft tissue around the eye anterior to the orbital septum **With evidence of external involvement**	co-amoxiclav 625mg PO q8h + clindamycin[4] 600mg PO q8h If severe: co-amoxiclav 1.2g IV q8h + clindamycin[4] 600mg IV q8h	co-trimoxazole 960mg PO q12h or doxycycline 200mg PO (loading dose) followed by 100mg PO q12h If severe: ciprofloxacin 400mg IV q12h + clindamycin 600mg IV q8h	[****]Always suspect orbital (post-septal) cellulitis unless there is a clear cause for pre-septal cellulitis e.g. trauma, surgery, insect bite, chalazion. Ophthalmology referral is needed. If MRSA is suspected replace flucloxacillin with vancomycin/ teicoplanin. Contact microbiologist in severe infections. Switch to oral therapy with clinical improvement. Total duration - 7 days. For children, immediate ophthalmology referral is needed.

Condition	Primary therapy	Alternative therapy/ Immediate beta- lactam hypersensitivity[1]	Comments
Without evidence of external involvement (with evidence of underlying sinusitis)	co-amoxiclav 625mg PO q8h		Contact microbiologist in severe infections or beta-lactam allergy.

Prepared in collaboration with the College of Ophthalmologists of Sri Lanka.

[1]Refer chapter 2
[2]Monitor renal functions and adjust doses (refer chapter 7).
[3]TDM is recommended (refer chapter 6). Monitor renal functions and adjust doses (refer chapter 7).
[4]For administration of clindamycin refer chapter 7.

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Chapter 16: Intra-abdominal Infection

- Uncomplicated intra-abdominal infections (IAIs), only involve a single organ and do not extend to the peritoneum.
- In complicated IAIs, the infectious process extends beyond the organ, causing either localized or diffuse peritonitis.
- The cornerstone of effective treatment of IAIs includes early recognition, adequate source control, appropriate antimicrobial therapy, and prompt physiologic stabilization using intravenous fluid therapy in critically ill patients.
- Adequate source control can shorten the course of antibiotic therapy.

Table 19: Empirical antimicrobial therapy for intra-abdominal infections

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Acute uncomplicated appendicitis (appendicitis with no perforation, abscess, or peritonitis)	Appendicectomy is the primary treatment		In the absence of perforation antibiotic therapy is limited to surgical prophylaxis
Acute uncomplicated appendicitis when surgery is not feasible (Appendicolith excluded)	co-amoxiclav 1.2g IV q8h or cefuroxime 1.5g IV q8h + metronidazole 500mg IV q8h	ciprofloxacin 400mg IV q12h + Metronidazole 500mg IV q8h	Specimens collected during surgery should be sent for culture and ABST. If the patient is with sepsis or septic shock, consider starting a carbapenem empirically. Contact microbiologist.

Condition	Primary therapy	Alternative therapy/ Immediate beta-lactam hypersensitivity[1]	Comments
Complicated appendicitis • gangrenous appendicitis • peri appendicular abscess • perforation/diffuse peritonitis	**Adequate source control** + piperacillin-tazobactam 4.5g IV q6-8h +/− gentamicin[2] 5mg/kg IV q24h (in critically ill patients) or ceftriaxone 2g IVq24h/ cefotaxime 2g IVq8h + metronidazole 500mg IV q8h +/− gentamicin[2] 5mg/kg IV q24h (in critically ill patients)	ciprofloxacin 400mg IV q12h + metronidazole 500mg IV q8h +/- gentamicin[2] 5mg/kg IV q24h (in critically ill patients) or amikacin[2] 15mg/kg IV q24 h + metronidazole 500mg IVq8h	Contact microbiologist.
Biliary tract infections **Uncomplicated cholecystitis**	co-amoxiclav 1.2g IV q8h or ceftriaxone 2g IV q24h/ cefotaxime 1g IVq8h +/- metronidazole 500mg IV q8h	ciprofloxacin 400mg IV q12h + /- metronidazole 500mg IV q8h	When early surgical treatment (within 7–10 days) is offered, post-operative antibiotics are unnecessary if source control is adequate. Biliary specimens collected during surgery should be sent for culture.

Condition	Primary therapy	Alternative therapy/ Immediate beta-lactam hypersensitivity[1]	Comments
Complicated cholecystitis Laparoscopic cholecystectomy/open cholecystectomy	piperacillin-tazobactam 4.5g IV q6-8h +/– gentamicin[2] 5mg/kg IV q24h (in critically ill patients) or imipenem 500mg IV q6h/ meropenem 1g IV q8h	ciprofloxacin 400mg IV q12h + metronidazole 500mg IV q8h + amikacin[2] 15mg/kg IV q24h	If the patient is in sepsis or septic shock, consider starting a carbapenem empirically. Contact microbiologist if the patient is immunocompromised or had recent antibiotic exposure.
Acute cholangitis	co-amoxiclav 1.2g IV q8h +/- gentamicin[2] 5mg/kg IV q24h or ceftriaxone 2g IV q24h/ cefotaxime 2g IV q8h + metronidazole 500mg IV q8h +/- gentamicin[2] 5mg/kg IV q24h	ciprofloxacin 400mg IV q12h + metronidazole 500mg IV q8h + /- gentamicin[2] 5mg/kg IV q24h	Source control with adequate biliary drainage will shorten the antibiotic duration. Send bile for culture and ABST. Contact microbiologist if the patient is immunocompromised or had recent antibiotic exposure.

Condition	Primary therapy	Alternative therapy/ Immediate beta-lactam hypersensitivity[1]	Comments
Biliary sepsis or healthcare-associated biliary infection of any severity	meropenem 1g IV q8h/ imipenem 500mg IV q6h +/- metronidazole 500mg IV q8h +/- teicoplanin 400mg IV q12h 3 doses followed by 400mg IV q24h or piperacillin-tazobactam 4.5g IV q6-8h + amikacin[2] 15mg/kg IV q24h +/- metronidazole 500mg IV q8h +/- teicoplanin 400mg IV q12h 3 doses followed by 400mg IV q24h	ciprofloxacin 400mg IVq12h + metronidazole 500mg IV q8h + amikacin[2] 15mg/kg IV q24h +/- teicoplanin 400mg IV q12h 3 doses followed by 400mg IV q24h	Contact microbiologist.

Condition	Primary therapy	Alternative therapy/ Immediate beta-lactam hypersensitivity[1]	Comments
Gastroduodenal ulcer perforation	co-amoxiclav 1.2g IV q8h +/− gentamicin[2] 5mg/kg IV q24h (in critically ill patients) or ceftriaxone 2g IV q24h / cefotaxime 2g IV q8h + metronidazole 500 mg IV q8h +/- gentamicin[2] 5mg/kg IV q24h (In critically ill patients)	ciprofloxacin 400 mg IV q12h/ gentamicin[2] 5 mg/Kg IV q24h + metronidazole 500 mg IV q8h	Surgical intervention is recommended along with antibiotic therapy.

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Diverticulitis • Mild (Localized sigmoid wall thickening / pericolic fat stranding)	co-amoxiclav 625mg PO q8h	ciprofloxacin 500mg PO q12h + metronidazole 400mg PO q8h	
• Moderate to Severe (Abscess /extraluminal air/ extraluminal contrast)	co-amoxiclav 1.2g IV q8h +/− gentamicin[2] 5 mg/kg IV q24h or ceftriaxone 2g IV q24h / cefotaxime 2g IV q8h + metronidazole 500 mg IV q8h +/− gentamicin[2] 5 mg/kg IV q24h or piperacillin-tazobactam 4.5g IV q6-8h +/− gentamicin[2] 5mg/kg IV q24h	ciprofloxacin 400 mg IV q12h + metronidazole 500mg IV q8h or amikacin[2] 15/kg IV q24h + metronidazole 500mg IV q8h	Drainage of abscess is necessary along with antibiotic therapy. If the patient is in sepsis or septic shock, consider starting a carbapenem empirically. Contact microbiologist.

Condition	Primary therapy	Alternative therapy/ Immediate beta-lactam hypersensitivity[1]	Comments
Pyogenic liver abscess	ceftriaxone 2g IV q24h/ cefotaxime 1g IV q8h + metronidazole 500mg IV q8h or piperacillin-tazobactam 4.5g IV q6-8h	ciprofloxacin 400mg IV q12h + metronidazole 500mg IV q8h	Melioidosis needs to be excluded. Aspirate should be sent for Gram stain, aerobic/anaerobic bacterial culture, testing for fungal and mycobacterial pathogens. *Entamoeba histolytica* should be considered based on epidemiologic factors.
Acute pancreatitis	Prophylactic antibiotics are not recommended.		Antimicrobial therapy is best indicated for culture-proven infection in pancreatic necrosis or when infection is strongly suspected (gas in the collection, bacteraemia, sepsis or clinical deterioration).
Severe pancreatitis/ Infected pancreatic necrosis	piperacillin–tazobactam 4.5g IV q6-8 h or imipenem 500 mg IV q6h/ meropenem 1g IV q8h (in critically ill patient)	ciprofloxacin 400mg IV q12h + metronidazole 500mg IV q8h + gentamicin[2] 5mg/kg IV q24h	Patients with 30% or more of necrosis are at a greater risk of developing infection.

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Peritonitis • **Spontaneous bacterial peritonitis** (SBP) / primary peritonitis (In SBP, bacterial infection in ascitic fluid is present without any intra-abdominal surgically treatable source of infection)	cefotaxime 2g IV q8h or ceftriaxone 2g IV 24h	levofloxacin* 750mg IV q24h	SBP is very common in patients with cirrhosis and ascites. Ascitic fluid should be sent for culture & ABST. *__Levofloxacin is a "Reserve Category" antibiotic__ (Annex 01). Contact microbiologist.
• **Secondary bacterial peritonitis** (Perforation of bowel and diverticula or post-operative peritonitis)	piperacillin-tazobactam 4.5g IV q6 - 8h +/- gentamicin[2] 5 mg/kg IV q24h or imipenem 500mg IV q6h/ meropenem 1g IV q8h (in critically ill patient with sepsis or septic shock)	ciprofloxacin 400mg IV q12h + metronidazole 500mg IV q8h + amikacin[2] 15mg/kg IV q24h	Early surgical source control and antibiotic therapy is required. Inability to control the septic source is associated with a very high mortality rate. Ascitic fluid should be sent for culture. Empirical anti MRSA and antifungal therapy is generally not indicated unless patient has risk factors. Contact microbiologist.

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Peritonitis related to peritoneal dialysis. • Moderate	Intra peritoneal intermittent dosing vancomycin 15-30mg/kg every 5-7days + ceftazidime 1-1.5g daily or Intra peritoneal continuous dosing vancomycin loading dose of 20-25mg/kg followed by a maintenance dose of 25mg/L in all exchanges + ceftazidime loading dose of 500mg/L followed by a maintenance dose of 125mg/L	Intra peritoneal intermittent dosing vancomycin 15-30mg/kg every 5-7days + gentamicin 0.6 mg/kg daily (gentamicin is not recommended for continuous dosing)	Send blood and other relevant specimens for culture. Vancomycin and ceftazidime can be mixed in the dialysis fluid of the same dialysis bag. Do not mix vancomycin and ceftazidime in a syringe or in an empty peritoneal dialysis fluid bag. If facilities are not available for measurement of serum vancomycin levels, vancomycin treatment should be monitored with serum creatinine. Timing of intermittent dosing depends on trough level of vancomycin. (repeat dose when trough level is 15mg/ml) Adjust doses according to renal functions. In intermittent dosing, the antibiotic-containing dialysis solution must be allowed to dwell for at least 6 hours to allow adequate absorption of the antibiotic into the systemic circulation. Contact microbiologist.

Condition	Primary therapy	Alternative therapy/ Immediate beta-lactam hypersensitivity[1]	Comments
Peritonitis related to peritoneal dialysis • Severe	In addition to above intra peritoneal antibiotics vancomycin[3] 1g IV q12h + ceftazidime 1g IV q8h	In addition to above intra peritoneal antibiotics vancomycin[3] 1g IV q12h + ciprofloxacin 400mg IV q12h	See above.

Prepared in collaboration with the College of Surgeons of Sri Lanka

[1]Refer chapter 2
[2]TDM is recommended refer chapter 6. Monitor renal functions and adjust doses refer chapter 7. Vestibular function should be assessed when continued for more than 5 days. Gentamicin when given in single daily dose, aim for a trough concentration of <1mg/L and peak levels of 10-12mg/L.
[3]TDM is recommended refer chapter 6. Monitor renal functions and adjust doses refer chapter 7.

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Table 20: Empirical antibiotics for oral cavity and associated structure infections.

Condition	Primary therapy	Alternative therapy / immediate beta-lactam hypersensitivity[1]	Comments
Acute suppurative sialadenitis/ suppurative parotitis	flucloxacillin 2g IV q6h + metronidazole 500mg IV q8h or co- amoxiclav 1.2g IV q8h	clindamycin[4] 450mg - 600mg IV q8h	If high risk of MRSA or immunocompromised, contact microbiologist.
Juvenile recurrent parotitis	co- amoxiclav PO/IV q8h		Refer BNF for children for paediatric doses. Selection of PO/IV route should be done according to clinical condition at the time of starting empirical antibiotics. Minimum of 7 days therapy is recommended.
Cervico-facial actinomycosis	benzylpenicillin 3-4MU IV q6h followed by phenoxymethylpenicillin 500mg -1g PO q6h	clindamycin[4] 600mg IV q8h followed by 450mg PO q6h. or doxycycline 200mg PO (loading dose) followed by 100mg PO q24h	2 - 6 weeks of parenteral therapy followed by oral therapy for a total duration of 6 - 12 months for serious infections and bulky disease, whereas a shorter duration for less extensive disease. Contact microbiologist.

Condition	Primary therapy	Alternative therapy / immediate beta-lactam hypersensitivity[1]	Comments
Dentoalveolar infections Tooth abscess/ inflamed wisdom tooth area / root canal infection			Surgical drainage and removal of necrotic tissue is essential. Local treatment may be adequate in mild cases.
Dentoalveolar infections with: • Fever>100°F • Malaise • Lymphadenopathy • Trismus • Increased swelling • Cellulitis • Osteomyelitis • Persistent infection	amoxicillin 500mg PO q8h + metronidazole 400mg PO q8h for 3-5 days or co-amoxiclav 625mg PO q8h	clindamycin 450mg PO q8h	**Conditions not requiring adjunctive antibiotics:** 1. Pain without signs and symptoms of infection 2. Symptomatic irreversible pulpitis 3. Acute peri-radicular periodontitis 4. Teeth with necrotic pulps and a radiolucency 5. Teeth with a sinus tract (chronic peri-radicular abscess) 6. Localized fluctuant swellings

Condition	Primary therapy	Alternative therapy / immediate beta-lactam hypersensitivity[1]	Comments
Ludwig's angina			Potentially life threatening. Manage the airway.
• Immunocompetent	benzylpenicillin 3MU IV q6h + metronidazole 500mg IV q8h or co-amoxiclav 1.2g IV q8h	clindamycin[4] 600mg – 900mg IV q8h	Intravenous antibiotics to be given for a minimum period of 48 hours or until patient responds adequately. Then switch to oral therapy. Culture and antibiotic sensitivity are advised in parapharyngeal space infections.
• Immunocompromised	piperacillin-tazobactam 4.5g IV q6-8h		If high risk of MRSA or immunocompromised contact microbiologist.
Parapharyngeal space infection/peritonsillar abscess	Refer chapter 14.		

Condition	Primary therapy	Alternative therapy / immediate beta-lactam hypersensitivity[1]	Comments
Periodontal disease • Gingivitis	0.2% chlorhexidine mouth wash q8-12h		Chlorhexidine gluconate may be incompatible with some ingredients in toothpaste; leave an interval of at least 30 minutes between using mouthwash and toothpaste. Debridement is important. No indication for antibiotics. Intravenous antibiotics may be required in severe infections.
• Necrotizing periodontal disease	amoxicillin 500mg PO q8h + metronidazole 400mg PO q8h or co-amoxiclav 625mg PO q8h	clindamycin 300-450mg PO q6-8h	Duration of treatment is usually 7 days. Intravenous antibiotics are usually not indicated. Drainage and removal of the cause is important in all forms.

Condition	Primary therapy	Alternative therapy / immediate beta-lactam hypersensitivity[1]	Comments
• Periodontitis/ abscesses of the periodontium	amoxicillin 500mg PO q8h + metronidazole 400mg PO q8h or co-amoxiclav 625mg PO q8h	clindamycin 300-450mg PO q6-8h or doxycycline 200mg PO (loading dose) followed by 100mg PO q24h	
• Chronic periodontitis			Chronic periodontal disease should be managed by controlling bacterial plaque with hygiene measures and debridement of pocket root surfaces. Systemic antimicrobial use will be ineffective in microbial elimination within plaque biofilm.
• Aggressive periodontitis	amoxicillin 500mg PO q8h + metronidazole 400mg PO q8h	doxycycline 200mg PO (loading dose) followed by 100mg PO q24h	

Condition	Primary therapy	Alternative therapy / immediate beta-lactam hypersensitivity[1]	Comments
Gangrenous stomatitis (Noma/ cancrum oris)	ampicillin 2g IV q6h for a minimum of 48 hours followed by amoxicillin 500mg PO q8h +/- metronidazole 500mg IV q8h or co-amoxiclav 1.2g IV q8h followed by 625mg PO q8h	clindamycin 300-450mg PO q6-8h	Correct underlying problems in the oral cavity, dehydration, malnutrition and debility

Prepared in collaboration with the College of Oral and Maxillofacial Surgeons of Sri Lanka.

[1]Refer chapter 2.
[4]For administration of clindamycin refer chapter 7.

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Chapter 18: Respiratory Tract Infections

- Respiratory and other relevant specimens should be sent for culture and other microbiology investigations when indicated.
- Blood cultures should be taken prior to antibiotics from patients with severe pneumonia, evidence of sepsis or from those empirically treated for MRSA or *Pseudomonas aeruginosa*.
- Treatment guidelines for tuberculosis are available in the National Manual for Tuberculosis Control (NPTCCD website).

Table 21: Empirical antimicrobials for respiratory tract infections

Condition	Primary therapy	Alternative therapy / immediate beta-lactam hypersensitivity[1]	Comments
Acute Bronchitis Antibiotics might be considered in: • a severe attack on initial presentation • persistent symptoms for 5-7 days with no evidence of resolution • patients with known cardiopulmonary disease • presence of abnormal lung signs • rising WBC and inflammatory markers	Antibiotics are usually not recommended as most are of viral origin. amoxicillin 500mg PO q8h or co-amoxiclav 625mg PO q8h or cefuroxime 500mg PO q12h Duration: 5 days	erythromycin 250-500mg PO q6h or clarithromycin 250-500mg PO q12h or doxycycline 200mg PO (first dose) followed by 100mg PO q24h Duration: 5 days	Avoid doxycycline in pregnancy and children. Fluroquinolones should be avoided. Caution: Ciprofloxacin, levofloxacin and moxifloxacin can mask / promote resistance of *Mycobacterium tuberculosis* and atypical mycobacterial infections. Exclude pulmonary TB if cough persists. Erythromycin is recommended in pregnancy.

Condition	Primary therapy	Alternative therapy / immediate beta-lactam hypersensitivity[1]	Comments
Persistent paroxysmal cough>14 days - consider pertussis (inspiratory whoop, post tussive vomiting)	clarithromycin 500mg PO q12h for 7-10 days or erythromycin 500mg PO q6h for 14 days	azithromycin 500mg PO on day one followed by 250mg PO q24h for 5 days or in macrolide intolerance co-trimoxazole 960mg PO q12h for 7 days	Per nasal swabs / nasopharyngeal swabs/ aspirates should be collected and sent to Medical Research Institute for culture/ PCR in suspected cases of pertussis. Contact microbiologist for collection and transport of specimens.
Acute bacterial exacerbation of chronic obstructive pulmonary disease (COPD) Patients without risk factors for Pseudomonas infection (refer comments for risk factors) a) Mild exacerbations	amoxicillin 500mg PO q8h or clarithromycin 500mg PO q12h Duration:3-5 days	doxycycline 200mg PO (first dose) followed by 100mg PO q24h or co-trimoxazole 960mg PO q12h	For mild exacerbations antibiotics may not be indicated as up to 50% are of viral origin. Antibiotics are indicated if at least 2 out of following 3 symptoms are present: 1. Increased dyspnoea 2. Increased sputum volume/ viscosity 3. Increased sputum purulence

Condition	Primary therapy	Alternative therapy / immediate beta-lactam hypersensitivity[1]	Comments
Acute bacterial exacerbation of chronic obstructive pulmonary disease (COPD) b) Moderate to severe exacerbations/ (Consider IV antibiotics if unable to take oral) If influenza suspected	co-amoxiclav 625mg PO q8h or co-amoxiclav 1.2g IV q8h or cefuroxime 750mg-1.5g IV q8h or ceftriaxone 1-2g IV q24h Duration:7-10 days oseltamivir 75mg PO q12h	clarithromycin 500mg PO/IV q12h or co-trimoxazole 960mg PO q12h	Risk factors for *Pseudomonas* infection: 1. Chronic colonization or prior infection with *Pseudomonas* (particularly within the past 12 months) 2. Very severe COPD (FEV1<30% predicted) 3. Bronchiectasis on chest imaging 4. Broad spectrum antibiotics used within the past 3 months 5. Chronic systemic glucocorticoid use Take nasopharyngeal/ throat swabs in viral transport medium for PCR/Ag detection. Contact microbiologist.
Acute bacterial exacerbation of chronic obstructive pulmonary disease (COPD) c) Patients with risk factors for *Pseudomonas* infection (refer comments for risk factors)	**Outpatient:** ciprofloxacin 500-750mg PO q12h **Inpatient:** ceftazidime 1-2g IV q8h/ piperacillin-tazobactam 4.5g IV q6-8h/ticarcillin–clavulanic acid 3.2g IV q8h Duration: 14 days	ciprofloxacin 400mg IV q12h	These patients should ideally be managed in a specialized unit under a respiratory physician's supervision.

Condition	Primary therapy	Alternative therapy / immediate beta-lactam hypersensitivity[1]	Comments
Acute infective exacerbation of bronchiectasis Clinical symptoms - change in character and severity of cough, change in volume, purulence and increased viscosity of sputum, increasing breathlessness from baseline, fatigue/ malaise, haemoptysis.	**Out-patient:** amoxicillin 500mg PO q8h or co-amoxiclav 625mg PO q8h or cefuroxime 500mg PO q12h **In-patient:** co-amoxiclav 1.2g IV q8h or cefotaxime 1-2g IV q8h or ceftriaxone 1-2g IV q24h Duration: 7-10 days	clarithromycin 500mg PO q12h for 7-10 days or doxycycline 200mg PO (first dose) followed by 100mg PO q24h Duration: 7-10 days	Caution: Ciprofloxacin, levofloxacin and moxifloxacin (quinolones) can mask / promote resistance of *Mycobacterium tuberculosis* and atypical mycobacterial infections. Send respiratory specimens for Mycobacterial diagnostics if TB or atypical mycobacteria is suspected. Anti-viral therapy is recommended for patients with clinical / laboratory evidence of Influenza infection. Contact microbiologist.

Condition	Primary therapy	Alternative therapy / immediate beta-lactam hypersensitivity[1]	Comments
Acute infective exacerbation of bronchiectasis Previous microbiologically confirmed or suspected infection with *Pseudomonas* spp.	**Out-patient:** ciprofloxacin 500-750mg PO q12h **In-patient:** ceftazidime 1-2g IV q8h or piperacillin–tazobactam 4.5g IV q6-8h or cefepime 1-2g IV q8-12h or meropenem 1g IV q8h or imipenem 500mg-1g IV q6-8h Duration: 14 days	Discuss with microbiologist.	For severe infections / patients with sepsis discuss with microbiologist / respiratory physician. Ertapenem is not effective for *Pseudomonas* spp.

Condition	Primary therapy	Alternative therapy / immediate beta-lactam hypersensitivity[1]	Comments
Empyema	co-amoxiclav 1.2g IV q8h or ceftriaxone 1-2g IV q24h / cefotaxime 1g IV q8h + metronidazole 500mg IV q8h	ciprofloxacin 400mg IV q12h + clindamycin 300-450mg PO q6-8h / 600mg IV q8h	Pus should be drained and sent for culture and ABST. Exclude *Mycobacterium tuberculosis* in sub-acute / chronic infections. Discuss with microbiologist for the duration of therapy. Piperacillin-tazobactam / meropenem may be started in patients with severe infection / poor response after discussing with the microbiologist/ respiratory physician.
If MRSA is suspected	Add vancomycin[3] 1g IV q12h	teicoplanin 400mg IV q12h for 3 doses followed by 400mg IV q24h	Duration of minimum 2 weeks.

Condition	Primary therapy	Alternative therapy / immediate beta-lactam hypersensitivity[1]	Comments
Lung abscess • Systemically well	amoxicillin 1g PO q8h + metronidazole 400mg PO q8h	clindamycin 300-450mg PO q6-8h	If guided aspiration / drainage is possible, pus should be sent for culture and ABST. If features of sepsis are present, blood culture should be sent.
• Systemically unwell	co-amoxiclav 1.2g IV q8h or ceftriaxone 1-2 g IV q24h/ cefotaxime 1-2 g IV q8h + metronidazole 500mg IV q8h	clindamycin[4] 600mg IV q8h + ciprofloxacin 400 mg IV q12h	If IV antibiotics are given, consider oral switch when sufficient clinical improvement is achieved. Contact microbiologist / respiratory physician for poorly responding infections, infections with suspected MDR organisms and for duration of treatment.
• If MRSA is suspected	Add vancomycin[3] 1g IV q12h	Add teicoplanin 400mg IV q12h for 3 doses followed by 400mg IV q24h	Exclude *Mycobacterium tuberculosis* infection.

Condition	Primary therapy	Alternative therapy / immediate beta-lactam hypersensitivity[1]	Comments
Pneumonia community acquired. • **Mild (CURB 65=0-1)** Out-patient a) No comorbidities: **CURB 65 score** can be used as a severity indicator.1 point is allocated for each of the following: • **C**onfusion (new onset) • **U**rea > 7mmol/l (20mg/dl) • **R**espiratory Rate > 30/min • **B**P (systolic< 90 or diastolic < 60mmHg) • **Age ≥ 65**years	amoxicillin 500mg-1g PO q8h or cefuroxime 500mg PO q12h Duration: 5 days	clarithromycin 500mg PO q12h or erythromycin 500mg PO q6h (for use in pregnancy) or doxycycline 200mg PO (first dose) followed by 100mg PO q24h Duration: 5 days	**CURB 65 score ≥ 1** needs hospital admission **CURB 65 score 4-5** may need ICU care (Outpatient settings- where urea is not available **CRB 65** may be used.**)** **Other factors to consider in hospitalization:** co-morbidities: poorly controlled DM, COPD, CRF, underlying malignancies etc. The decision to hospitalize a patient will ultimately depend on the judgment of the clinician. If antimicrobials were used within previous 3 months or in immediate beta-lactam allergy, contact microbiologist.

Condition	Primary therapy	Alternative therapy / immediate beta-lactam hypersensitivity[1]	Comments
Pneumonia community acquired. • **Mild (CURB 65=0-1)** Out-patient b) With comorbidities: alcoholism, COPD, bronchiectasis, DM	co-amoxiclav 625mg PO q8h/ cefuroxime 500mg PO q12h + clarithromycin 500mg PO q12h for a minimum duration of 5 days	clarithromycin 500mg PO q12h	
• **Moderate (CURB 65 = 2)** Patient requires hospitalization.	co-amoxiclav 1.2g IV q8h/ cefuroxime 1.5g IV q8h + clarithromycin 500mg PO q12h	levofloxacin* 750mg PO/IV q24h	*__Levofloxacin is a "Reserve Category" antibiotic__ (Annex 01). Erythromycin is the preferred macrolide during pregnancy.

Condition	Primary therapy	Alternative therapy / immediate beta-lactam hypersensitivity[1]	Comments
Pneumonia community acquired. • **Severe (CURB 65 = 3-5)** May need ICU admission.	cefotaxime 1-2 g IV q8h / ceftriaxone 1-2g IV q24h + clarithromycin 500mg IV/PO q12h	levofloxacin* IV 500mg q12h	*__Levofloxacin is a "Reserve Category" antibiotic__ (Annex 01). Contact microbiologist if patient presents with sepsis, haemoptysis, multilobar infiltrates, and leucopenia. Specific combination therapy is recommended for PVL (Panton-valentine leukocidin) producing CA-MRSA pneumonia.
• For suspected community acquired MRSA (CA- MRSA) pneumonia	Add vancomycin[3] 1g IV q12h	Add teicoplanin 400mg IV q12h for 3 doses then 400mg IV q24h	**Risk factors for *Pseudomonas* infection** • Chronic colonization or prior infection with *Pseudomonas* (particularly within the past 12 months) • Very severe COPD (FEV1<30% predicted) • Bronchiectasis on chest imaging • Broad spectrum antibiotics used within past 3 months. • Chronic systemic glucocorticoid use
• With risk factors for *Pseudomonas*: • Cystic fibrosis • COPD • Bronchiectasis	piperacillin-tazobactam 4.5g IV q6-8h or meropenem 1g IV q8h or imipenem 500mg IV q6h	ciprofloxacin 400mg IV q12h + gentamicin[2] 5-7mg/kg IV q24h	

Condition	Primary therapy	Alternative therapy / immediate beta-lactam hypersensitivity[1]	Comments
Suspected viral pneumonia	oseltamivir 75mg PO q12h Duration: 5 days		Effective only in pneumonia due to influenza virus. Send specimens for viral studies before starting antivirals.
Hospital acquired pneumonia (HAP) or ventilator-associated pneumonia (VAP) • **Early onset:** 3- 5 days after admission/ intubation **and No risk factors** for multi-drug resistant organisms (refer comments)	ceftriaxone 2g IV q24h/ cefotaxime 1g IV q8h + clarithromycin 500mg PO/IV q12h	levofloxacin* 750mg IV q24h or 500mg IV q12h	*__Levofloxacin is a "Reserve Category" antibiotic__ (Annex 01). **Risk factors for multi-drug resistant organisms:** • Recent hospitalization • Recent use of broad-spectrum antibiotics during preceding 90 days • Haemodialysis • Critical illness • Presence of comorbidities (such as severe lung disease or immunosuppression) • Colonization with multidrug-resistant bacteria

Condition	Primary therapy	Alternative therapy / immediate beta-lactam hypersensitivity[1]	Comments
• **Early onset: HAP/VAP with risk factors for MDR organisms** (refer comments) or • **Late onset HAP/VAP:** (>5 days after admission/ intubation	piperacillin-tazobactam 4.5g IV q6-8h / cefepime 1-2g IV q8-12h / meropenem 1g IV q8h +/- ciprofloxacin 400mg IV q12h / amikacin[2] 15mg/kg IV q24h/ gentamicin[2] 5-7mg/kg IV q24h	ciprofloxacin 400mg IV q12h + amikacin[2] 15mg/kg IV q24h or gentamicin[2] 5-7mg/kg IV q24h	For risk factors refer comment on page 107. Therapy should be guided by local antibiotic sensitivity data. Contact microbiologist. In severe infections and in obese patients, ciprofloxacin IV 400mg q8h can be given.
• **If MRSA is suspected**	Add vancomycin[3] 1g IV q12h	Add teicoplanin 400mg IV q12h for 3 doses followed by 400mg IV q24h	.

Prepared in collaboration with the Sri Lanka College of Pulmonologists and the Sri Lanka College of Internal Medicine

[1]Refer chapter 2
[2]TDM is recommended (refer chapter 6). Monitor renal functions and adjust doses (refer chapter 7). Vestibular function should be assessed when continued for more than 5 days.
[3]TDM is recommended (refer chapter 6). Monitor renal functions and adjust doses (refer chapter 7).
[4]For administration of clindamycin, refer chapter 7.

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Chapter 19: Sepsis/ Septic Shock

- Sepsis and septic shock are medical emergencies. Intravenous empirical broad spectrum antibiotic therapy with one or more agents to cover all likely pathogens should be started immediately, within the first hour of recognition of septic shock and definite / probable sepsis.
- For adults with possible sepsis without shock, rapid assessment for likelihood of infection is required. If concern for infection persists, administer antibiotics within three hours from the time when sepsis was first recognized.
- All patients presenting with sepsis should be evaluated for the presence of a focus of infection to control the source of sepsis.
- Septic screen with blood cultures, urine cultures (specially in elderly patients irrespective of the presence of typical symptoms) and other relevant specimens for culture should be collected prior to starting antibiotics. However, collection of specimens should not delay the administration of appropriate antibiotics.
- Empirical antifungal drugs should be considered in patients with risk factors for fungal infections.
- The antimicrobial regimen should be assessed daily. Clinical improvement and/or evidence of infection resolution to antibiotics may take 48 hours or more. Therefore, frequent change of antibiotics should be avoided unless a new focus of infection is suspected. If the presenting clinical syndrome is determined to be due to a non-infectious cause, the antimicrobial therapy should be stopped promptly.
- Empirical therapy should be changed to targeted therapy when culture and ABST results are available. De-escalation of antibiotics should be considered when possible.
- Unnecessary prolongation of empirical antibiotics should be avoided. Response to therapy should be assessed with clinical and investigation parameters.

- **If the source of sepsis is known, please refer to the relevant section of this guideline.**
- **Please refer table 22 below for selection of empirical antimicrobials for sepsis and septic shock of unknown source.**
- **Doses given in the tables are for patients with normal organ functions. Please refer Chapter 07 for dosing adjustments for continuation of antimicrobials in patients with deranged renal function.**

Table 22: Empirical antimicrobial therapy for sepsis/septic shock

Condition	Primary therapy	Alternative therapy / immediate beta lactam hypersensitivity[1]	Comments
Community acquired sepsis and septic shock	ceftriaxone 2g IV q24h/ cefotaxime 1g IV q8h + gentamicin[2] 5mg/kg IV q24h +/- metronidazole 500mg IV q8h or meropenem 1g IV q8h meropenem should be restricted for instances where 3rd generation cephalosporin use cannot safely be recommended	ciprofloxacin 400mg IV q12h + clindamycin[4] 600-900mg IV q6h + gentamicin[2] 5mg/kg IV q24h	Contact microbiologist for continuation of gentamicin/amikacin after 48 hours or for alternative therapy. Add vancomycin/teicoplanin if MRSA is suspected or in a known colonizer. Antifungals are considered in patients with risk factors for invasive candidiasis: E.g. immunosuppressed status (neutropenia, chemotherapy, transplant, chronic liver dysfunction), invasive vascular devices, total parenteral nutrition, recent abdominal surgery, high APACHE (Acute Physiology and Chronic Health Evaluation) score, prolonged antibiotic exposure and hospitalization, candida colonization at multiple sites

Condition	Primary therapy	Alternative therapy / immediate beta lactam hypersensitivity[1]	Comments
Healthcare associated sepsis and septic shock	piperacillin-tazobactam 4.5g IV q6-8h/ meropenem 1g IV q8h + amikacin[2] 15mg/kg IV q24h **If MRSA is suspected or in a known colonizer:** add teicoplanin 400mg IV q12h for 3 doses followed by 400mg IV q24h or vancomycin[3] 1g IV q12h	ciprofloxacin 400mg IV q12h + amikacin[2] 15mg/kg IV q24h **If MRSA is suspected or in a known colonizer:** add teicoplanin 400mg IV q12h for 3 doses followed by 400mg IV q24h or vancomycin[3] 1g IV q12h	However individual patient factors should be assessed even among the group of patients mentioned in page 111 when starting antifungals. Contact mycologist/ microbiologist for opinion on empirical antifungals.
Post-splenectomy sepsis	ceftriaxone 2g IV q24h/ cefotaxime 1g IV q8h +/- vancomycin[3] 1g IV q12h		Patients should be investigated for malaria and treated accordingly if there is a history of recent visit to an endemic country. In patients with immediate beta-lactam allergy contact microbiologist.

Prepared in collaboration with the College of Anaesthesiologists and Intensivists of Sri Lanka and The Ceylon College of Critical Care Specialists

[1]Refer Chapter 2
[2]TDM is recommended (refer chapter 6). Monitor renal functions and adjust doses (refer chapter 7). Vestibular function should be assessed when continued for more than 5 days.
[3]TDM is recommended (refer chapter 6). Monitor renal functions and adjust doses (refer chapter 7).
For critically ill patients, consider a loading dose of vancomycin (refer chapter 7).

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Chapter 20: Skin and Soft Tissue Infections

- This chapter addresses only common bacterial infections of acute onset.

Table 23: Empirical antimicrobial therapy for skin and soft tissue infections

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]/ high risk of MRSA	Comments
Erysipelas localized infection	amoxicillin 500mg PO q8h or cephalexin 500mg PO q8h or flucloxacillin 500mg PO q6h	erythromycin 500mg PO q6h or clindamycin 300mg PO q6-8h or co-trimoxazole 960mg PO q12h	

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]/ high risk of MRSA	Comments
Erysipelas If signs of systemic infection present	benzylpenicillin 2MU IV q6h or flucloxacillin 1g IV q6h or co-amoxiclav 1.2g IV q8h	vancomycin[3] 1g IV q12h	
Cellulitis • Mild (Outpatient therapy)	amoxicillin 500mg PO q8h or cephalexin 500mg PO q8h or flucloxacillin 500mg PO q6h	erythromycin 500mg PO q6h or clindamycin 300-450 mg PO q6-8h or co-trimoxazole 960mg PO q12h	Continue antibiotic therapy for 5 days. Extension of therapy is considered up to 10 days if there is lack of symptom resolution at 5 days.

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]/ high risk of MRSA	Comments
Cellulitis • Moderate (Inpatient therapy)	benzylpenicillin 2-4MU IV q4-6h or flucloxacillin 1-2g IV q6h	vancomycin[3] 1g IV q12h +/- clindamycin[4] 600-900mg IV q8h	In patients at risk for Gram negative infections or severe forms (neutropenic and immunocompromised patients) who do not respond to first-line therapy or patients with sepsis or septic shock, contact microbiologist. Send a blood culture before starting antibiotics. Duration: 14 days With good clinical response IV therapy can be converted to oral therapy.
Cellulitis • Severe (Inpatient therapy)	co-amoxiclav 1.2g IV q8h/ flucloxacillin 1-2g IV q6h +/- clindamycin[4] 600-900mg IV q8h	vancomycin[3] 1g IV q12h +/- clindamycin[4] 600-900mg IV q8h	

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]/ high risk of MRSA	Comments
Purulent cellulitis with furuncles (Outpatient therapy)	flucloxacillin 500mg PO q6h or cephalexin 500mg PO q6h	co-trimoxazole 960mg PO q12h or doxycycline 200mg PO (loading dose) followed by 100mg PO q12h	Incision & drainage should be combined with antibiotic treatment. In patients at risk for Gram negative infections or severe forms (neutropenic and immunocompromised patients) who do not respond to first-line therapy or patients with sepsis or septic shock, contact microbiologist.
Purulent cellulitis with carbuncles or abscesses (Inpatient therapy)	flucloxacillin 1-2g IV q6h + /- clindamycin[4] 600-900mg IV q8h	vancomycin[3] 1g IV q12h +/- clindamycin[4] 600-900mg IV q8h	

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]/ high risk of MRSA	Comments
Necrotizing fasciitis Types: Monomicrobial Polymicrobial Gas gangrene Fournier's Gangrene	piperacillin-tazobactam 4.5g IV q6-8h / ticarcillin-clavulanic acid 3.2g IV q8h + clindamycin[4] 600-900mg IV q8h +/- vancomycin[3] 1g IV q12h / teicoplanin 400mg IV q12 h for three doses then 400mg IV q24h	meropenem 1g IV q8h / imipenem 500mg IV q6h + clindamycin[4] 600-900mg IV q8h +/- vancomycin[3]1g IV q12h / teicoplanin 400mg IV q12 h for three doses then 400mg IV q24h **In immediate beta-lactam hypersensitivity[1]** ciprofloxacin 400mg IV q12h + clindamycin[4] 600-900mg IV q8h +/- vancomycin[3] 1g IV q12h / teicoplanin 400mg IV q12h for three doses then 400mg IV q24h	Early and adequate surgical debridement is required. Blood culture and infected fluid/tissue specimen culture should be arranged. In critically ill patients presenting with sepsis/ septic shock and in a setting with high ESBL/MDRO, consider carbapenem instead of piperacillin-tazobactam. Contact microbiologist. Vancomycin/ teicoplanin should be added if suspecting MRSA or if not responding within 48 hours.

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Cutaneous abscesses, furuncles, carbuncles	For small lesions <5cm, I & D would be sufficient. Antibiotic treatment is not indicated. For large lesions >5cm/ undrainable areas/ multiple lesions/ high risk patient for severe infection: flucloxacillin 500mg-1g PO q6h or cephalexin 500mg PO q8h	clindamycin 300-450mg PO q6-8h or co-trimoxazole 960mg PO q12h	I & D and send pus for culture and ABST. If no response after 2-3 days review for complications and consider IV therapy. If the MRSA risk is high, consider adding vancomycin/ teicoplanin. Contact microbiologist.
Diabetic foot ulcer • Mild infection	co-amoxiclav 625mg PO q8h	clindamycin 300-450mg PO q6-8h + ciprofloxacin 500mg PO q12h	Antibiotic therapy is not recommended for ulcers without signs of inflammation. Use rotational antiseptics.

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Diabetic foot ulcer • Severe infection	piperacillin-tazobactam 4.5g IV q6-8h/ ticarcillin-clavulanic acid 3.2g IV q8h +/- vancomycin[3] 1g IV q12h/ teicoplanin 400mg IV q12h for three doses followed by 400mg IV q24h	**In immediate beta-lactam hypersensitivity[1]** vancomycin[3] 1g IV q12h/ teicoplanin 400mg IV q12h for three doses followed by 400mg IV q24h + ciprofloxacin 400mg IV q12h	Exclude osteomyelitis. Contact microbiologist. Vancomycin/ teicoplanin should be added if suspecting MRSA or if not responding within 48 hours.
Impetigo Bullous/ non-bullous	Topical 2% fusidic acid q12h for 5 days +/- flucloxacillin 500mg PO q6h / cephalexin 500mg PO q8h	erythromycin 500mg PO q6h **If MRSA is suspected:** co-trimoxazole 960mg PO q12h or clindamycin 300-450mg PO q6-8h or doxycycline 200mg PO (loading dose) followed by 100mg PO q12h	Crusts need to be removed with soap and water or saline before local application. Oral antibiotics are recommended for patients with numerous lesions or in outbreaks. Duration 7 days.

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Mastitis • Mild (symptoms <24hours) If symptoms are not resolving within 12 to 24 hours with physiological methods, consider antibiotics.	flucloxacillin 500mg PO q6h or cephalexin 500mg PO q8-12h	erythromycin 250mg-500mg PO q6h or clindamycin 300mg PO q6h	Breast feeding can be continued or milk from the infected breast can be expressed manually or by a pump.
• Moderate-severe mastitis (symptoms >24hours/ fever/ unwell/ breast abscess)	flucloxacillin 1-2g IV q6h	**In immediate beta-lactam hypersensitivity[1]/ high risk of MRSA:** vancomycin[3] 1g IV q12h or teicoplanin 400mg IV q12h for three doses then 400mg IV q24h or clindamycin[4] 600-900mg IV q8h	Percutaneous aspiration / I&D if there is an abscess and pus should be sent for culture and sensitivity. Switch to oral therapy when symptoms resolve.

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Paronychia (Acute) If soft tissue swelling is present without fluctuance, the infection may resolve with only warm soaks 3-4 times daily	flucloxacillin 500mg PO q6h	erythromycin 500mg PO q6h or clindamycin 300-450mg PO q6-8h	I & D if there is an abscess. Send pus for culture.
Surgical site infections • Mild	Systemic antibiotics are not necessary		Manage with antiseptics.
• Mild to moderate infections with surrounding cellulitis Non-GI Tract surgery	flucloxacillin 500mg PO q6h or co-trimoxazole 960mg PO q12h	clindamycin 300-450 mg PO q6-8h	Send pus for culture prior to antibiotic therapy. Antibiotic choice in surgical site infections may differ according to the organism profile and antibiogram of surgical site infections of the hospital.
GI Tract surgery	co-amoxiclav 625mg PO q8h	ciprofloxacin 400mg IV q12h + clindamycin[4] 600mg IV q8h	

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Surgical site infections • Severe infections with systemic symptoms Non-GI Tract surgery	flucloxacillin 1-2g IV q6h/ co-amoxiclav 1.2g IV q8h +/- gentamicin[2] 5mg/kg IV q24h	vancomycin[3] 1g IV q12h/ teicoplanin 400mg IV q12h for three doses then 400mg IV q24h + ciprofloxacin 400mg IV q12h	Contact microbiologist. Send pus/tissue specimens for culture prior to antibiotic therapy. Vancomycin/ teicoplanin should be added if suspecting MRSA. Antibiotic choice in surgical site infections may differ according to the organism profile and antibiogram of surgical site infections of the hospital.
GI Tract surgery	ticarcillin-clavulanic acid 3.2g IV q8h or piperacillin-tazobactam 4.5g IV q6-8h	gentamicin[2] 5mg/kg IV q24h + ciprofloxacin 400mg IV q12h + metronidazole 500mg IV q8h	

Prepared in collaboration with the College of Surgeons of Sri Lanka.

[1]Refer Chapter 2
[2]TDM is recommended (refer Chapter 6). Monitor renal functions and adjust doses (refer Chapter 7). Vestibular function should be assessed when continued for more than 5 days.
[3]TDM is recommended (refer Chapter 6). Monitor renal functions and adjust doses (refer Chapter 7). According to the patient's body weight a loading dose of vancomycin should be given.
[4]For administration of clindamycin, refer Chapter 7.

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- Urine cultures should be collected before starting empirical antibiotics.
- Continuation of antibiotic therapy should be guided by culture and ABST results.
- All male patients with UTI should be investigated to exclude underlying urinary tract abnormalities.
- Patients should be advised on proper collection of urine samples.
- It is important to indicate the type of specimen on the request form for specimens other than mid-stream urine samples (e.g. from an indwelling urinary catheter, in-out urinary catheter, urine from renal pelvis, ureter, suprapubic).
- Screening and treatment of asymptomatic bacteriuria (with or without a urinary catheter) is not recommended unless prior to urological procedures which anticipate mucosal bleeding or early post kidney transplant period.
- Recurrent UTIs could be due to re-infections or relapses. Recurrent UTIs are defined as ≥2 UTI episodes within 6 months or ≥3 UTI episodes within 12 months in adults. Relapses are due to the same bacterial strain as in the previous UTI. Re-infections are caused by a different strain of the same bacterial species of the previous episode or a different species. In such patients, empirical antibiotic management should be guided by the choices given in the tables, until culture results are available.

Table 24: Empirical antimicrobial therapy for Urinary Tract Infections (UTI) in adults

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Cystitis **Acute uncomplicated cystitis** Cystitis in otherwise healthy non-pregnant women	nitrofurantoin 50mg PO q6h/ 100mg PO q12h (sustained release capsules) or cephalexin 500mg PO q12h	norfloxacin 400mg PO q12h or co-trimoxazole 960mg PO q12h	Previous antibiotic therapy, previous episodes of UTI and susceptibility patterns should be considered when selecting antibiotics. Do not use nitrofurantoin if CrCl<45 ml/min. Avoid multiple antibiotics. Duration of therapy: 5 days for nitrofurantoin and 3 days for other antibiotics.
Complicated cystitis • Cystitis in patients with anatomical and functional anomalies • Cystitis with underlying disease which increase the risk of more serious outcome or treatment failure • Cystitis in men	nitrofurantoin 50mg PO q6h/ 100mg PO q12h (sustained release capsules) or norfloxacin 400mg PO q12h or cefuroxime 500mg PO q12h or co-amoxiclav 625mg PO q8h	pivmecillinam 200mg PO q8h **In immediate beta-lactam hypersensitivity[1]** nitrofurantoin/norfloxacin can be used	Duration of therapy: 7 days. If the patient cannot tolerate oral antibiotics, consider IV preparations. Recurrent UTIs could be due to re-infections or relapses. Treatment should be guided by previous culture and ABST.

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Acute Prostatitis	ciprofloxacin 500mg PO q12h	co-trimoxazole 960mg PO q12h	For mild cases with prompt responses 14 days of antibiotic is recommended. For delayed response or severe cases longer duration of therapy is needed. If there is a risk of STI refer to guidelines issued by NSACP. If there is associated sepsis, consider intravenous antibiotics.
Pyelonephritis **Acute uncomplicated pyelonephritis in non-pregnant women** Pyelonephritis in the absence of structural or functional anomalies of the urinary tract • Out-patient • In-patient	co-amoxiclav 625mg PO q8h co-amoxiclav 1.2g IV q8h +/- gentamicin[2] 5mg/kg IV q24h (for 48 hours)	ciprofloxacin 500mg PO q12h ceftriaxone 1-2g IV q24h/ cefotaxime 1g IV q8h +/- gentamicin[2] 5mg/kg IV q24h (for 48 hours)	Patients who don't have clinical evidence of sepsis and are able to take oral medication, can be managed as outpatient. Urine culture and susceptibility tests should always be performed. Blood culture should be done in patients with sepsis. Review intravenous antibiotics in 48 hours and consider stepping down to oral antibiotics where possible depending on the clinical improvement and sensitivity pattern. A combination of antibiotics may be considered in sepsis or if there are concerns about antibiotic resistance.

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
See above	see above	**In immediate beta-lactam hypersensitivity[1]** ciprofloxacin 400 mg IV q12h +/- gentamicin[2] 5mg/kg IV q24h (for 48 hours)	Duration of treatment: 7-14 days according to the antibiotic used. Contact microbiologist.
Complicated pyelonephritis • pyelonephritis in patients with anatomical and functional anomalies in the urinary tract • pyelonephritis in patients with underlying disease which increases the risk of more serious outcome or treatment failure. • pyelonephritis in men	co-amoxiclav 1.2g IV q8h + gentamicin[2] 5mg/kg IV q24h / amikacin[2] 15mg/kg IV q24h (for 48 hours) or ceftriaxone 1-2 g IV q24h / cefotaxime 1g IV q8h + gentamicin[2] 5mg/kg IV q24h / amikacin[2] 15mg/kg IV q24h (for 48 hours)	cefepime 1-2g IV q12h/ piperacillin-tazobactam 4.5g IV q8h/ ticarcillin-clavulanic acid 3.2g IV q8h +/- gentamicin[2] 5mg/kg IV q24h / amikacin[2] 15mg/kg IV q24h (for 48 hours) **In immediate beta-lactam hypersensitivity[1]** ciprofloxacin 400mg IV q12h + gentamicin[2] 5mg/kg IV q24h/ amikacin[2] 15mg/kg IV q24h	Contact microbiologist for advice on choice and duration of antibiotic therapy in complicated pyelonephritis. Review aminoglycoside therapy at 48 hours.

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Uncomplicated or complicated pyelonephritis with sepsis/ septic shock/ emphysematous pyelonephritis	piperacillin-tazobactam 4.5g IV q8h +/- gentamicin[2] 5mg/kg IV q24h / amikacin[2] 15mg/kg IV q24h (for 48 hours) or meropenem 1g IV q8h/ imipenem 500mg IV q6h +/- gentamicin[2] 5mg/kg IV q24h / amikacin[2] 15mg/kg IV q 24h (for 48 hours)	**In immediate beta lactam hypersensitivity[1]** ciprofloxacin 400mg IV q12h + amikacin[2] 15mg/kg IV q24h (for 48 hours)	Contact microbiologist for advice on choice and duration of antibiotic therapy. Consider surgical opinion.
Catheterized patient Asymptomatic bacteriuria	Screening for and treatment of catheter associated asymptomatic bacteriuria is not recommended except in pregnant women, patients who undergo urologic procedures or early post kidney transplant period. Antimicrobial prophylaxis should not be routinely used.		

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Catheter-Associated Urinary Tract Infections Cystitis in men and non-pregnant women Without evidence of upper UTI	nitrofurantoin 50mg PO q6h or 100mg PO q12h (sustained release capsules) or norfloxacin 400mg PO q12h	co-amoxiclav 625mg PO q8h or co-trimoxazole 960mg PO q12h or pivemecillinam 200mg PO q8h **In immediate beta lactam hypersensitivity[1]** nitrofurantoin, norfloxacin or co-trimoxazole can be given	Urinary catheter should be removed or replaced. A urine specimen for culture should be obtained from a new catheter or mid-stream sample if catheter is removed, prior to initiating antimicrobial therapy. Do not use nitrofurantoin if CrCl<45 ml/min. Duration: 7 days if responds promptly after change of catheter and 10-14 days is recommended for those with delayed response or pyelonephritis regardless of whether the patient remains catheterized or not. Contact microbiologist.

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Catheter-Associated Urinary Tract Infections upper UTI without sepsis in men and non-pregnant women	ticarcillin-clavulanic acid 3.2g IV q8h + /- gentamicin[2] 5mg/kg IV q24h / amikacin[2] 15mg/kg IV q24h (for 48 hours)	**In immediate beta-lactam hypersensitivity** ciprofloxacin 400mg IV q12h +/- amikacin[2] 15 mg/kg IV q24h (for 48 hours)	Refer page 130 for comments.
Catheter-Associated Urinary Tract Infections upper UTI with sepsis or septic shock	piperacillin-tazobactam 4.5g IV q8h +/- amikacin[2] 15mg/kg IV q24h or meropenem 1g IV q8h/ imipenem 500mg IV q6h +/- amikacin[2] 15mg/kg IV q24h (for 48 hours)	**In immediate beta lactam hypersensitivity[1]** ciprofloxacin 400mg IV q12h + amikacin[2] 15mg/kg IV q24h (for 48 hours)	

Prepared in collaboration the with the Ceylon College of Physicians

[1]Refer Chapter 2

[2]TDM is recommended (refer Chapter 6). Monitor renal functions and adjust doses (refer Chapter 7). Vestibular function should be assessed when continued for more than 5 days.

UTI in Pregnancy – Refer chapter 27 on empirical antibiotics for pregnancy related infections.

UTI in childhood – Refer chapter 26 on empirical antibiotics for paediatric infections.

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SECTION C

Chapter 22: Special Infections

This chapter includes the choice of antimicrobials for the treatment and prevention of several selected infections.

Table 25: Empiric antibiotic therapy for brucellosis, enteric fever, leptospirosis, melioidosis, rickettsial infections (including typhus) and tetanus

Condition	Primary therapy	Alternative therapy	Comments
Brucellosis **Non-focal**			
▪ Adults and children>8yrs	doxycycline 100mg PO q12h for 6 weeks + gentamicin[2] 5mg/kg/day IV or IM q24h for 7-10 days	doxycycline 100mg PO q12h for 6 weeks + rifampicin 15mg/kg PO (600-900mg) divided in q12h/q8h for 6 weeks	Send samples for serological diagnosis (blood and CSF) and culture for *Brucella* spp. (blood and bone marrow). Consult microbiologist for suspected/ confirmed cases or those presenting with focal / complicated infections including endocarditis and neuro-brucellosis who need prolonged treatment and alternative therapy. Doxycycline to be considered in <8 years only if no other options available. Refer to BNF for gentamicin dosage in paediatric population.
▪ Children <8yrs	co-trimoxazole 5mg/kg PO (TMP component) q12h for 6 weeks + rifampicin 15-20mg/ kg/day PO divided in q12h/q8h for 6wks		

Condition	Primary therapy	Alternative therapy	Comments
Enteric fever Mild-Moderate / uncomplicated (GI manifestations only) Severe or complicated cases Eradication of chronic carriage	ciprofloxacin* 400mg IV q12h or 500mg PO q12h for 7-14 days ceftriaxone 2g IV q24h for 10-14 days ciprofloxacin 500mg PO q12h for 28 days depending on susceptibility of the isolate	azithromycin 1g PO single dose followed by 500mg PO q24h for 5-7days or chloramphenicol* 500mg PO q6h for 14 days/ 12.5-25mg/kg IV q6h for 14 days	Obtain blood samples for culture. Tailor treatment according to latest local susceptibility data. Clinical improvement precedes defervescence. In cases of continuing fever, contact microbiologist and exclude endocarditis and other complications. *Empirical treatment should only be based on local or individual susceptibility patterns for these options.
Leptospirosis In mild illness Moderate-severe disease	doxycycline 100mg PO q12h for 7 days benzylpenicillin 1.5 MU IV q6h or ceftriaxone 1g IV q24h/ cefotaxime 1g IV q6-8h for 7 days	azithromycin 1g PO loading dose on day 1 followed by 500mg PO q24h for 2 more days in mild disease ampicillin 500mg – 1g IV q6h for 7 days or doxycycline 100mg IV (preferred in severe disease)	Pre-exposure prophylaxis: Doxycycline 200mg PO once weekly. Start 1 to 2 days before exposure and continue throughout the period of the exposure. Currently, there is no recommended pre-exposure prophylaxis that is safe for pregnant and lactating women. Contact microbiologist for treatment options in immediate beta-lactam hypersensitivity.

Condition	Primary therapy	Alternative therapy	Comments
Melioidosis Intensive phase ▪ Adults Single focus mild to moderate infection	ceftazidime 120 mg/kg/day IV up to 2g q6-8h	for non-CNS infections imipenem 50mg/kg/day IV q8h	Intensive phase/induction stage should be followed by eradication stage. The duration and dose of intensive phase may vary according to severity and site from 2 to 8 weeks. Contact microbiologist in immediate beta-lactam hypersensitivity.
Severe infection	meropenem 1-2g IV q8h		
CNS infection	meropenem 2g IV q8h		
▪ Children Single focus mild to moderate infection	ceftazidime 50 mg/kg/day IV q6h	for non-CNS infections imipenem *<1 week, >1.5 kg*: 25 mg/kg IV q12h *1-4 weeks, >1.5 kg*:25 mg/kg IV q8h *4 weeks-3 months, >1.5 kg*: 25 mg/kg IV q6h *>3 months*: 15-25 mg/kg IV q6h (not to exceed 2 g/day) *>12 years*: 10-15 mg/kg IV q6h	
CNS infection/severe infection	meropenem 50 mg/kg IV up to 2g		

Condition	Primary therapy	Alternative therapy	Comments
Melioidosis Adjunct therapy ▪ **Adults**	co-trimoxazole *<40kg:* 10+50 mg/kg/day PO in two divided doses *40-60kg:* 240+1200mg PO q12h *>60kg:* 320+1600mg PO q12h + folic acid 5mg PO q24h		Oral co-trimoxazole is added during intensive phase therapy in cutaneous melioidosis, osteomyelitis or septic arthritis, central nervous system infection, deep seated collections, or infections with poor response to treatment.
▪ **Children**	co-trimoxazole 6+30 mg/kg up to 240+1200 mg PO q12h + folic acid *For < 4 years:*0.3 mg PO q24h *For >4yers:* 0.4 mg PO q24h		

Condition	Primary therapy	Alternative therapy	Comments
Melioidosis Eradication phase ▪ **Adults**	cotrimoxazole *>60kg:* 320/1600mg PO q12h *40-60kg:* 240/1200mg PO q12h *<40 kg*: 160 mg/800mg PO q12h + folic acid 5mg PO q24h	doxycycline 100 mg PO q12h or co-amoxiclav 625mg PO q8h	The duration and dose of eradication phase may vary from 3- 6 months according to severity and site.
▪ **Children**	cotrimoxazole 6+30 mg/kg up to 240+1200 mg PO q12h + folic acid *For < 4 years:*0.3 mg PO q24h *For >4yers:* 0.4 mg PO q24h		

Condition	Primary therapy	Alternative therapy	Comments
Rickettsial infections (Scrub typhus, spotted fever group rickettsioses, typhus fever and other miscellaneous infections such as Q fever and ehrlichiosis) ▪ **Adult**	doxycycline 200mg PO/IV loading dose on day 1 followed by 100mg PO/IV q12h for 5–7 days (10-14 days in severe disease)	chloramphenicol 500mg IV q6h or 50 mg/kg PO per day in four divided doses (maximum dose 4g/d) for 7 – 10 days or azithromycin 500mg PO q24h for 5 days	Azithromycin is recommended for pregnant women and patients with doxycycline allergy. Doxycycline treatment should result in prompt defervescence. Persistent fever > 48 hours should raise the need to consider alternative diagnosis. Treatment decisions for Rickettsial pathogens should never be delayed while awaiting laboratory confirmation as this can lead to severe disease and long-term sequelae or death.
▪ **Children**	doxycycline PO/IV	chloramphenicol PO/IV or azithromycin PO	Refer to BNF for Children for doses.

Condition	Primary therapy	Alternative therapy	Comments
Tetanus	tetanus immunoglobulin (TIG) 500IU IM (Part of TIG dose can be infiltrated around the wound if identified) + metronidazole 500mg IV q6h or 400mg PO q8h for 7-10 days	intravenous immunoglobulin (IVIG) 200-400mg/kg can be given. + benzylpenicillin 2-4MU IV q4-6h for 7-10 days or doxycycline 200mg PO loading dose on day 1 followed by 100mg PO q12h for 7-10 days	TIG or IVIG should be given as soon as the diagnosis of tetanus is considered. IV or intrathecal preparations of TIG can be considered if available. If wound is identified, debridement is essential. Vaccination with tetanus toxoid before discharge is required as patients with tetanus will not develop immunity following infection.

[1]Refer chapter 2.
[2]TDM is recommended (refer chapter 6). Monitor renal functions and adjust doses (refer chapter 7). Vestibular function should be assessed when continued for more than 5 days.

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Chapter 23: Trauma, Bites and Burns

- Antibiotic prophylaxis is recommended only for certain categories of trauma.
- The need for tetanus immunization should be assessed on each trauma victim.
- Common indications for empirical antibiotic therapy or prophylaxis and appropriate regimens are given in the tables.
- Antibiotics suggested as prophylaxis to be evaluated by the end of indicated time frame to stop if no evidence of infection or to continue if evidence suggestive of active infection seen.

Table 26: Empirical and prophylactic antibiotic therapy for selected types of trauma

Type of trauma	Primary therapy/ prophylaxis	Alternative therapy/ prophylaxis	Comments
Head and neck trauma • Penetrating cranio-cerebral injury	cefuroxime 1.5g IV stat followed by 750mg IV q8h + metronidazole 500mg IV q8h	co-amoxiclav 1.2g IV q8h or **In immediate beta-lactum hypersensitivity**[1] vancomycin[3] 1g IV q12h + metronidazole 500mg IV q8h	Duration: 5 days
• Depressed skull fractures	Antimicrobial prophylaxis is not required. If there is cranial CSF leak, consider pneumococcal vaccine.		
• Simple basal skull fracture with or without CSF leak	If the patient develops signs of meningitis, refer to empirical antibiotics for meningitis associated with neuro-trauma (chapter 12).		

Type of trauma	Primary therapy/ prophylaxis	Alternative therapy/ prophylaxis	Comments
Penetrating abdominal trauma	co-amoxiclav 1.2g IV q8h +/- gentamicin[2] 5mg/kg IV q24h or cefuroxime 1.5g IV stat followed by 750mg IV q8h + metronidazole 500mg IV q8h +/- gentamicin[2] 5mg/kg IV q24h	ciprofloxacin 400mg IV q12h + metronidazole 500mg IV q8h +/- gentamicin[2] 5mg/kg IV q24h	Reassess after 24 hours regarding continuation of antibiotics. Discontinue prophylactic antibiotics after 24 hours if there is no acute hollow viscous injury. If there are ruptured viscera, consider treatment than prophylaxis.

Type of trauma	Primary therapy/ prophylaxis	Alternative therapy/ prophylaxis	Comments
Thoracic trauma Penetrating chest injury requiring chest drain placement	cefuroxime 1.5g IV stat followed by 750mg IV q8h + metronidazole 500mg IV q8h or co-amoxiclav 1.2g IV q8h only for 24 hours	clindamycin[4] 600mg IV q6-8h	Reassess after 24 hours to decide on continuation. Prophylaxis is not indicated for blunt chest trauma.
Open limb fractures • Type I and II (Refer table 27 for classification)	flucloxacillin 2g IV q6h	clindamycin[4] 600mg IV q6h	Metronidazole IV should be added in the presence of faecal or potential clostridial contamination (e.g. farm related injuries). Review the requirement of continuation of antibiotics beyond 24hours.
• Type III	cefuroxime 1.5g IV stat followed by 750mg IV q8h + metronidazole 500mg IV q8h +/- gentamicin[2] 5mg/kg IV q24h	clindamycin[4] 600mg IV q6-8h + gentamicin[2] 5mg/kg IV q24h	In type III fractures, antibiotics should be continued for 72 hours after injury or not more than 24 hours after soft tissue coverage has been achieved.

Table 27: Open Fractures – Gustilo Classification

Type I	Open fracture with a skin wound < 1 cm in length and clean
Type II	Open fracture with a laceration > 1 cm in length without extensive soft tissue damage, flaps, or avulsions
Type III	Open segmental fracture with > 10 cm wound with extensive soft tissue injury or a traumatic amputation (special categories in Type III include gunshot fractures and open fractures caused by farm injuries)
Type IIIA	Adequate soft tissue coverage
Type IIIB	Significant soft tissue loss with exposed bone that requires soft tissue transfer to achieve coverage
Type IIIC	Associated vascular injury that requires repair for limb preservation.

Table 28: Empirical therapy for bites and infected burns

Type of trauma	Primary therapy	Alternative therapy	Comments
Bites (Human and animal)	co-amoxiclav1.2g IV or co-amoxiclav 625mg PO q8h Infected bites: 5 days Prophylaxis: only 3 days	metronidazole 400mg PO q8h + doxycycline 200mg PO (loading dose) followed by 100mg PO q24h for 2-7 days Infected bites: 5 days Prophylaxis: only 3 days	Risk of tetanus/rabies and blood-borne infection to be considered.
Burns • **with no evidence of infection**	Available evidence does not support systemic antibiotic therapy for clinically non-infected burn wounds.		
• **with evidence of infection**	flucloxacillin 2g IV q6h	clindamycin[4] 600mg IV q6h	Select antibiotics to cover *Pseudomonas* spp. and *Enterobacterales* , based on culture and severity of infection.
• **with evidence of infection and critically ill**	piperacillin-tazobactam 4.5g IV q8h +/- vancomycin[3] 1g IV q12h	ciprofloxacin 400mg IV q12h + vancomycin[3] 1g IV q12h	

[1]Refer chapter 2.

[2]TDM is recommended (refer chapter 6). Monitor renal functions and adjust doses (refer chapter 7). Vestibular function should be assessed when continued for more than 5 days.
[3]TDM is recommended (refer chapter 6). Monitor renal functions and adjust doses (refer chapter 7). According to the patient's body weight a loading dose of vancomycin should be given.
[4]For administration of clindamycin, refer chapter 7.

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SECTION D

Chapter 24: Infections in Patients with Immunodeficiency

- Patients with immune deficiency are at risk of getting infections with commonly encountered pathogens as well as with opportunistic bacteria, viruses, fungi and parasites. They also have a greater risk of reactivation of latent infections.
- The risk of infection and the type of pathogens depend on the cause and severity of immuno-suppression and the site of infection. They can have a prolonged period of replication and take longer for clearance of the infectious agents and therefore, may need a longer duration of treatment.
- Appropriate samples should be sent for aetiological diagnosis after discussing with microbiologist/virologist/ mycologist/ parasitologist.
- Although a diverse group of conditions can cause secondary immunodeficiency, infections seen among the following groups of immunocompromised patients are addressed in this chapter.
    1. Solid organ transplant (SOT) recipients
    2. Human immunodeficiency virus infection/ acquired immunodeficiency syndrome (HIV/AIDS) patients
    3. Blood and other malignancies
    4. Patients on long term corticosteroids therapy, antimetabolites and biologics (immunosuppressive therapy)
- Empirical therapy for infections in neutropenic patients is described in chapter 26.
- Separate guidelines on empirical and prophylactic use of antimicrobials in patients with inborn errors of immunity (primary immune deficiencies) and HSCT recipients are available in the official website of SLCM.
- Treatment guidelines for tuberculosis are available in the National Manual for Tuberculosis Control.
- Persons with HIV infection may be at greater risk for acquisition of STIs. Reactivation of genital viral infections including HSV and HPV occurs frequently and can have a protracted course in patients with HIV infection and in transplant recipients. Refer to the guidelines issued by National STD/AIDS Control Programme (NSACP).

Table 29: Pathogens causing infections with greater severity in patients with secondary immunodeficiency

Bacteria	Fungi	Viruses	Parasites
Streptococcus pneumoniae *Listeria monocytogenes* *Nocardia* spp. *Salmonella* spp. *Legionella* spp. *Mycobacterium tuberculosis* non-tuberculous mycobacteria	*Candida* spp *Cryptococcus* spp. *Pneumocystis jirovecii* *Histoplasma capsulatum* *Coccidioides* spp. *Blastomyces* spp. *Aspergillus* spp. *Fusarium* spp. Mucorales group	HSV VZV CMV EBV HHV-6 Hepatitis B virus BK virus Respiratory viruses	*Toxsoplasma gondii* *Cryptosporidium parvum* *Strongyloidiasis stercoralis*

Table 30: Special investigations for aetiological diagnosis (in addition to routine bacterial cultures)

Suspected condition/infection	Microbiological investigations
Acute renal dysfunction/ Chronic renal nephropathy (especially in renal transplant recipients)	Quantitative PCR for CMV, BK virus, Adenovirus
Central line associated blood stream infections (CLABSI)	Blood from central line: fungal culture Blood from peripheral vein: fungal culture (*Candida* spp. grows in aerobic bacterial blood culture bottles as well)

Suspected condition/infection	Microbiological investigations
Community acquired pneumonia/ pneumonitis and Hospital acquired pneumonia	Sputum/endotracheal aspirate/broncho alveolar lavage (BAL): • Direct microscopy for fungi and parasites including worms (*Strongyloides stercoralis*) • PCR (e.g. GeneXpert) for *Mycobacterium tuberculosis* • Real time multiplex PCR for respiratory viruses and bacteria, quantitative PCR for CMV, HSV and EBV • Fungal culture BAL/induced sputum: Microscopy and PCR for *Pneumocystis jirovecii* BAL/Serum: *Aspergillus* spp. antigen (galactomannan)/ PCR for *Aspergillus* spp. Serum: Aspergillus precipitants, 1,3 Beta-D-glucan test Blood: Bacterial culture and fungal culture Urine: Legionella and pneumococcal urinary antigen Biopsy samples: direct microscopy, fungal culture and histopathology special staining for fungi
Intra-abdominal infections	Blood, peritoneal fluid/pus/surgical specimens: fungal direct microscopy, mycobacterial and fungal culture Serum: 1,3 Beta D glucan test Biopsy specimens: histopathology special staining for fungi
Colitis/Enteritis/Gastritis	Biopsy: CMV and adenovirus PCR

Suspected condition/infection	Microbiological investigations
Acute gastroenteritis Chronic gastroenteritis	Faeces: • *Clostridioides difficile* toxin/enzyme detection • Microscopy of modified Zeihl Neelsen (acid-fast) stained smear for cryptosporidium oocyst • Antigen detection test for *Cryptosporidium* spp. • Macroscopic worm identification and differentiation of strongyloides and hookworm larvae by culture Blood: culture for mycobacteria if disseminated *Mycobacterium avium* complex (MAC) is suspected especially in HIV/AIDS
Skin and soft tissue infections	Pus/tissue/blister fluid/scrapings from ulcers or skin lesions: • Ziehl-Neelsen and modified Ziehl-Neelsen stain • Fungal direct microscopy • Direct microscopy for protozoa • Tzanck smear • Fungal and mycobacterial culture • Histology with special stains for fungi where necessary • HSV, VZV and enterovirus PCR • If suggestive of Kaposi sarcoma: HHV-8 PCR • If suggestive of HPV: PCR MRSA screening

Suspected condition/infection	Microbiological investigations
Central nervous system infections	CSF: • Modified Ziehl-Neelsen stain • Fungal direct microscopy, India ink stain • PCR (Eg: GeneXpert) for *Mycobacterium tuberculosis* • HSV, VZV, EBV, CMV, HHV-6, BKV and JCV quantitative PCR • Enterovirus PCR CSF and urine: Cryptococcal antigen test Blood: CMV, EBV, adenovirus, VZV, HSV quantitative PCR Serology: Toxoplasma IgM, IgG antibodies
Sinus infections	Superficial / endoscopic/surgical collection of necrotic tissue (urgent sampling)/sinus aspirate: fungal direct microscopy and culture

Table 31: Empirical antimicrobial therapy for common infections in patients with secondary immunodeficiency

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Asymptomatic bacteriuria/ candiduria	Empirical treatment is not indicated. In renal transplant recipients, repeat culture with appropriate technique to rule out contamination. During the first 3 months of post-transplant, consider treatment for 5–7 days; beyond 3 months, post-transplant, avoid treatment unless associated with a rise in serum creatinine. Treatment is indicated if awaiting instrumentation. Await culture susceptibility results and select a narrow-spectrum antibiotic according to antibiotic sensitivity pattern.		
Symptomatic urinary tract infection	Similar to non-immunocompromised patients. Refer chapter 21.		
Symptomatic candiduria	fluconazole 3-6mg/kg PO or IV q24h		
Community acquired pneumonia/Hospital acquired pneumonia (HAP should be suspected if the patient has been hospitalised during the preceding 3 months)	Similar to non-immunocompromised patients. Refer chapter 18. Anti-pseudomonal and anti-MRSA cover should be provided if risk factors for these infections are present. oseltamivir 75 mg PO q12h if suggestive of viral pneumonia.		Empirical antifungal chemotherapy is only indicated when clinical and radiological presentation strongly suggests a fungal origin. If not responding to initial empirical treatment, uncommon bacterial, fungal and parasitic infections should be suspected. Contact microbiologist.

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Central nervous system infections e.g. acute meningitis, chronic meningitis, meningoencephalitis, brain abscesses or focal neurological deficits	ampicillin 2g IV q4h + cefotaxime 2g IV q6h/ ceftriaxone 2g IV q12h + vancomycin[3] 30–45 mg/kg IV q8–12h + aciclovir 10 mg/kg IV q8h	chloramphenicol 1-1.5g IV q6h + vancomycin[3] 30-45mg/kg IV q8–12h + cotrimoxazole 5mg/kg (trimethoprim component) PO q5-8 h + aciclovir 10mg/kg IV q8h	Dexamethasone 0.15 mg/kg IV started before or with the first dose of antibiotic. Then continue 6 hourly for 2- 4 days. Add metronidazole when brain abscess is suspected. If not responding to initial antimicrobials, mycobacterial, fungal and parasitic infections should be suspected. Contact microbiologist.
Post liver transplant intra-abdominal infections	piperacillin-tazobactam 4.5g IV q6h	meropenem 1g IV q8h **In immediate beta-lactam hypersensitivity[1]** ciprofloxacin 400mg IV q12h + metronidazole 500mg IV q8h	Consider antifungal in the early post-transplant period if risk factors are present. If CMV colitis is suspected IV ganciclovir should be considered. Contact microbiologist.
Moderate to severe gastroenteritis (≥6 stools per day or bloody stool)	ciprofloxacin 500mg PO q12h **In severe illness** ceftriaxone 1-2g IV q24h	ciprofloxacin 400mg IV q12h	Blood cultures are indicated when fever is present.

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
For patients with chronic diarrhoea (>14 days) without severe clinical signs	Empiric antibiotics therapy is not indicated.		
***Clostridioides difficile*-associated infections (CDI)**	Refer chapter 13		Immunocompromised patients are at increased risk for CDI.
Oropharyngeal Candidiasis • **Mild** • **Moderate to severe**	nystatin suspension 500,000 units (5ml) swish and swallow q6h for 7-14 days fluconazole 100-200 mg PO q24h for 10 days	For fluconazole-refractory disease, itraconazole solution 200 mg PO q24h for up to 28 days	For people living with HIV, antiretroviral therapy is strongly recommended to reduce the incidence of recurrent opportunistic infections.
Candida oesophagitis	fluconazole 200–400 mg PO (3–6 mg/kg) q24h for 14–21 days For patients who cannot tolerate oral therapy, fluconazole 400mg (6 mg/kg) IV q24h	For fluconazole-refractory disease, itraconazole solution 200 mg PO q24h or voriconazole* 200 mg (4mg/kg) IV/PO q12h for 14–21 days	For people living with HIV, antiretroviral therapy is strongly recommended to reduce the incidence of recurrent opportunistic infections. ***Voriconazole is a "Reserve Category" antifungal** (Annex 01).

Condition	Primary therapy	Alternative therapy/ In immediate beta-lactam hypersensitivity[1]	Comments
Bacterial skin and soft tissue infections	Refer chapter 20		
Mucocutaneous Herpes Simplex Virus infection	aciclovir 400mg PO 5 times per day for 7 days or aciclovir 5mg/kg IV q8h for 5-7 days		Continue treatment until lesions have completely healed.
Varicella zoster virus infection (chicken pox)	aciclovir 800mg PO 5 times per day for 7 days Patients with complications, aciclovir 10mg/kg IV infusion q8h for 5 days		Continue treatment until lesions have completely healed.
Herpes Zoster (shingles)	aciclovir 800mg PO 5 times per day for 7-10 days or in severe cases aciclovir 10 mg/kg IV q8h for 7-14 days		IV aciclovir can be considered with following risk factors. • Advanced age > 60y • Corticosteroid dose > 7.5 mg to 10 mg prednisone-equivalent dose (PEQ) • History of recurrent shingles • Presence of ocular/neurologic or disseminated disease. Continue treatment until lesions have completely healed.

[1]Refer chapter 2

[3]TDM is recommended (refer Chapter 6). Monitor renal functions and adjust doses (refer chapter 7). According to the patient's body weight a loading dose of vancomycin should be given.

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Chapter 25: Febrile Neutropenia/ Infections in HSCT Recipients

- Empiric antimicrobial therapy for infections in HSCT (haemopoietic stem cell transplant) recipients is similar to that of febrile neutropenia.
- In febrile neutropenic patients, urgent therapy with intravenous broad-spectrum antimicrobials and assessing the patient's hemodynamic stability is crucial.
- Septic screen including blood cultures (preferably 2) has to be performed before commencing antibiotics.
- Empirical therapy should be based on local antimicrobial susceptibility pattern and reviewed when culture results are available.
- If the focus of infection is known, site specific treatment should be started without delay.
- Those who have received intensive chemotherapy for solid malignancies and patients with aggressive haematological malignancies are at a higher risk for severe prolonged neutropenia and require immediate attention.
- Neutropenic patient with severe sepsis may not have fever and other clinical features typical of bacterial infections, particularly the elderly or patients on corticosteroids.

  - **Febrile neutropenia:** absolute neutrophil count of <500 cells/mm^3 or that is expected to decrease to < 500 cells/mm^3 during the next 48 hours and single oral temperature of ≥ 38.3^{0}C or a temperature of ≥38^{0}C sustained over 1 hour.

  - **Duration of therapy** is decided by the duration of neutropenia, causative organism and the site of infection. Appropriate antimicrobials should be continued at least for the duration of neutropenia (until absolute neutrophil count is > 500 cells/mm^3) or longer if clinically indicated. Patients should be monitored for adverse effects if prolonged antimicrobial courses are used.

Table 32: Empirical therapy for patients with febrile neutropenia

Condition	Primary therapy	Alternative therapy / Immediate beta-lactam hypersensitivity[1]	Comments
Febrile neutropenia in low-risk adults • Outpatient status at the time of development of fever • Anticipated short duration of severe neutropenia (≤100 cells/mm^3 for <7days) • Good performance status • No comorbidities • No hepatic insufficiency • No renal insufficiency • MASCC risk index score 21 or above	ciprofloxacin 500mg PO q12h + co-amoxiclav 625 mg PO q8h or ciprofloxacin 400mg IV q12h + co-amoxiclav 1.2g IV q8h	ciprofloxacin 500mg PO q12h + clindamycin 300-450mg PO q6h or ciprofloxacin 400mg IV q12h + clindamycin[4] 600mg IV q8h	If patients are discharged on oral antibiotics, ensure careful observation and access to medical care 24/7. Review in 3-5 days to evaluate response and culture results. Possibility of ciprofloxacin resistance should be considered if there is a recent exposure to fluoroquinolones. Contact microbiologist.

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Febrile neutropenia in high-risk patients	piperacillin-tazobactam 4.5g IV q6h or ticarcillin-clavulanate 3.2g IV q8h or cefepime 1-2g IV q8-12h +/- gentamicin[2] 5mg/kg IV q24h/ amikacin[2] 15mg/kg IV q24h	ceftazidime 1-2g IV q8h **In immediate beta-lactam hypersensitivity[1]** ciprofloxacin 400mg IV q12h +/- amikacin[2] 15mg/kg q24h	Combination therapy could be considered if antibiotic resistance is suspected (due to recent antibiotic exposure or institutional resistance pattern) or proven with previous culture results. Contact microbiologist if fever persists beyond 96 hours of antibacterial therapy or if there is clinical deterioration.
Patients colonized with MRSA / clinical evidence of a vascular catheter related infection / skin and soft tissue infection/ pneumonia/ in a unit with a high incidence of MRSA infection	Add vancomycin[3] 15mg/kg IV 12h in addition to above antibiotics	Add teicoplanin 400mg IV q12h for 3 doses followed by 400mg q24h in addition to above antibiotics	Teicoplanin is preferred in patients with renal impairment.

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Patients with risk factors for candida infections	Add fluconazole 400mg IV/PO q12h to above antibiotics		Risk factors for candida infections: Patients who have persistent or recurrent fever after 4-7 days of broad-spectrum antibiotics or overall duration of neutropenia for>7 days and no identified source of fever
Patients with risk factors for mould infections e.g. neutropenia lasting >10 days, allogenic HSCT recipients, treatment with high dose corticosteroids.	Add voriconazole* 6mg/kg IV q12h 2 doses followed by 4mg/kg IV q12h or voriconazole* 400mg PO q12h followed by 200mg PO q12 h	amphotericin B* deoxycholate 1mg /kg IV q24h	If the patient has renal insufficiency, liposomal amphotericin B* 3-5mg/kg IV once daily may be started after discussing with microbiologist. Read the product leaflet carefully before using both products of amphotericin B*. ***Amphotericin B and voriconazole are "Reserve Category" antifungals** (Annex 01).

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Febrile neutropenia in critically ill or haemodynamically unstable patients	meropenem 1-2g IV q8h/ imipenem 1g IV q8h or 500mg IV q6h + vancomycin[3] 1g IV q12h +/- amikacin[2]15mg/kg IV q24h	ciprofloxacin 400mg IV q12h + teicoplanin 400mg IV q12h for 3 doses followed by 400mg IV q24h + amikacin[2] 15mg/kg IV q24h/ gentamicin[2] 5mg/kg IV q24h	If typhlitis is suspected add metronidazole.

Prepared in collaboration with Sri Lanka College of Oncologists

[1]Refer Chapter 2
[2]TDM is recommended (refer Chapter 6). Monitor renal functions and adjust doses (refer chapter 7). Vestibular function should be assessed when continued for more than 5 days.
[3]TDM is recommended (refer Chapter 6). Monitor renal functions and adjust doses (refer chapter 7). According to the patient's body weight a loading dose of vancomycin should be given.
[4]For administration of clindamycin, refer Chapter 7.

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- Pregnant women with evidence of sepsis should be assessed by a senior medical professional as early as possible and guidelines for the management of sepsis should be followed.
- Risk of infection to the fetus and benefits and toxicity of antimicrobials to both the mother and the fetus should be considered carefully. Refer to chapter 5 on safety of antimicrobials in pregnancy and lactation.

Table 33: Empirical antimicrobials for infections in pregnancy

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Asymptomatic bacteriuria in pregnancy			Routine screening with urine culture is currently not practised. If asymptomatic bacteriuria is confirmed, treat for 4-7 days according to antibiotic sensitivity.
Lower UTI in pregnancy	nitrofurantoin 50mg PO q6h or 100mg (sustained- release) PO q12h	cefalexin 500mg PO q12h Contact microbiologist in immediate beta-lactam hypersensitivity	Avoid nitrofurantoin in 3rd trimester and in women with an eGFR of <45ml/minute. Treat for 7days. Perform urine cultures before starting antibiotics.

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Pyelonephritis in pregnancy	cefuroxime 750mg IV q8h	cefotaxime 1g IV q8h Contact microbiologist in sepsis/ immediate beta-lactam hypersensitivity[1]	Perform blood and urine cultures before starting antibiotics. Switch to oral therapy following clinical response. Complete 7-10 days depending on severity and response.
Septic abortion **If critically ill**	co-amoxiclav 1.2g IV q8h + gentamicin[2] 5 mg/kg IV q24h + metronidazole 500mg IV q8h / clindamycin[4] 600mg IV q6h piperacillin-tazobactam 4.5g IV q6-8h / meropenem 1g IV q8h + clindamycin[4] 600mg IV q6h	ceftriaxone 1-2g IV q24h + metronidazole 500mg IV q8h / clindamycin[4] 600mg IV q6h **In immediate beta-lactam hypersensitivity[1]** ciprofloxacin 400mg IV q12h + gentamicin[2] 5 mg/kg IV q24h + clindamycin[4] 600mg IV q6h	Antibiotics should be started promptly prior to evacuation of the products of conception and continued afterwards. Contact microbiologist if suspecting STI. Send blood for cultures. If risk factors for MRSA are present replace clindamycin with vancomycin and metronidazole.
Preterm prelabour rupture of membranes (PPROM) from 24+ weeks of gestation	erythromycin 250mg PO q6h for 10 days or until the woman is in established labour (whichever is sooner)		Obtain a vaginal swab for culture during the speculum examination for diagnosing PPROM. Assess mother and fetus regularly to detect infection.

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Chorioamnionitis (Intra amniotic infection syndrome - IAIS) **If critically ill**	ampicillin 2g IV q6h + gentamicin[2] 5mg/ kg IV q24h + metronidazole 500mg IV q8h piperacillin-tazobactam 4.5g IV q6-8h or meropenem 1g IV q8h	cefotaxime 1g IV q8h + metronidazole 500mg IV q8h **In immediate beta-lactam hypersensitivity[1]** clindamycin[4] 600mg IV q6h + gentamicin[2] 5mg/kg IV q24h	Send relevant specimens for culture including blood cultures. If risk factors for MRSA are present add vancomycin or in instances where clindamycin is used, replace clindamycin with vancomycin and metronidazole.
Intrapartum prophylaxis for group B streptococcal (GBS) infection	Intrapartum benzylpenicillin 3g (5 MU) IV loading dose followed by 1.2g (2 MU) IV q4h until delivery	Intrapartum ampicillin 2g IV loading dose followed by 1g IV q4h until delivery **In immediate beta lactam hypersensitivity[1]** clindamycin[4] 900 mg IV q8h or vancomycin[3] 1g IV q12h until delivery	Intrapartum antibiotics are indicated in • GBS carriage • GBS bacteriuria • previously GBS infected baby • maternal pyrexia in labour (≥38°C) • rupture of membranes ≥ 18hours.

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Postpartum endometritis • **Mild disease**	co-amoxiclav 625mg PO q8h or ampicillin 2g IV q6h + gentamicin[2] 5mg/kg IV q24h + clindamycin[4] 600mg IV q6h / metronidazole 500mg IV q8h	cefuroxime 500mg PO q12h/ ceftriaxone 1-2g IV q24h + metronidazole 400mg PO q12h **In immediate beta lactam hypersensitivity[1]** gentamicin[2] 5 mg/kg IV q24h + clindamycin[4] 600mg IV q6h/ metronidazole 500 mg IV q8h	Contact microbiologist if suspecting STI.
• **Moderate disease**	ampicillin 2g IV q6h + gentamicin[2] 5mg/kg IVq24h + clindamycin[4] 600mg IV q6h / metronidazole 500mg IV q8h	ceftriaxone 1-2g IV q24h + metronidazole 500mg IV q8h	

Condition	Primary therapy	Alternative therapy / immediate beta-lactam hypersensitivity[1]	Comments
Postpartum endometritis • **If critically ill**	piperacillin-tazobactam 4.5g IV q6-8h or meropenem 1g IV q8h	**In immediate beta lactam hypersensitivity[1]** ciprofloxacin 400mg IV q12h + gentamicin[2] 5mg/kg IV q24h + clindamycin[4] 600-900mg IV q6h	Contact microbiologist if suspecting STI.
Episiotomy infections • **Superficial**	co-amoxiclav 625mg PO q8h or cefuroxime 500mg PO q12h + metronidazole 400mg PO q8h	clindamycin 300mg PO q6h +/- gentamicin[2] 5mg/ kg IV q24h	
• **Deep infections/ necrotizing fasciitis/ myonecrosis**	piperacillin–tazobactam 4.5g IV q6-8h / ticarcillin-clavulanate 3.2g IV q8h + clindamycin[4] 600-900mg IV q8h	ceftazidime 1-2g IVq8h + clindamycin[4] 600-900mg IV q8h **In immediate beta-lactam hypersensitivity[1]** ciprofloxacin 400mg IV q12h + gentamicin[2] 5mg/kg IV q24h + clindamycin[4] 600-900mg IV q8h	Prompt surgical interventions are required. If risk factors for MRSA are present, replace clindamycin with vancomycin and metronidazole.

Condition	Primary therapy	Alternative therapy / immediate beta-lactam hypersensitivity[1]	Comments
Influenza in pregnancy	oseltamivir 75mg PO q12h for 5 days		Oseltamivir should be started within 48 hours of onset of symptoms in a suspected or confirmed influenza infection during pregnancy at any trimester. But it is still recommended to start antiviral therapy even after 48 hours in late presentations. Send specimens for viral studies before starting antivirals if facilities are available.
Chickenpox	aciclovir 800mg PO 5 times per day for 7 days		Therapy should ideally be given within the first 24 hours of onset of rash. Intravenous aciclovir should be given under specialist care to all pregnant women with severe chickenpox. Neonates of mothers who have chickenpox 7 days prior to or 7 days after delivery should be given a single dose of varicella zoster immunoglobulin. Contact virologist/microbiologist.

Condition	Primary therapy	Alternative therapy/ immediate beta-lactam hypersensitivity[1]	Comments
Post exposure prophylaxis following a significant exposure to a case of chicken pox or shingles	< 20 weeks of gestation: single dose of varicella zoster immunoglobulin (VZIG) >20 weeks of gestation: single dose of varicella zoster immunoglobulin or aciclovir 800mg PO q6h from day 7 to 14 after exposure	If VZIG is not available, aciclovir 800mg PO q6h from day 7 to 14 after exposure can be considered. Contact virologist.	When contact occurs with chickenpox or shingles, a careful history must be taken to confirm the significance of exposure and the susceptibility of the patient. If exposure is significant, immunity for VZV should be established. If patient is not having evidence of immunity, refer to VOG as soon as possible after the first exposure (up to 10days) for administering VZIG or considering prophylactic aciclovir.
Vulvovaginal candidiasis **Uncomplicated infection (first or single isolated infection)**	clotrimazole pessary 500mg intravaginally at night as a single dose	clotrimazole pessary 100-200mg intravaginally at night for 7 consecutive nights or miconazole vaginal cream (2%) 5g intravaginally at night for 7 consecutive nights	Oral therapies must be avoided in pregnancy. Topical imidazoles are a safe and effective alternative. Refer to VOG for the management of non-responding/complicated/recurrent infections.

Prepared in collaboration with the Sri Lanka College of Obstetricians and Gynaecologists, Sri Lanka

[1]Refer Chapter 2
[2]TDM is recommended (refer Chapter 6). Monitor renal functions and adjust doses (refer chapter 7). Vestibular function should be assessed when continued for more than 5 days.
[3]TDM is recommended (refer Chapter 6). Monitor renal functions and adjust doses (refer chapter 7). According to the patient's body weight a loading dose of vancomycin should be given.
[4]For administration of clindamycin, refer Chapter 7.

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Chapter 27: Infections in Children

- This chapter includes the initial empirical therapy recommended for infections commonly encountered among children.
- Relevant specimens for microbiological investigations should be collected before starting empirical antimicrobials.
- Opinion of the paediatrician should be obtained in following occasions:
  - Immediately, when managing neonates/infants/children with evidence of sepsis/septic shock
  - Immediately, when managing infections in immunocompromised/neutropenic patients with or without fever
  - As early as possible when managing neonates/infants/children who are clinically stable but systemically unwell or with suspected/previously diagnosed ongoing medical/surgical conditions
  - When there is poor response to initial empirical therapy or clinical deterioration within 48hours
- Empirical therapy should be reviewed in 48 hours (or earlier if indicated), with a view of narrowing down initial broad spectrum empirical therapy with 'Watch category' (Annex 1) antimicrobials and combinations of beta- lactams.
- Empirical therapy is expected to cover common pathogens with predicted sensitivity patterns and may not be effective in the treatment of uncommon/rare pathogens with different sensitivity patterns.
- Culture and ABST results should be used for further management when available.
- BNF for Children should be referred to calculate the dosage regimes for different age groups (preterm babies are considered as neonates up to 180 days depending on the gestational age).
- Contraindications, cautions, adverse drug reactions and drug interactions described in the BNF for Children should be carefully considered before prescribing antimicrobials and appropriate monitoring should be continued during treatment.
- Allergy to any of the antimicrobials should be clearly documented in a manner that is visible to prescribers and nursing staff administering medicine.
- Refer Annex 2 for further details on prescribing antibacterials for children.

Table 34: Empirical therapy for infections in children

Condition	Primary therapy	Alternative therapy	Comments
Sepsis			
Neonatal sepsis • Early onset sepsis (EOS) < 72 hours of age Suspected EOS Severe EOS*	 benzylpenicillin IV + gentamicin IV benzylpenicillin IV + cefotaxime IV		Collect blood culture before giving the first dose of antibiotics. However, antibiotics should not be delayed if blood culture facilities are not readily available. Contact paediatrician/neonatologist immediately. IV ampicillin is preferred when there is a possibility of *Listeria monocytogenes* infection. Exclude CNS involvement by performing lumbar puncture (LP) as early as possible.
• Late onset sepsis (LOS) >72 hours of age Severe LOS* (Risk of Multi Drug Resistant Organisms - MDRO)	cefotaxime IV meropenem IV + vancomycin IV	flucloxacillin IV + gentamicin IV	MDRO risk factors include: low birth weight, prematurity, invasive procedures, IV lines in situ, antibiotic use and NICU stay. If risk factors for MRSA are present, add IV vancomycin.
• Probable necrotizing enterocolitis (NEC)	cefotaxime IV + metronidazole IV	piperacillin-tazobactam IV (after excluding CNS infection)	Contact paediatrician immediately. Antifungal therapy with fluconazole should be considered for premature infants with a history of recent or prolonged antibiotic therapy or for infants with very low birth weight.

Condition	Primary therapy	Alternative therapy	Comments
Sepsis			
Sepsis beyond neonatal period • Unknown focus of sepsis in **haemodynamically stable immunocompetent** child	cefotaxime IV/ ceftriaxone IV		Collect blood and urine for culture. Contact paediatrician immediately. Consider adding IV vancomycin if suspecting MRSA (having long lines, undergoing haemodialysis, having prosthesis in situ etc.) Consider possible immunodeficiencies in children with unusual presentations / recurrent infections. Adding IV amikacin should be considered when suspecting Gram negative sepsis depending on the possible focus and when there is a possibility of healthcare associated infection. IV ciprofloxacin and IV amikacin can be used as alternatives to beta-lactams when there is a history of immediate beta-lactam hypersensitivity.
• Unknown focus of sepsis in **haemodynamically unstable immunocompetent** child	cefotaxime IV/ ceftriaxone IV + gentamicin IV/ amikacin IV	piperacillin-tazobactam IV +/- IV amikacin (if meningitis is unlikely)	
• Unknown focus of sepsis in **haemodynamically unstable Immunocompromised** child including neutropenic child with evidence of sepsis	meropenem IV +/- gentamicin IV	piperacillin-tazobactam IV +/- amikacin IV (if meningitis is unlikely)	

Condition	Primary therapy	Alternative therapy	Comments
Sepsis			
Febrile neutropenia in haemodynamically stable child	piperacillin-tazobactam IV	meropenem IV	Refer to paediatrician immediately.
Central nervous system infections**			
Meningitis in neonates	benzylpenicillin IV + cefotaxime IV (meningitis dose)		Perform blood and CSF cultures as early as possible. Refer BNF for Children for meningitis doses.
Meningitis beyond neonatal period	ceftriaxone IV/ cefotaxime IV (meningitis dose) +/- vancomycin IV		
Shunt infection, post-neurosurgery, head trauma or CSF leak	vancomycin IV + ceftazidime IV		
Encephalitis	aciclovir IV		Send CSF for viral studies including HSV PCR.
Brain abscess	cefotaxime IV/ ceftriaxone IV + metronidazole IV	**In immediate beta- lactam hypersensitivity[1]** vancomycin IV + ciprofloxacin IV + metronidazole IV	Consider adding IV vancomycin if MRSA is suspected. The cephalosporin should be IV ceftazidime/ IV cefepime if *Pseudomonas* is suspected.

Condition	Primary therapy	Alternative therapy	Comments
Bacterial endocarditis			
Endocarditis - native valves/ late prosthetic valve, after 1 year of surgery	benzylpenicillin IV/ ceftriaxone IV + gentamicin IV	**In immediate beta- lactam hypersensitivity[1]** vancomycin IV + gentamicin IV	At least 3 blood cultures from different venipuncture sites should be obtained, with the first and last samples drawn at least 1 hour apart.
Endocarditis - early prosthetic valve or nosocomial	vancomycin IV + gentamicin IV + cefepime IV/ ceftazidime IV		At least 3 blood cultures from different venipuncture sites should be obtained, with the first and last samples drawn at least 1 hour apart. Contact paediatric cardiologist and microbiologist.
Urinary tract infections**			
UTI **1-3 months of age** Refer to the section on neonatal sepsis for the management of neonates suspected to have UTI	co-amoxiclav IV/ cefuroxime IV/ cefotaxime IV		Collect urine sample for culture before starting antibiotics. Infants younger than 3 months with a possible UTI should be referred for specialist care immediately and the treatment should be with parenteral antibiotics.

Condition	Primary therapy	Alternative therapy	Comments
Urinary Tract Infections**			
Afebrile UTI /lower UTI (bacteriuria without systemic symptoms or signs)			Empirical therapy is not recommended unless the child has significant symptoms.
• **3 months - 3years of age**	co-amoxiclav PO/ cefalexin PO/ cefuroxime PO	**In immediate beta-lactam hypersensitivity[1]** nitrofurantoin PO / co-trimoxazole PO	Reassess 48 hours after initiating empirical therapy. Children <3 years should be given IV antibiotics initially if oral therapy is not tolerated or compliance is poor.
• **3 years or above**	cefalexin PO/ co-amoxiclav PO/ cefuroxime PO/ nitrofurantoin PO	nalidixic acid PO / co-trimoxazole PO	Empiric therapy for recurrent UTI can be guided by previous ABST. Children on prophylactic antibiotics should not receive the same antibiotic for empirical therapy. Do not use nitrofurantoin if eGFR is <45 ml/min.

Condition	Primary therapy	Alternative therapy	Comments
Urinary tract infections**			
Febrile UTI/ Upper UTI **≥3 months of age** (bacteriuria and fever of ≥38°C or bacteriuria with loin pain/ tenderness)	co-amoxiclav PO/ cefalexin PO/ cefuroxime PO or co-amoxiclav IV/ cefuroxime IV/ ceftriaxone IV/ cefotaxime IV	**In immediate beta-lactam hypersensitivity[1]** gentamicin*** IV/ amikacin*** IV/ ciprofloxacin PO/IV	Start IV therapy and refer for specialist care if the child is, 1. not tolerating oral therapy 2. ill or septic 3. having possible obstructive uropathy 4. immunosuppressed The latter 3 groups need **immediate** specialist care.
Bone and joint infections			
Septic arthritis / Acute osteomyelitis • **< 3 months** **Septic arthritis/ Acute osteomyelitis** • **3 months to < 5 years**	cefotaxime IV ceftriaxone IV/ cefotaxime IV	**In immediate beta- lactam hypersensitivity[1]** ciprofloxacin IV + clindamycin IV/ vancomycin IV **In immediate beta- lactam hypersensitivity[1]** ciprofloxacin IV + clindamycin IV/ vancomycin IV	In all suspected acute septic arthritis/ osteomyelitis blood and synovial fluid aspirates and bone biopsies for culture should be obtained. Urgent surgical intervention reduces the risk of serious complications in septic arthritis but should not delay antibiotics. If community acquired MRSA is suspected, consider adding IV vancomycin or IV clindamycin. Total 3 weeks of IV antibiotics are indicated for neonates.

Condition	Primary therapy	Alternative therapy	Comments
Bone and joint infections			
Septic arthritis / Acute osteomyelitis • **5 years and above**	flucloxacillin IV	cefuroxime IV / ceftriaxone IV **In immediate beta- lactam hypersensitivity[1]** clindamycin IV	See page 178.
Respiratory tract infections			
Acute cough with upper respiratory tract infection	Antibiotics are not indicated		Most commonly due to vial aetiology. Review if symptoms are persistent or worsening.
Bronchiolitis	Antibiotics are not indicated		
Acute cough with high risk of complications or systemically unwell	amoxicillin PO	clarithromycin PO	High risk category involves children with comorbidities and younger children born prematurely.
Community acquired pneumonia • **Non-severe**	amoxicillin PO +/- clarithromycin PO	cefuroxime PO + /- clarithromycin PO **In immediate beta- lactam hypersensitivity[1]** vancomycin IV/ teicoplanin IV + clarithromycin PO	

Condition	Primary therapy	Alternative therapy	Comments
Respiratory tract infections			
Community acquired pneumonia • **Severe**	co-amoxiclav IV/ cefuroxime IV/ ceftriaxone IV/ cefotaxime IV + clarithromycin PO	**In immediate beta- lactam hypersensitivity[1]** vancomycin IV/ teicoplanin IV + ciprofloxacin IV	Blood cultures should be collected. Consider IV vancomycin if MRSA is suspected. Contact microbiologist if melioidosis is suspected based on clinical or epidemiological features.
Hospital acquired pneumonia • **Non-severe/ early onset and not at risk of harbouring MDRO**	co-amoxiclav PO/ IV or cefuroxime PO/ IV	**In immediate beta lactam hypersensitivity[1]** ciprofloxacin PO/ IV	
Hospital acquired pneumonia • **Severe/ late onset/ symptoms of sepsis/ at risk of harbouring MDRO**	piperacillin-tazobactam IV	**In immediate beta- lactam hypersensitivity[1]** ciprofloxacin IV + teicoplanin IV/ vancomycin IV	Conditions with a high risk of harbouring MDRO include severe lung disease, immunosuppression, recent use of broad-spectrum antibiotics, prior colonization with MDRO, recent contact with health care settings etc.

Condition	Primary therapy	Alternative therapy	Comments
Respiratory tract infections			
Ventilator associated pneumonia • **Onset <5days after intubation** • **Onset ≥ 5days after intubation**	ceftriaxone IV/ cefotaxime IV piperacillin-tazobactam IV	**In immediate beta- lactam hypersensitivity[1]** ciprofloxacin IV + teicoplanin IV/ vancomycin IV	Contact microbiologist.
Aspiration pneumonia	co-amoxiclav PO/ IV	**In immediate beta lactam hypersensitivity[1]** clindamycin IV/ PO + ciprofloxacin IV	
Empyema	co-amoxiclav IV/ PO + clindamycin IV or cefuroxime IV/ PO + clindamycin IV	**In immediate beta lactam hypersensitivity[1]** clindamycin IV + ciprofloxacin IV	

Condition	Primary therapy	Alternative therapy	Comments
Respiratory tract infections			
Probable pertussis (Cough for two or more weeks with one of the following - paroxysms of cough, inspiratory whoop, post-tussive emesis without another known cause) • **< 1 month of age** • **≥ 1 month**	azithromycin PO clarithromycin PO/ erythromycin PO/ azithromycin PO	**If macrolides are contraindicated** co- trimoxazole PO	
Oto-laryngeal/ Oral/ Sinus/ Upper airway infections			
Sore throat/ Tonsillitis If bacterial infection is suspected	phenoxymethylpenicillin PO or amoxicillin PO	**In immediate beta- lactam hypersensitivity**[1] clarithromycin PO	Most commonly due to viral aetiology. Antibiotics are indicated if systemically unwell/ high risk of complications/ pus on tonsils/ severely inflamed tonsils
Scarlet fever	phenoxymethylpenicillin PO or amoxicillin PO	**In immediate beta- lactam hypersensitivity**[1] clarithromycin PO	Scarlet fever is a bacterial illness that develops in children who have streptococcal sore-throat. Patients will have distinctive pink-red rash.

Condition	Primary therapy	Alternative therapy	Comments
Oto-laryngeal/ Oral/ Sinus/ Upper airway infections			
Otitis externa Antibiotics are indicated if there is evidence of cellulitis /disease extending outside the ear canal/ systemic infection	flucloxacillin PO/ co-amoxiclav PO + ciprofloxacin ear drops	**In immediate beta- lactam hypersensitivity[1]** clarithromycin PO + ciprofloxacin ear drops	
Malignant (necrotizing) otitis externa	ceftazidime IV or piperacillin-tazobactam IV	**In immediate beta- lactam hypersensitivity[1]** ciprofloxacin IV + ciprofloxacin ear drops	Refer for specialist care.
Acute otitis media Antibiotics are indicated if: <5 months of age/ systemically unwell/ <2 years of age with bilateral acute otitis media/ evidence of otorrhoea/ having cranio-facial malformations	amoxicillin PO/ co-amoxiclav PO	**In immediate beta- lactam hypersensitivity[1]** clarithromycin PO	Refer for specialist care if severe infection or evidence of complications are present.

Condition	Primary therapy	Alternative therapy	Comments
Oto-laryngeal /Oral/ Sinus/Upper airway infections			
Epiglottitis / bacterial tracheitis (laryngo-tracheo-bronchitis)	cefotaxime IV/ ceftriaxone IV	**In immediate beta- lactam hypersensitivity[1]** levofloxacin IV + clindamycin IV	Consider IV vancomycin if MRSA is suspected. **Levofloxacin is a "Reserve Category" antibiotic** (Annex 01).
Acute bacterial cervical lymphadenitis/ Acute bacterial parotitis	co-amoxiclav PO/ IV	**In immediate beta- lactam hypersensitivity[1]** clarithromycin PO or clindamycin PO/ IV	Antibiotics are not indicated for otherwise well child with few systemic symptoms or generalized lymphadenopathy.
Mastoiditis without intracranial involvement	co–amoxiclav IV	**In immediate beta- lactam hypersensitivity[1]** clindamycin IV	Refer to an ENT surgeon.
Mastoiditis with intracranial involvement	ceftriaxone IV/ cefotaxime IV + metronidazole IV + vancomycin IV	**In immediate beta- lactam hypersensitivity[1]** ciprofloxacin IV + metronidazole IV + vancomycin IV	Refer to an ENT surgeon.

Condition	Primary therapy	Alternative therapy	Comments
Oto-laryngeal /Oral/ Sinus/Upper airway infections			
Retro pharyngeal cellulitis/ abscess • **Mild** • **Severe**	co-amoxiclav IV ceftriaxone IV + metronidazole IV	**In immediate beta-lactam hypersensitivity[1]** clindamycin IV +/- ciprofloxacin IV	Refer to an ENT surgeon.
Eye infections			
Pre-septal/ periorbital cellulitis	co-amoxiclav PO/IV	**In immediate beta-lactam hypersensitivity[1]** clindamycin PO/IV +/- ciprofloxacin PO/IV	Review within 24-36 hours.
Orbital cellulitis	ceftriaxone IV + clindamycin IV	**In immediate beta-lactam hypersensitivity[1]** ciprofloxacin IV + clindamycin IV	Refer to an eye surgeon. Add IV vancomycin if MRSA is suspected.

Condition	Primary therapy	Alternative therapy	Comments
Eye infections			
Ophthalmia neonatorum	cefotaxime IV single dose (immediately) + chloramphenicol eye drops If *C. trachomatis* infection is suspected add azithromycin PO		Need urgent ophthalmology review. Send specimens (swabs) for chlamydia and gonococcus after discussing with the district clinics of NSACP. Investigate for maternal infection (refer to NSACP guideline) Consider HSV if vesicles are present and add IV aciclovir.
Intra-abdominal/ Gastrointestinal tract infections			
Community acquired complicated intra-abdominal infections • **Mild to moderate**	cefuroxime IV + metronidazole IV or co-amoxiclav IV or cefotaxime IV/ ceftriaxone IV + metronidazole IV	**In immediate beta-lactam hypersensitivity[1]** ciprofloxacin IV + metronidazole IV +/- gentamicin IV	Source identification and control is vital.

Condition	Primary therapy	Alternative therapy	Comments
Intra-abdominal/ Gastrointestinal tract infections			
Community acquired complicated intra-abdominal infections • **Severe/ health care associated infections**	piperacillin-tazobactam IV or meropenem IV	**In immediate beta-lactam hypersensitivity[1]** ciprofloxacin IV + metronidazole IV +/- gentamicin IV	Source identification and control is vital.
Acute gastroenteritis **Watery diarrhoea**	Antibiotics are not indicated.		Most cases of acute gastroenteritis are caused by viruses and are self-limiting.
Blood and mucus diarrhoea • **Patient systemically well** • **Patient systemically unwell**	Antibiotic therapy is not usually indicated. ciprofloxacin PO or azithromycin PO or cotrimoxazole PO		The risk of haemolytic uraemic syndrome increases if antibiotics are given. IV cefotaxime/ceftriaxone may be indicated in severe illness caused by S*higella* spp.
Suspected cholera	doxycycline PO		

Condition	Primary therapy	Alternative therapy	Comments
Skin and soft tissue infections			
Cellulitis • **Mild**	phenoxymethylpenicillin PO or flucloxacillin PO	**In immediate beta-lactam hypersensitivity**[1] erythromycin PO	
• **Moderate to severe**	flucloxacillin IV or ceftriaxone IV	**In immediate beta-lactam hypersensitivity**[1] clindamycin IV	If rapidly progressive add IV clindamycin. If risk factors for MRSA are present add IV vancomycin.
Necrotizing fasciitis	piperacillin-tazobactam IV + clindamycin IV	**In immediate beta-lactam hypersensitivity**[1] ciprofloxacin IV + clindamycin IV	If risk factors for MRSA are present, add IV vancomycin. May consider IV meropenem in immunocompromised children.
Impetigo	Topical fusidic acid 2% ointment/ cream on crusted areas 3 times a day or cephalexin PO if widespread or large lesions	**In immediate beta-lactam hypersensitivity**[1] erythromycin PO	

Prepared in collaboration with Sri Lanka College of Paediatricians

[1]Refer Chapter 2

* Severe sepsis: ICCPS definition in neonates

Sepsis plus cardiovascular organ dysfunction, acute respiratory distress syndrome, or ≥ 2 other organ dysfunctions
cardiovascular dysfunction - presence of 1 of the following despite isotonic IV fluid bolus ≥ 40 mL/kg in 1 hour, decrease in blood pressure as defined as blood pressure < fifth percentile for age or systolic blood pressure > 2 standard deviations below normal for age, vasoactive drug required to maintain normal blood pressure (dopamine > 5 mcg/kg/minute, or any dose of dobutamine, epinephrine, or norepinephrine), ≥ 2 of unexplained metabolic acidosis with base deficit > 5mEq/L, arterial lactate > 2 times upper limit of normal, urine output < 0.5mL/kg/hour, capillary refill > 5 seconds, core to peripheral temperature gap > 3°C, respiratory dysfunction - presence of 1 of partial pressure of arterial oxygen (PaO_2)/fraction of inspired oxygen (FiO_2) < 300 in absence of lung disease or cyanotic heart disease

** Refer to Sri Lanka College of Paediatricians (SLCP) website for detailed guidelines on management of CNS infections and UTI in children (https://slcp.lk/books-guidelines/)

***Avoid aminoglycosides in children with or at risk of having hypovolaemia or kidney injury or damage. If started, arrange monitoring of renal functions and discuss with microbiologist for alternative antibacterials if aminoglycoside levels cannot be monitored.

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SECTION E

Chapter 28: Medical Prophylaxis

This chapter provides indications and recommendations for preventing infections in specific medical conditions.

Table 35: Prophylactic antibiotics for indicated medical conditions

Condition	First choice	Alternative choice	Comments
1A. Post splenectomy antibiotic prophylaxis	phenoxymethylpenicillin PO *Adults and children over 5 years:* 250mg q12h *Children 1-5 years:* 125mg q12h *Children <1 year:* 62.5mg q12h or amoxicillin PO *Adults*: 250mg q24h *Children:* 20mg/kg q24h (up to 250mg)	**In immediate beta-lactam hypersensitivity**[1] erythromycin PO *Adults and children over 2 years:* 250mg q24h *Children 1 month–2 years:* 10 mg/kg (up to 250mg) q24h	Antibiotic prophylaxis needs to be given irrespective of vaccinations. Duration in adults: At least for 2 years after splenectomy Duration in children: At least up to the age of 5 years Lifelong prophylaxis should be considered for the following categories. 1) Immunodeficient patients 2) History of severe sepsis 3) Patients who underwent splenectomy for a haematological disorder or malignancy that requires ongoing treatment

1B. Post splenectomy vaccine prophylaxis:

- For elective splenectomy, all indicated vaccines should be administered approximately 10 to 12 weeks prior to surgery and completed at least 14 days prior to surgery. If it cannot be completed, resume vaccination 14 days after splenectomy. Following emergency splenectomy, all indicated vaccines should be initiated as soon as possible 2 weeks or more after surgery.
- All vaccines could be given simultaneously to different sites.
- For those who require chemotherapy or other immunosuppressive treatment following splenectomy, vaccination should be completed at least 2 weeks prior to commencement. If it is not possible, vaccination should be delayed at least 3 months post therapy.

Adults

1. **Pneumococcal vaccines**
   - Unvaccinated: single dose of pneumococcal conjugate vaccine (PCV), followed by 1 dose of 23-valent pneumococcal polysaccharide vaccine (PPSV23) 8 weeks later.
   - Patients who have previously received PPSV23: administer a dose of PCV 1 year later.
   - Patients who have previously received PCV: 1 dose of PPSV23 8 weeks later.
   - Revaccination: single dose of PPSV23 vaccine should be given 5 years after the initial dose and another dose should be given after completing 65 years of age, timed > 5 years after the previous dose.
2. **Haemophilus influenzae type b (Hib) vaccine**
   - Single dose regardless of previous vaccine status.
   - Revaccination not needed.
3. **Meningococcal vaccine**
   - Single dose of conjugate MenACWY, irrespective of previous vaccine status.
   - Booster: every 5 years.
4. **Seasonal influenza vaccine**
   - Single dose annually at the start of influenza season.
   - Repeat annually at the start of influenza season.

Children

1. **Pneumococcal vaccines**
   - **Pneumococcal conjugate vaccine (PCV):**
     - Unvaccinated children 2 months-1 year: 2 doses 8 weeks apart and a booster at 1 year and a 2nd booster after 8 weeks.
     - Unvaccinated children 1-2 years: 2 doses 8 weeks apart and a booster at least 6 months after the 2nd dose.
     - Children ≥2 years: single dose if they have not received a dose previously.

   - **Pneumococcal 23-valent polysaccharide vaccine (PPSV23):**
     - Children aged ≥2 years: 1 dose of PPSV23 > 8 weeks after completing all recommended doses of PCV.
     - Then a booster only once after 5 years.

2. ***Haemophilus influenzae* type b (Hib) vaccine (**should be initiated at 2 months of age as per standard schedule).
   - Children <5 years unvaccinated or who have received only one dose before 12 months of age: 2 doses 8 weeks apart.
   - Those who have received >2 doses before 12 months of age: 1 additional dose.
   - Unimmunized children ≥5 year: single dose.
   - No re-vaccination required.

3. **Meningococcal vaccine (Conjugate MenACWY vaccine)**
   - Children <1 year: 2 doses at least 4 weeks apart, booster every 5 years thereafter.
   - Children ≥1 year: Single dose, booster every 5 years thereafter.

4. **Seasonal influenza vaccine**
   - 1 dose at the start of influenza season (children 6 months - 9 years receiving the vaccine for the 1st time - 2 doses one month apart).
   - Repeat annually at the start of influenza season.

Condition	First choice	Alternative choice	Comments
2. Rheumatic fever	benzathine penicillin IM *Adult and children >27kg:* 900mg (1.2 MU) every 3-4 weeks *Children ≤ 27kg:* 450mg (600,000 units) every 3-4 weeks	phenoxymethylpenicillin PO 250mg q12h for all ages **In immediate beta-lactam hypersensitivity[1]** azithromycin PO *Weight > 27 kg:* 250 mg q24h *Weight ≤ 27 kg:* 5 mg/kg (up to 250 mg) q24h or erythromycin PO 250mg q12h for all ages (10 mg/kg q12h)	Duration: - If no rheumatic carditis: Continue prophylaxis 5 years after the acute rheumatic fever or until age 21 years, whichever is longer. - Carditis without residual valvular disease: Continue prophylaxis for 10 years after the acute rheumatic fever or until age 21 years, whichever is longer. - Carditis with residual valvular disease: Continue prophylaxis for 10 years since the last episode or until age 40 years, whichever is longer. Lifelong prophylaxis may be needed.

3. Prevention of Infective Endocarditis (IE)

Antibiotic prophylaxis is needed for patients with the following high risk cardiac conditions (A) undergoing procedures mentioned below (B).

A. High risk cardiac conditions

1. Patients with previous IE
2. Patients with prosthetic valves
3. Congenital Heart Diseases (CHD)*:
   - Untreated cyanotic congenital heart defects
   - Surgically or trans-catheter corrected congenital heart defects with post-operative palliative shunts, conduits or other prostheses
   - Completely repaired congenital heart defects without prosthetic material or device, during the first 6 months after the procedure
4. Patients with Ventricular Assist Device (VAD) as destination therapy
5. Patients with trans-catheter mitral valve or tricuspid valve repair

***Except for the conditions listed above, antibiotic prophylaxis is no longer recommended for any other form of CHD.**

B. Procedures

1. Dental Procedures

All dental procedures that involve manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa **except,**

- routine anaesthetic injections through non-infected tissue
- taking dental radiographs
- shedding of deciduous teeth
- bleeding from trauma to the lips or oral mucosa

2. Non-Dental Procedures

Invasive respiratory procedures

- An invasive procedure of the respiratory tract that involves incision or biopsy of the respiratory mucosa (e.g. tonsillectomy, adenoidectomy, bronchoscopy only if the procedure involves incision of the respiratory tract mucosa).
- For the procedures carried out to treat established infection in the respiratory tract (e.g. drainage of an abscess or empyema), include an agent active against viridans streptococci in the therapeutic regimen. Include anti-staphylococcal antibiotic in the regimen if the infection is known/ suspected to be caused by *S. aureus*. Contact microbiologist if needed.

Invasive gastrointestinal (GI) or genitourinary (GU) tract procedures

- If the patient is having an established GI or GU tract infection or for those who receive antibiotic therapy to prevent wound infection or sepsis associated with a GI or GU tract procedure, include an agent active against enterococci in a peri-operative therapeutic regimen.
- In elective procedures of the urinary tract, if the patient is having enterococcal urinary tract infection or colonization, antibiotic therapy should be given to eradicate enterococci from the urine before the procedure. Contact microbiologist if needed.

Procedures involving infected skin and musculoskeletal tissue.

- The therapeutic regimen should include coverage against staphylococci and beta-haemolytic streptococci.

3. Cardiac or vascular interventions

- In all patients undergoing implantation of a prosthetic valve, any type of prosthetic graft/ occluder device or CIED, peri-operative antibiotic prophylaxis is recommended.

Condition	First choice	Alternative choice	Comments
3. Infective Endocarditis Prophylaxis is indicated for patients with risk conditions undergoing procedures mentioned in pages 194 and 195.	amoxicillin PO *Adults:* 2g *Children:* 50 mg/kg or ampicillin IV or IM *Adults:* 2g *Children:* 50 mg/kg	cefalexin PO *Adults:* 2g *Children:* 50 mg/kg or ceftriaxone IV or IM *Adults:* 1g *Children:* 50 mg/kg **In immediate beta-lactam hypersensitivity[1]** doxycycline PO *Adults:* 100mg *Children <45kg:*2.2mg/kg *≥45kg:* 100mg or azithromycin PO/ clarithromycin PO *Adults:* 500mg *Children:* 15mg/kg	Prophylaxis should be given as a single dose 30-60 minutes before the procedure.

Condition	First choice	Alternative choice	Comments
4. Meningitis • Significant exposures to invasive **meningococcal** infections (after exposure risk assessment)**	ciprofloxacin PO single dose *Adults:* 500mg *Children:* *Infants <1 year:* 30mg/kg to a maximum 125mg *1- <5 years:* 125mg *≥5-11 years:* 250mg *≥12 years:* 500mg	ceftriaxone IM single dose *Adults:* 250mg *Children:* *1 month-11 years:* 125mg *≥ 12-18 years:* 250mg or rifampicin PO q12h for 2 days *Adults:* 600mg *Children:* *Neonate - < 1 year:*5mg/kg *≥ 1-11 years:* 10mg/kg (max.600mg) *≥ 12-18 years:* 600mg	**Indications for prophylaxis - contact microbiologist. **Pregnant Women:** Single dose of ciprofloxacin 500mg PO/ ceftriaxone 250mg IM/ azithromycin 500mg PO
• Significant exposures to invasive ***Haemophilus influenzae* type b** infections (after exposure risk assessment)**	rifampicin PO q24h for 4 days *Adults:*600mg *Children:* *1 -<3 months:* 10mg/kg *≥ 3 months-11 years:*20mg/kg (max.600mg) *≥ 12-18 years:* 600mg	ceftriaxone IM/IV q24h for 2 days *Adults and children older than 12 years:*1g *Children younger than 12 years:* 50mg/kg (max.1g)	**Indications for prophylaxis - contact microbiologist.

Condition	First choice	Alternative choice	Comments
5. Cirrhosis • For prevention of SBP The antibiotic prophylaxis should strictly be restricted to patients at high risk of SBP. i) patients with acute GI bleeding ii) patients with low protein content in ascitic fluid and no prior history of SBP (primary prophylaxis) iii) patients with a previous history of SBP (secondary prophylaxis)	norfloxacin PO 400mg q24h	ciprofloxacin PO 750mg once a week/ ciprofloxacin 500 mg q24h or co-trimoxazole PO 960mg q24h for 5 days per week/ co-trimoxazole PO 960mg q24h	Duration needs to be decided by the attending physician
• For patients with active variceal bleeding	ceftriaxone IV 1g q24h for 7 days	norfloxacin PO 400mg q12h for 7 days or ciprofloxacin PO 500mg q12h for 7 days	

Condition	First choice	Alternative choice	Comments
• Patients with gastro-intestinal bleeding prior to endoscopy	norfloxacin PO 400mg 1 hour before procedure and then q12h for 1-2 days	If oral therapy is not feasible ciprofloxacin IV 400mg at induction and then q12h for 1-2 days	
6. Recurrent cellulitis associated with lymphoedema (Considered in patients who have 2 or more attacks of cellulitis per year)	phenoxymethylpenicillin PO 250 mg (500mg if BMI is >33 kg/m^2) q12h or benzathine penicillin IM 1.2MU every 2-4 weeks	clarithromycin PO 250mg q24h	No clinical consensus exists regarding effectiveness and duration. Following two years of successful prophylaxis, discontinuation should be considered.
7. Pre exposure prophylaxis for Leptospirosis	Refer page 135		

Prepared in collaboration with Ceylon College of Physicians and Sri Lanka College of Cardiology

[1]Refer chapter 2

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Chapter 29: Prophylaxis: Surgical

- Identification of **specific surgical procedures** in which prophylactic antibiotics are beneficial**, the optimal agents, timing** and **duration** are important aspects that need consideration when administering prophylactic antibiotics for the prevention of surgical site infections.
- Antibiotic prophylaxis is one of the measures to prevent surgical site infections. Refer Hospital Infection Prevention and Control Manual 2021 of Sri Lanka College of Microbiologists (available on the website https://slmicrobiology.lk/hospital- infection-prevention-and-control-manual-2/) for other patient care recommendations to prevent surgical site infections.

Table 36: Classification of surgical wounds and surgical procedures (NICE Guidelines–UK 2021)

Type of surgery	Description
Clean	An incision in which no inflammation is encountered in a surgical procedure, without a break in sterile technique, and during which the respiratory, alimentary and genitourinary tracts are not entered.
Clean-contaminated	An incision through which the respiratory, alimentary or genitourinary tract is entered under controlled conditions but with no contamination encountered.
Contaminated	An incision undertaken during an operation in which there is a major break in sterile technique or gross spillage from the gastrointestinal tract, or an incision in which acute, non-purulent inflammation is encountered. Open traumatic wounds that are more than 12 –24 hours old also fall into this category.
Dirty or infected	An incision undertaken during an operation in which the viscera are perforated or when acute inflammation with pus is encountered during the operation (for example, emergency surgery for faecal peritonitis), or for traumatic wounds where treatment is delayed, or there is faecal contamination or devitalized tissue present.

General recommendations for surgical prophylaxis:

- Antibiotic prophylaxis is recommended in clean-contaminated or contaminated procedures and in certain clean procedures where there are severe consequences of infection, even if infection is unlikely.
- Antibiotic prophylaxis is indicated in the following clean surgical procedures.
  - Surgery involving introduction of prosthetic material
  - Surgery where consequences of infection would be catastrophic. e.g. neurosurgery, open heart surgery, orthopaedic surgery or ophthalmic surgery
  - Surgery in patients with impaired host defences
- Antibiotic prophylaxis is not routinely indicated for clean, non-prosthetic and uncomplicated surgery.
- In contaminated surgeries either antibiotic prophylaxis or therapy is recommended depending on patient's clinical condition.
- The use of antibiotics in dirty procedures or established infection is classified as treatment of presumed infection, not prophylaxis.
- Vancomycin/ teicoplanin can be used in MRSA colonized patients in high-risk surgeries (cardio-thoracic/ orthopaedic etc., where routine MRSA screening is indicated) or if the MRSA rates are high in these units.

Timing:

- Successful prophylaxis requires the delivery of the antibiotic to the operative site before contamination occurs. Thus, the antibiotic should be administered at such a time as to provide serum and tissue concentrations exceeding the minimum inhibitory concentration (MIC) of the antibiotic for the probable organisms associated with the procedure, at the time of incision, and for the duration of the procedure.
- The optimal time for administration of preoperative doses is within 60 minutes before surgical incision/procedure. However, vancomycin and ciprofloxacin infusions should be started 120 minutes prior to surgical incision/ procedure because of the prolonged infusion times required for these drugs. Oral ciprofloxacin is given 60-90 minutes before the surgical incision/ procedure.

- Consider prophylaxis earlier for surgeries in which a tourniquet is used (e.g. in orthopaedic surgery where application of a tourniquet is required) prophylaxis needs to be given at least 10 minutes prior to application of tourniquet.

Dosing and duration:

- Prophylactic antibiotic therapy should generally be limited to a single dose. However, if further doses are considered it should not be continued for more than 24 hours after the end of surgery or confined to a maximum of three doses. However, the prophylaxis may be continued for up to 48 hours in certain cardio-thoracic surgeries as the available data is not sufficient to decide the optimal duration.
- Re-dosing during surgery is indicated with certain antibiotics when the duration of surgery exceeds two times the half-life of the antibiotic given or if there is a significant blood loss of >1.5L (or 25% of total blood volume) (refere table 37).
- The practice of continuing prophylactic antibiotics until surgical drains have been removed is not proven to be beneficial.
- The pharmacokinetics of drugs may be altered in obese patients, so dosage adjustments based on body weight maybe warranted in these patients.
- Gentamicin dose should be calculated according to ideal body weight, and in case of obese patients it is calculated according to adjusted body weight (refer chapter 7).

Table 37: Route and doses of antibiotics for surgical prophylaxis (in alphabetical order)

Antibiotic	Route	Adult Dose	Paediatric dose	Re-dosing interval during surgery (from initiation of pre-op dose) if indicated
ampicillin	IV	2g	50mg/kg	2 hours
cefazolin (1st gen. cephalosporin recommended in international guidelines for surgical prophylaxis)	IV	2g	30mg/kg	4 hours
cefotaxime	IV	1g	50mg/kg	3 hours
ceftriaxone	IV	2g	50-75mg/kg	NA
cefuroxime	IV	1.5g	50mg/kg	4 hours
ciprofloxacin*	IV	200-400mg	10mg/kg	NA
ciprofloxacin	Oral	500-750mg	15mg/kg	NA
clindamycin*	IV	600-900mg	10mg/kg	6 hours
co-amoxiclav	IV	1.2g	30mg/kg	2 hours
flucloxacillin	IV	1-2g	50mg/kg	2 hours
fluconazole	IV	400mg	30mg/kg	NA
gentamicin	IV	5mg/kg	2.5mg/kg	NA
metronidazole*	IV	500mg	15mg/kg	NA
piperacillin-tazobactam	IV	4.5g	100mg/kg	2 hours
teicoplanin	IV	6mg/kg	10mg/kg	NA
vancomycin*	IV	15mg/kg	15mg/kg	NA

** To be given as infusion. Refer chapter 7*

Table 38: Antibiotics recommended for prophylaxis in common surgical procedures

Type of surgery	First choice	Alternative choice	Comments
Cardiac, thoracic and vascular surgery • **Cardiac surgery and cardiology procedures** e.g. coronary artery bypass graft (CABG), valvular surgeries, repair of congenital anomalies, placement of implantable cardiac devices including ventricular assist devices and pacemakers	cefuroxime IV/ co-amoxiclav IV	**In immediate beta-lactam hypersensitivity[1] or in units with high prevalence of MRSA and for patients colonized with MRSA:** vancomycin IV/ teicoplanin IV	Vancomycin dose should not exceed more than 1.5g per dose in adults. Gentamicin can be added as a single dose when Gram negative pathogens are a concern.
• **Thoracic surgeries** e.g. insertion of prosthetic material, video-assisted thoracoscopic surgery (VATS), mediastinoscopy, pneumonectomy/ lobectomy	cefuroxime IV/ co-amoxiclav IV	**In immediate beta-lactam hypersensitivity[1] or in units with high prevalence of MRSA and for patients colonized with MRSA:** vancomycin IV/ teicoplanin IV	

Type of surgery	First choice	Alternative choice	Comments
• **Vascular surgery** e.g. reconstruction of abdominal aorta, aneurysm repair, thrombo-endarterectomy, vein bypass, procedures on the leg that involve a groin incision (except for varicose veins) or implantation of foreign material, lower extremity amputation for ischemia	cefuroxime IV/ co-amoxiclav IV +/- gentamicin IV	vancomycin IV/ teicoplanin IV + gentamicin IV	Vancomycin dose should not exceed more than 1.5g per dose in adults. Metronidazole IV can be added for amputations of an ischaemic limb.
ENT surgery • Prophylaxis is recommended for clean contaminated procedures that involve an invasion through oral, nasal, pharyngeal or oesophageal mucosa and stapedectomy • Grommet insertion	cefuroxime IV +/- metronidazole IV or co-amoxiclav IV topical ciprofloxacin 0.3% ear drops	clindamycin IV	Prophylaxis is not recommended for clean ear surgery (e.g. tympanostomy with tube placement, tympanoplasty), simple septorhinoplasty, endoscopic sinus surgery, clean head and neck surgeries (e.g. thyroidectomy, salivary gland excisions, parathyroidectomy) and tonsillectomy. Single topical dose is recommended after grommets insertion.

Type of surgery	First choice	Alternative choice	Comments
Endoscopic procedures • Percutaneous endoscopic gastrostomy (PEG)/ percutaneous endoscopic jejunostomy PEJ) placement	cefuroxime IV/ co-amoxiclav IV	clindamycin IV	Contact microbiologist for prophylaxis in complicated endoscopic surgeries. .
• Interventional endoscopic ultrasound guided (EUS) procedures (e.g. EUS-FNA of cystic lesion) • Endoscopic retrograde cholangiopancreatography (ERCP)	ciprofloxacin PO/IV or co-amoxiclav IV		Ciprofloxacin orally given within 60 to 90 minutes prior to procedure or IV beginning within 120 minutes prior to procedure (infusion given over 60 minutes). Contact microbiologist for prophylaxis in complicated endoscopic surgeries.

Type of surgery	First choice	Alternative choice	Comments
General Surgery • Hernia repair with mesh	cefuroxime IV/ co-amoxiclav IV	clindamycin IV	
• Breast surgeries (breast cancer surgery, reshaping procedures, breast surgery with implants)	cefuroxime IV/ co-amoxiclav IV	vancomycin IV/ teicoplanin IV + gentamicin IV	
Gastro-intestinal Surgery **Upper GI Surgery** e.g. oesophageal/ gastro-duodenal procedures involving entry into lumen of gastrointestinal tract (bariatric, pancreatico-duodenectomy, gastrectomy, oesophagectomy, fundoplication), procedures without entry into GI tract (antireflux, highly selective vagotomy) for high-risk patients	cefuroxime IV/ co-amoxiclav IV	vancomycin IV/ clindamycin IV + gentamicin IV	In complicated surgeries (e.g. gastric stasis, perforation, spillage at operation) antibiotics may be continued up to 48 hours.

Type of surgery	First choice	Alternative choice	Comments
Lower GI Surgery			
• Small intestinal surgery (unobstructed)	cefuroxime IV/ co-amoxiclav IV	clindamycin IV + gentamicin IV	
• Small intestinal surgery (obstructed)	cefuroxime IV + metronidazole IV or co-amoxiclav IV	metronidazole IV + gentamicin IV	
• Appendectomy	cefuroxime IV + metronidazole IV or co-amoxiclav IV	clindamycin IV/ metronidazole IV + gentamicin IV	Patients with complicated appendicitis (with infectious complications), should receive empirical therapy before surgery and therapy is tailored according to sensitivity results.
• Colorectal surgery	cefuroxime IV/ co-amoxiclav IV + metronidazole IV	clindamycin IV/ metronidazole IV + gentamicin IV	Antibiotics may be continued for up to 48 hours in complicated surgeries and review the need after 48 hours.

Type of surgery	First choice	Alternative choice	Comments
Hepatobiliary • Elective laparoscopic cholecystectomy for biliary pain and low risk of infection (no current or previous acute cholecystitis / no common bile duct calculi /no immune suppression or no prosthetic implants)	Antibiotic prophylaxis is not indicated.		The biliary tract is usually sterile. Patients with bacteria in the bile at the time of surgery may be at higher risk of postoperative infection; however, some studies have found no association between the presence of bacteria in the bile and infection.
• Elective laparoscopic cholecystectomy with risk of infection • Open procedures (cholecystectomy/ liver or pancreatic resection)	cefuroxime IV/ co-amoxiclav IV	vancomycin IV / clindamycin IV + gentamicin IV	Patients with pre-existing infection in the hepato-biliary tract should receive empirical antimicrobials for the infection before surgery and targeted according to sensitivity results.
• Complicated open hepatopancreatobiliary surgery (resections including Whipple / with biliary stent or drain)	co-amoxiclav IV/ cefuroxime IV + metronidazole IV or piperacillin-tazobactam IV	vancomycin IV + ciprofloxacin IV + metronidazole IV	

Type of surgery	First choice	Alternative choice	Comments
Head, Neck and Neurosurgeries • Clean (e.g.thyroidectomy, lymph node biopsy, parotidectomy)	Antibiotic prophylaxis is not indicated.		Prophylaxis is not indicated for clean head and neck surgeries.
• Clean head and neck surgeries with prosthesis	cefuroxime IV / co-amoxiclav IV	**In immediate beta-lactam hypersensitivity[1]:** clindamycin IV **In units with high prevalence of MRSA and for patients colonized with MRSA:** vancomycin IV	
• Clean-contaminated head and neck surgeries	cefuroxime IV + metronidazole IV or co-amoxiclav IV	**In immediate beta-lactam hypersensitivity[1]:** clindamycin IV **In units with high prevalence of MRSA:** vancomycin IV + metronidazole IV	Duration of antibiotics for clean contaminated surgeries depends on the patient's condition.

Type of surgery	First choice	Alternative choice	Comments
Neurosurgeries • Elective craniotomy and cerebrospinal fluid shunting procedures • Implantation of intrathecal pumps, spinal surgery with/without implants	cefuroxime IV	**In immediate beta lactam hypersensitivity[1]:** clindamycin IV **In units with high prevalence of MRSA and for patients colonized with MRSA:** vancomycin IV	For spinal surgeries with implants, the antibiotics may be continued for 24 hours.
Obstetric and Gynaecological surgery • Insertion of IUD, hysteroscopy, assisted delivery, miscarriage, diagnostic laparoscopy and laparoscopic sterilization (not entering uterine cavity/ vagina), dilatation and curettage	Antibiotic prophylaxis is not indicated.		Screening for *Chlamydia trachomatis* in high-risk population should be considered before IUD insertion and hysteroscopy.

Type of surgery	First choice	Alternative choice	Comments
• Hysterosalpingography	Antibiotic prophylaxis is not indicated.	clindamycin IV + gentamicin IV	Patients should be screened and treated for *Chlamydia trachomatis* before uterine instrumentation procedures. Antibiotic prophylaxis (e.g. doxycycline) can be considered if screening is not done. Evidence favours giving prophylaxis before skin incision than giving after cord clamping for caesarean section.
• Caesarean section (Elective/ Emergency)	cefuroxime IV/ co-amoxiclav IV		
• Hysterectomy (abdominal/ laparoscopic/ vaginal) • Perineal procedures	cefuroxime IV + metronidazole IV or co-amoxiclav IV		
Ophthalmic surgery • Cataract surgery, vitrectomy, keratoplasty, intraocular lens implantation, glaucoma procedures, strabotomy, retinal detachment repair, laser in situ keratomileusis, laser-assisted subepithelial keratectomy	Topical moxifloxacin or gatifloxacin eye drops or neomycin–polymyxin B–gramicidin eye drops or 5%betadine eye drops		Aseptic procedures such as appropriate draping and pre-op assessment are better and effective methods for prevention of post-surgical eye infections. The addition of subconjunctival, intracameral or intravitreal cefuroxime or fourth generation fluoroquinolones at the end of the procedure is optional.

Type of surgery	First choice	Alternative choice	Comments
Oro maxillofacial surgeries e.g. orthognathic surgeries, temporomandibular joint surgery, surgical extractions of third molars, open reduction and internal fixation of compound mandibular fractures, major resections of tumors/ cysts, complex implants and intraoral bone grafting procedures	cefuroxime IV + metronidazole IV or co-amoxiclav IV	clindamycin IV	Prophylactic antibiotic use is not routinely recommended for clean facial surgeries and tonsillectomy.

Type of surgery	First choice	Alternative choice	Comments
Orthopaedic surgery			
• Clean operations involving hand, knee or foot and not involving implantation of foreign materials	Antibiotic prophylaxis is not indicated.		
• Total joint replacement/ internal fixation of closed fractures/hip fracture repair/spinal surgery/implantation of internal fixation devices (nails, screws, plates, wires), procedures involving other foreign material	cefuroxime IV +/- gentamicin IV or flucloxacillin IV + gentamicin IV	**In immediate beta-lactam hypersensitivity[1] or in units with high prevalence of MRSA and for patients colonized with MRSA:** vancomycin IV/ teicoplanin IV + gentamicin IV	The prophylactic antimicrobial infusions should be completed 10 minutes prior to inflation of the proximal tourniquet. Gentamicin is added when Gram negatives are a concern and should be limited to a single dose. Flucloxacillin adult dose should be 2g IV.

Type of surgery	First choice	Alternative choice	Comments
Peritoneal dialysis catheter placement	cefuroxime IV	vancomycin IV	In settings with high prevalence of MRSA vancomycin is preferred.
Plastic surgery • Clean with risk factors or clean contaminated	cefuroxime IV/ co-amoxiclav IV	vancomycin IV/ clindamycin IV	

Type of surgery	First choice	Alternative choice	Comments
Solid organ transplant surgery • Renal transplant • Heart transplant • Lung transplant	cefuroxime IV/ co- amoxiclav IV	**In immediate beta-lactam hypersensitivity[1] or in units with high prevalence of MRSA and for patients colonized with MRSA:** vancomycin IV/ teicoplanin IV +/- gentamicin IV	Gentamicin should be considered in the possibility of Gram negative infection and should be limited to a single dose. Other antibiotics should be continued for <48 hours.
• Pancreas or pancreas-kidney transplant	cefuroxime IV/ co- amoxiclav IV		IV fluconazole should be used as a single dose in patients with higher risk of fungal infection in patients undergoing pancreas or pancreas-kidney transplant.
• Liver transplant	cefotaxime IV / ceftriaxone IV + ampicillin IV **+/-** fluconazole IV or piperacillin-tazobactam IV +/- fluconazole IV	**In immediate beta-lactam hypersensitivity[1]** vancomycin IV/ teicoplanin IV + gentamicin IV +/- fluconazole IV	Antifungals should be used according to the individual risk and given as a single dose.

Type of surgery	First choice	Alternative choice	Comments
Urological surgeries/ procedures	• Prior to urological procedures/surgeries entering urinary tract, patients should be screened and treated for asymptomatic bacteriuria or UTI according to the antibiotic sensitivity. • Antibiotic prophylaxis for patients with hip or knee prostheses is recommended during genitourinary surgeries/procedures which carry high risk of bacteraemia, within two years of prosthesis implant.		
• Flexible cystoscopy/ urodynamic studies/ catheterization, or catheter changes/ clean surgeries in low-risk patients (e.g. circumcision, orchidectomy, orchidopexy, varicocelectomy), inguino-scrotal surgery (non-prosthetic surgeries)	Antibiotic prophylaxis is not indicated.		Prophylaxis is not indicated in healthy people. However, prophylaxis is indicated in adults and children with strongly suspected or already proven urinary tract abnormalities when they undergo imaging procedures involving the urinary tract/ urodynamics/ voiding cystourethrography (VCUG) and in children with urological malformations or a previous history of recurrent UTI before cystoscopy, ureteroscopy, and all other endoscopic procedures.

Type of surgery	First choice	Alternative choice	Comments
• Lower tract instrumentation with risk factors for infection (TURP, TURBT) Trans-rectal ultrasound (TRUS) prostate biopsy • Rigid cystoscopy • Ureteroscopy	cefuroxime IV/ co-amoxiclav IV +/- gentamicin IV	gentamicin IV +/- clindamycin IV or ciprofloxacin PO/IV or co-trimoxazole PO	
• Clean urologic procedures without entry into the urinary tract (e.g.nephrectomy and adrenalectomy)	cefuroxime IV	vancomycin IV/ clindamycin IV	
• Clean urologic procedures with entry into the urinary tract (e.g. bladder reconstruction, nephroureterectomy and prostatectomy	cefuroxime IV/ co-amoxiclav IV	gentamicin IV +/- clindamycin IV	

Type of surgery	First choice	Alternative choice	Comments
• Clean-contaminated procedures of the urinary tract (often entering the gastrointestinal tract/vagina) (e.g.radical cystectomy with urinary diversion/ ileal conduit/ neobladder)	cefuroxime IV + gentamicin IV +/- metronidazole IV	ciprofloxacin IV/ gentamicin IV + metronidazole IV/ clindamycin IV	
• Urinary stone surgery (e.g. shock wave lithotripsy (high risk procedures), percutaneous nephrolithotripsy, transurethral ureterolithotripsy	cefuroxime IV/ co-amoxiclav IV	gentamicin IV / ciprofloxacin IV / or co-trimoxazole PO	For low-risk shock wave lithotripsy procedures, antibiotic prophylaxis is not indicated. High risk shock wave lithotripsy procedures include: the presence of bacteriuria, infected stone, endoscopic manipulation, repeated procedures, history of febrile urinary tract infection, stone diameter ≥2 cm, hydronephrosis etc.

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Annex 1

AWaRe Classification of Antimicrobials 2024 - Ministry of Health Sri Lanka (General Circular No: 01-13/2024)

Antibacterials		
ACCESS	**WATCH**	**RESERVE**
Amoxicillin	Amikacin	Ampicillin/sulbactam
Amoxicillin/clavulanic acid	Azithromycin	Aztreonam
Ampicillin	Cefixime	Ceftazidime/avibactam
Benzathine-benzylpenicillin	Cefotaxime	Cefepime
Benzylpenicillin	Ceftazidime	Cefoperazone/sulbactam
Cefalexin	Ceftriaxone	Colistin (polymyxin E)
Cefazolin	Chloramphenicol	Daptomycin
Cefuroxime	Ciprofloxacin	Fosfomycin
Clarithromycin	Ertapenem	Fusidic acid
Clindamycin	Imipenem/cilastatin	Levofloxacin
Cloxacillin	Mecillinam	Linezolid
Doxycycline	Meropenem	Minocycline
Erythromycin	Netilmicin	Moxifloxacin
Flucloxacillin	Ofloxacin	Polymyxin-B
Gentamicin	Piperacillin/tazobactam	Rifampicin
Metronidazole	Pivmecillinam	Tigecycline
Nitrofurantoin	Rifamycin	
Norfloxacin	Rifaximin	
Ornidazole	Roxithromycin	

Phenoxymethylpenicillin	Secnidazole	
Procaine-benzylpenicillin	Spectinomycin	
Sulfamethoxazole/trimethoprim	Spiramycin	
Tetracycline	Streptomycin	
Tinidazole	Sulfadiazine	
Trimethoprim	Sulfadiazine/trimethoprim	
	Teicoplanin	
	Vancomycin	
Anti-Fungal		
Access	**Watch**	**Reserve**
Griseofulvin	Fluconazole	Amphotericin B
	Itraconazole	Anidulafungin
	Terbinafine	Caspofungin
		Flucytocine
		Posaconazole
		Voriconazole
Anti-Viral		
Access	**Watch**	**Reserve**
Acyclovir (Oral)	Acyclovir IV	Cidofovir
	Oseltamivir	Foscarnet
	Valganciclovir Oral	Ganciclovir IV
		Ribavirin IV

Annex 2

Prescribing antibacterials for children

Following are some important considerations when antibacterials are prescribed for children.

1. Some antibacterials have to be used cautiously in children. Prescribers are expected to compare the risks vs. benefits before deciding to prescribe such antibacterials. Examples include ceftriaxone in neonates (risk of kernicterus), azithromycin/erythromycin in neonates under 2 weeks (risk of hypertrophic pyloric stenosis). Always check the most recent version of BNF-C if you are in doubt.
2. Paediatric doses have to be calculated based on their age and weight. One size does not fit all in children. Hence mg/kg dose recommendations might vary within different age groups in children (e.g. neonates, 1-5 years, 6-11 years, etc.). Extra cautions have to be taken in calculating the dose. Checking the calculation twice or getting it done by two people is always recommended. For intravenous administration, adhere to the recommended dilution volume and rate of infusion.
3. Prescribers should be very familiar with the strengths of different paediatric dosage forms available in Sri Lanka (e.g. syrups, tablets, powder for solution for infusion, etc.)
4. For oral administration, suitable dosage forms have to be selected. Tablets should not be broken/crushed. Capsules should not be opened and the contents given to children. If a child cannot swallow, prescribe suitable dosage forms like liquid preparations or dispersible tablets. They should not be given with food. Manipulating the adult dosage forms not only affect the bioavailability, but also can predispose to antibacterial resistance.
5. If antibacterial suspensions are prescribed on-discharge, parents should be trained about reconstitution, storage and administration them. Advice should be given regarding accurate measuring device. An oral syringe is the preferred measuring device.
6. Generally, the vials of antibacterials available in the ward setting are of adult size. When a small dose is taken for a child, follow the manufacturer's recommendations regarding the balance reconstituted solution. Always use sterile water for reconstitution to reconstitute the powder.

7. Anti-bacterial medicines should not be discarded in an untreated form. Never discard unused/balance antibacterial medicines into the wash basin sink or toilet. The liquid ones may be diluted in water, left for two weeks and disposed to the sewer. If diluted with hot water, it can be disposed soon.

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