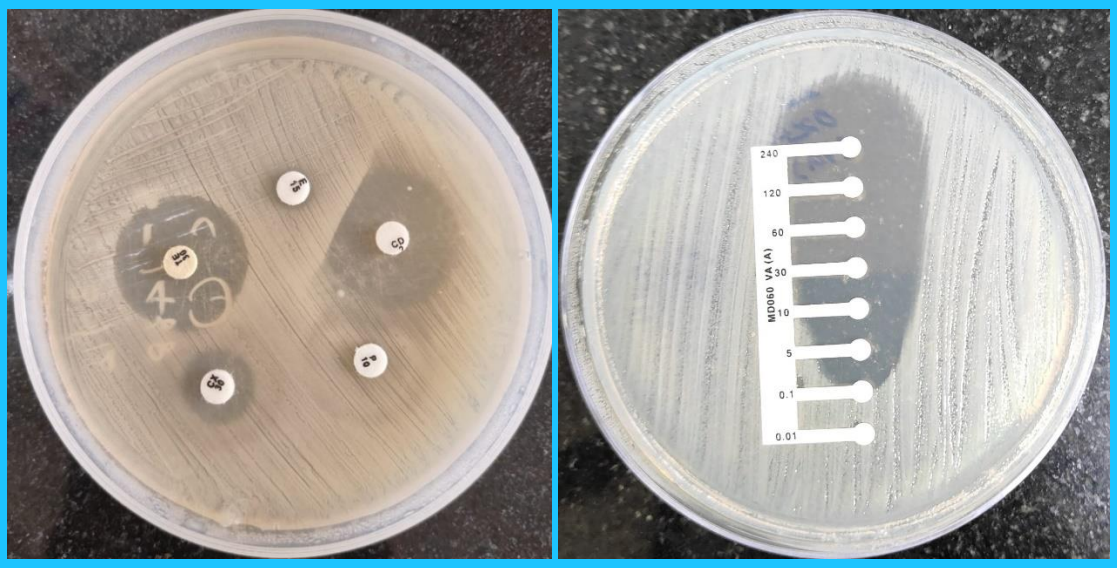
# GUIDANCE TO

# ANTIMICROBIAL THERAPY

# TAMIL NADU




**Directorate of Medical Education & Research (DME&R)**

**GOVERNMENT OF TAMILNADU**

# GUIDANCE TO

# ANTIMICROBIAL THERAPY

# TAMIL NADU

# 2nd Edition



Room G11, Directorate of Medical Education and Research
Kilpauk, EVR Periyar Salai, Chennai 600010

Secretariat
Date: 29.May.2025


Ma. Subramanian BA, BL.
Hon'ble Minister for Health & Family Welfare
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## Foreword

Antimicrobial resistance (AMR) has emerged as a silent pandemic that threatens global health security and the progress we have made in modern medicine. Addressing this challenge requires a collective, coordinated, and evidence-based response.

It gives me great pleasure to introduce the Guidance to Antimicrobial Therapy – 2nd Edition, an important step forward in Tamil Nadu's commitment to promoting rational antibiotic use and strengthening antimicrobial stewardship across all levels of our healthcare system.

This comprehensive guide has been developed by a team of dedicated experts, including clinicians, infectious disease specialists, and microbiologists from both government and private sectors.

The Department of Health & Family Welfare, Government of Tamil Nadu is proud that our Directorate of Medical Education & Research has formulated these guidelines inculcating inputs from various specialists. This book is not merely a clinical reference; it is a vital tool in our broader public health strategy to combat AMR, protect our communities, and preserve the effectiveness of life-saving medicines for future generations.

Tamil Nadu is the forerunner for "Makkalai Thedi Maruthuvam" scheme for the whole India. This scheme bagged Award "UN Interagency Task Force Awards (UNIATF) 2024" for Tamil Nadu endowed for their innovative program.

I extend my sincere appreciation to all contributors who have worked tirelessly to bring out this second edition. I urge all healthcare professionals across Tamil Nadu to utilize this guide responsibly and consistently in their clinical practice.

Together, let us stand united in our fight against antimicrobial resistance.

(Ma. SUBRAMANIAN)

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## FOREWORD

In an era marked by rapid medical advancements and the global challenge of antimicrobial resistance, the prudent and informed use of antimicrobial agents has never been more critical. "Guidance to Antimicrobial Therapy" was developed to serve as a practical and accessible reference for healthcare professionals tasked with the complex responsibility of selecting and managing antimicrobial treatments.

This guide aims to bridge the gap between evolving microbiological science and everyday clinical practice. Whether faced with a common community-acquired infection or a multidrug-resistant organism in a critically ill patient, clinicians require accurate, timely, and concise information to make therapeutic decisions that optimize patient outcomes while minimizing harm.

Drawing on current evidence, established guidelines, and expert consensus, this book provides:

- Clear recommendations for empirical and targeted antimicrobial therapy.
- Concise summaries of pharmacologic properties, spectra of activity, and key adverse effects.
- Practical approaches to antimicrobial stewardship, dosage adjustments, and special population considerations.

It is our hope that this guide will not only support clinicians in delivering safe and effective care but also contribute to the larger mission of preserving the efficacy of antimicrobials for future generations.

We extend our sincere gratitude to the many contributors, reviewers and healthcare professionals whose insights and dedication have informed this work.

- May this guide serve as a valuable companion in your clinical journey.

**(P.SENTHILKUMAR)**

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# Foreword

Antimicrobial resistance (AMR) represents one of the most pressing public health challenges of our time. The inappropriate and irrational use of antibiotics has contributed significantly to the emergence and spread of resistant pathogens, threatening our ability to treat common infections and perform routine medical procedures safely.

In this context, the Guidance to Antimicrobial Therapy – 2nd Edition has been meticulously developed to support clinicians in making evidence-based, judicious decisions in antimicrobial prescribing across healthcare facilities in Tamil Nadu. This edition reflects our continued commitment to strengthening antimicrobial stewardship and improving patient care through standardised, rational therapeutic approaches.

This comprehensive guide has been prepared by a distinguished panel of clinicians, infectious disease specialists, and microbiologists from both the government and private sectors.

Notably, this edition introduces color-coded antibiotic classifications based on the WHO AWaRe (Access, Watch, Reserve) framework, enhancing clarity in selection and stewardship.

It is important to remember that while this guide provides standard recommendations, individual treatment decisions should be informed by local microbiological data, patient-specific factors, and clinical judgement.

I commend the expert contributors and the editorial team for their dedicated efforts in producing this valuable resource. I trust that this guide will serve as an essential tool for all healthcare professionals and will contribute meaningfully to the rational use of antimicrobials across our state.

**Dr. A. Arun Thamburaj, I.A.S.,**
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Date ; 09-09-2025
Place: Chennai

**Foreword**

The practice of antimicrobial therapy lies at the intersection of clinical acumen, microbiological insight, and an ever-evolving understanding of resistance patterns and pharmacology. In an era where antimicrobial resistance poses a global threat to public health, the importance of thoughtful, evidence-based prescribing has never been greater.

This guide has been developed to provide healthcare professionals with a practical and accessible reference for the selection, dosing, and monitoring of antimicrobial agents across a range of clinical scenarios. Whether in primary care, hospital settings, or specialty practice, the goal is to support timely and effective decision-making that prioritizes both patient outcomes and stewardship principles.

We have aimed to synthesize current guidelines, emerging evidence, and expert consensus into a concise format that facilitates use at the bedside. Each section is designed to be clear, clinically relevant, and adaptable to the diverse needs of practitioners. Where possible, local resistance trends, formulary preferences, and cost considerations have been taken into account.

This guidance is not a substitute for clinical judgment, but rather a tool to enhance it. We should not forget the formula of Antibiotics. Three Antibiotics is equal to one fungal infection. Rational use of Antibiotics is mandatory and also updating knowledge of Antibiotics and Resistance is important for all Doctors.

We hope this guide will serve as a trusted companion in your clinical practice and contribute to the safe, rational, and effective use of antimicrobial agents

Director of Medical Education & Research,
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Date ; 03-06-2025
Place: Chennai

**Foreword**

It gives me immense pleasure to present this *Guidance to Antimicrobial Therapy Book*, a timely and essential resource for healthcare professionals involved in the rational use of antimicrobial agents. The growing threat of antimicrobial resistance (AMR) has emerged as a significant public health challenge, not only globally but also within our local healthcare settings. Addressing this concern demands a concerted, evidence-based approach, and this guide serves as a vital tool in that endeavour.

This book provides clear, concise, and clinically relevant guidelines to assist prescribers in making informed decisions regarding antimicrobial therapy. It reflects current best practices, incorporates local epidemiological data where applicable, and aligns with national and international antimicrobial stewardship goals. I commend the authors and contributors for their meticulous work in compiling a reference that is both practical and scientifically robust.

As medical educators and healthcare providers, we bear the responsibility to ensure that future generations inherit effective treatments. This guidebook will serve not only as a reference for clinicians but also as an educational tool for medical students, residents, and allied healthcare professionals.

I hope that this publication will encourage judicious antimicrobial use and inspire further initiatives in stewardship, surveillance, and infection prevention.

Antimicrobial resistance is one of the stake of “ONE HEALTH”.

I extend my sincere appreciation to the editorial team, contributors, and all those involved in bringing this valuable guide to fruition.

3/06/2025

Additional Director of Medical Education & Research,
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## List of Abbreviations:

**ABM**-Acute bacterial Meningitis

**AMA**-Anti Microbial Agent

**AmpC**-Ambler C Classification Betalactamase

**AMR**-AntiMicrobial Resistance

**AMS**-AntiMicrobial Stewardship

**ART**-Anti Retroviral Therapy

**BMT**-Bone Marrow Transplant

**CAP**- Community acquired Pneumonia

**CAUTI-**Catheter Associated Urinary Tract Infection

**CDC**-Centre for Disease Control

**CDI**-Clostridium difficile Infection

**CLABSI**-Central Line Associated Blood Stream Infection

**CMI**-Cell Mediated Immunity

**CP-CRE**-Carbapenamase Producing Carbapenem Resistant

**CRO**-Carbapenem Resistant Organism

**CRP**- C Reactive Protein

**CSF**-Cerebro Spinal Fluid

**DLC**-Differential Leucocyte Count

**DTP**-Difficult To Treat Pseudomonas aeruginosa

**ESBL**-Extended Spectrum Beta Lactamase

**GNB**-Gram Negative Bacilli

**HAP**-Hospital Acquired Pneumonia

**HBV**-Hepatitis B Virus

**HCP**-Health Care Personnel

**HCV**-Hepatitis C virus

**HIV**-Human Immuno Deficiency Virus

**HSCT**-Hematopoietic Stem Cell Therapy

**IE**-Infective Endocarditis

**LFT**-Liver Function Test

**MRSA**-Methicillin Resistant Staphylococcus aureus

**MSSA**-Methicillin Sensitive Staphylococcus aureus

**NACO**-National AIDS Control Organization

**NC**-No Change

**Non CP-CRE**-Non Carbapenamase Producing Carbapenem Resistant

**NTEP**-National Tuberculosis Elimination Program

**PCT**-Procalcitonin

**PEP**-Post Exposure Prophylaxis

**PJI-**Prosthetic Joint Infection

**PMN**-Poly Morpho Nuclear Leucocytes

**RFT**-Renal Function Test

**SSI**-Surgical Site Infection

**TBM**-Tuberculous Meningitis

**TLC**-Total Leucocyte Count

**UTI**-urinary Tract Infection

**VAP-**Ventilator Associated Pneumonia

**VGS**-Viridans Group Streptococci

**VRE**-Vancomycin Resistant Enterococci

**WFI**-Water For Injection

**WHO**-World Health Organisation

# Ink & Insight

The Guidance to Antimicrobial Therapy – 2nd Edition – has been developed with a clear goal: to combat antimicrobial resistance (AMR) by optimizing antimicrobial use in the healthcare facilities of Tamil Nadu.

This edition is the result of collaborative efforts by a panel of eminent clinicians, infectious disease specialists, and microbiologists from both the government and private sectors.

The guidelines presented for empirical therapy, malaria treatment, and tuberculosis management are based on well-established national protocols, ensuring consistency with India's public health policies. To aid rapid and informed decision-making, antibiotics in this book are color-coded according to the WHO **AWaRe** (**Access**, **Watch**, **Reserve**) classification using **green**, **orange**, and **red** indicators.

Building on the foundation of the first edition, this updated version includes new chapters on antibiotic resistance mechanisms, rabies prophylaxis, and the use of antimicrobials during pregnancy and lactation. These additions aim to broaden the scope of the book and address key challenges faced by healthcare providers in diverse clinical settings.

All therapeutic recommendations adhere to internationally recognized standards, however, it is important to acknowledge that individual treatment decisions should be tailored to local epidemiology and patient-specific factors.

In addition to therapy guidance, this book emphasizes the critical importance of standard precautions—especially hand hygiene—as an essential strategy in preventing the spread of AMR within healthcare environments.

**Best wishes,**

**Editorial Team**

**Guidance to Antimicrobial Therapy TN– 2nd Edition**

# Guidance to Antimicrobial Therapy-Tamil Nadu

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# Chapter – 1: Introduction

Antimicrobial resistance is the ability of microorganisms to withstand the effects of antimicrobial drugs and it develops when an antibiotic loses its ability to effectively stop microbial growth. Antibiotic resistance is a growing global health concern, as it can lead to longer hospital stays, higher healthcare costs, and increased mortality rates. When antibiotics are overused or misused, bacteria are exposed to drugs unnecessarily, and those that survive develop resistance to the antibiotics used.

Antimicrobial resistance (AMR) jeopardizes not only public health but also economic growth and security. Based on high-level predictions and global reports, AMR has the potential to result in 10 million fatalities worldwide by 2050[1]. The Centers for Disease Control and Prevention (CDC) has estimated that antibiotic resistance increases direct healthcare expenditures in the United States by $20 billion annually, excluding the estimated $35 billion in productivity losses.

The wide spread of antimicrobials has resulted in the expression of resistance to these antimicrobial agents. Resistance-encoding genes have been probably present for thousands of years, either as a defence against antibiotics or for unknown purposes, and the incorporation of these genes by human commensal and pathogenic flora has been quickly followed.

Various programs and strategies have been developed over the years to reduce antimicrobial resistance and promote the proper and effective use of antibiotics. The antimicrobial stewardship programs (ASPs) have attracted a lot of attention as one of the most important strategies for combating AMR. Antimicrobial stewardship is a coordinated approach to promote the appropriate use of antibiotics and other antimicrobial agents in healthcare settings.

Since the 1940s, different educational programs, management strategies, clinical protocols, and guidelines have been developed by infectious-disease organizations to control and prevent microbial infections in various sectors. In the United States, the Centers for Disease Control and Prevention (CDC) launched the first educational program in 2009 to advocate for the rational use of antibiotics in acute-care settings, and improved antibiotic use as a strategy was adopted in 2013 to address the problem. In 2015, World Health Organization (WHO) issued a global action plan (GAP) on the appropriate use and effects of antibiotics on humans and animals along with the validity of antibiotics for future generations as the main aim of GAP.

AMS has a positive impact in hospitals with shorter lengths of stay, shorter treatment duration without an increase in mortality, and a decrease in colonization and infection with resistant bacteria. Many studies have been conducted on interventions aimed at outpatient prescribers proving the prominent reduction in antibiotic

prescriptions and resistance rates. The government urged in 2017 that all hospitals include stewardship programs in their organizational mandates. In 2017, European Commission issued reports that highlighted the successful implementation of AMS in clinical communities of different countries.

The analysis of the different classes of antibiotics, when applying the WHO **AWaRe (Access, Watch, Reserve)** categorization, found a high level of consumption of Watch group drugs like cephalosporins and quinolones in some of the countries, and a very high level of consumption of third generation cephalosporins in all states in India[3]. To promote responsible use of antibiotics and slow the spread of antibiotic resistance, the WHO Global Programme of Work includes a target that at least "60% of total antibiotic prescribing at the country level should be Access antibiotics by 2023[2]"

Antimicrobial stewardship (AMS) refers to interventions and control programs for the optimization of antibiotic usage. Antimicrobial stewardship is growing fastly in numbers with diverse contexts ranging from hospitals to the veterinary community. Despite much acceptance, the term is still facing many challenges in different communities. There are different ways to view antimicrobial stewardship such as a collection of coordinated interventions, a program, a philosophy, and an ethic.

Antimicrobial stewardship policies are mainly focused on the optimization of antibiotic usage to reduce antimicrobial resistance and improvement of patients' outcomes and hospital hygiene in different healthcare centers. This may involve creating criteria for the use of antibiotics, such as limiting their use to specific indications or restricting certain antibiotics to specific patient populations

The infectious diseases team should follow evidence-based recommendations for the duration of the treatment. The IV drugs should be shifted to the oral route of administration to shorten the patient's stay at the hospital to avoid catheter associated infections. The treatment plan for gram positive and gram-negative bacteria is also established based on the identified pathogen(s) to avoid unnecessary prolonged treatments.

This book is aimed to provide Diagnostic guidance, Clinical guidance on the management of common infections including empiric antibiotic treatment at the first clinical presentation including Anaerobic infection, Definitive treatment guidance for pathogens after culture report available, National Treatment guidelines for Malaria, Tuberculosis and Vaccination schedule, Prophylaxis guidance for surgery, Infective Endocarditis, Post exposure prophylaxis for Hepatitis B virus, Human Immunodeficiency Virus, Antibiotic activity Spectrum, Intrinsic resistance / Expected resistance of organisms and Dosing guidance including "**No Antibiotic**" approach when appropriate.

# Chapter-2: Antimicrobial Stewardship

Antimicrobial stewardship (AMS) is defined as "**coordinated interventions designed to improve and measure the appropriate use of antimicrobials by promoting the selection of the optimal antimicrobial regimen, dose, duration of therapy and route of administration**".

Today, AMS is one of three "pillars" of an integrated approach to health systems strengthening. The other two are infection prevention and control (IPC) & Medicine and patient safety.

| **Think D8 – before prescribing Antibiotics[2]** | |
|---|---|
| **Diagnose** | What is the clinical diagnosis?<br>Is there evidence of a significant bacterial infection? |
| **Decide** | Are antibiotics really needed?<br>Do I need to take any cultures or other tests? |
| **Drug** | Which antibiotic to prescribe?<br>Is it an Access or Watch or Reserve antibiotic?<br>Are there any allergies, interactions or other contraindications? |
| **Dose** | What dose, how many times a day?<br>Are any dose adjustments needed, for example, because of renal impairment? |
| **Delivery** | What formulation to use? Is this a good quality product?<br>If intravenous treatment is needed, when is step down to oral delivery possible? |
| **Duration** | For how long? What is the stop date? |
| **Discuss** | Inform the patient of the diagnosis, likely duration of symptoms and any likely medicine toxicity and what to do if not recovering. |
| **Document** | Write down all decisions and the management plan |

## Aims of Antimicrobial Stewardship

- to optimize the use of antibiotics;
- to promote behaviour change in antibiotic prescribing and dispensing practices;
- to improve quality of care and patient outcomes;
- to save on unnecessary health-care costs;
- to reduce further emergence and spread of AMR;
- to prolong the lifespan of existing antibiotics;
- to limit the adverse economic impact of AMR; and
- to build the best-practices capacity of health-care professionals regarding the rational use of antibiotics

**Steps of rational antibiotic use**:

### • Step 1: Making a clinical diagnosis:

It often helps us to predict causative pathogens fitting in to a clinical syndrome which would tailor the correct antibiotic rather than blindly relying on fever, procalcitonin levels, WBC counts, cultures or radiology to make a diagnosis of infection.

A risk assessment of the patient, likely to have an infectious disease should be done followed by appropriate culture to diagnose the same.

### • Step 2: Limit the Empiric Antibiotic Therapy

Empirical antibiotics should be started based on the likely infective syndrome.

## • Step 3: Know Your Bugs

After identifying the clinical syndrome- Elucidate possible sources of infection - Predict possible microbial pathogens - Predict the local resistance pattern based on institutional antibiogram.

## • Step 4: Choose the Appropriate Antibiotic

- Based on the spectrum of the antibiotic taking into account possible resistant patterns
- Use the correct dose, route and duration
- Ensure chosen antibiotic has adequate tissue penetration at the site of infection
- Optimize PK-PD parameters according to co-morbidities

## • Step 5: De-escalation/modification

- Modify empiric broad spectrum antibiotics depending on culture and antimicrobial susceptibility reports and patient status
- Stop polymyxins and glycopeptides if no carbapenem resistant organisms (CRO) or methicillin resistant Staphylococcus aureus (MRSA) identified on cultures –
- Avoid double or redundant gram negative or anaerobic coverage
- If etiology is not due to infectious origin-Discontinue antibiotics
- De-escalate combination therapy to a single agent

- Change a broad spectrum antibiotic to a narrow spectrum one
- Change IV to oral antibiotics
- De-escalation will reduce mortality and length of hospital stay.

## • Step 6: NO Antibiotic Approach[2]:

**Restrict the use of antibiotics in the following clinical situations**

| Infection | Can it be safely treated without antibiotics? | Comment |
|---|---|---|
| **Acute diarrhoea** | Yes, in the majority of cases (unless there is significant bloody diarrhoea) | Mostly infection is of viral origin and the illness is usually self-limiting. The cornerstone of treatment is rehydration and electrolyte replacement. |
| **Bronchitis** | Yes | Nearly all cases have a viral origin and there is no need for antibiotics. |
| **COPD Exacerbations** | Yes, in most mild Cases | Most exacerbations of COPD are not triggered by bacterial infections; only certain cases will benefit from antibiotic treatment. |
| **Otitis media** | Yes, in most mild Cases | Most mild cases of acute otitis media can be managed symptomatically and do not require antibiotic treatment. |

| | | |
|---|---|---|
| **Pharyngitis** | Yes, in most mild Cases | Most cases do not require antibiotics because the infection is viral. |
| **Sinusitis** | Yes, in most mild Cases | Most cases do not require antibiotics as the infection is viral |
| **Skin and soft tissue infections (mild)** | Only for certain conditions and in certain patients | In cases of wounds at low risk of becoming infected, antibiotic treatment is not needed.<br>In cases of animal bites, only wounds in high-risk anatomical locations and patients with severe immunosuppression benefit from antibiotic treatment. |

- Patients treated with symptomatic care only (no antibiotic care) should be clearly informed of what danger signs to monitor and what to do if they occur.
- Stop antibiotics when Microbial colonization is reported.

## • Step 7: Reduce the Duration of Therapy

Duration of therapy should be optimized to minimum possible to reduce selection pressure. Practice guidelines and recommendations for optimum duration of therapy for various infectious disease syndromes, suggest the following durations:

**Community acquired pneumonia : 5 days**

**Hospital acquired pneumonia : 8 days**

**Skin and Soft tissue infections : 5 days**

| | | |
|---|---|---|
| **Urinary tract infections – cystitis** | **:** | **3-5 days** |
| **Pyelonephritis** | **:** | **5-14 days** |
| **Catheter associated UTI** | **:** | **7 days** |
| **Staphylococcal aureus bactraemia –** | | |
| **low risk of complications** | **=** | **2 weeks** |
| **high risk of complications** | **=** | **4-6 weeks** |
| **Intra-abdominal infection** | **:** | **4-7 days** |
| **Surgical antibiotic prophylaxis** | **:** | **1 dose** |

A stop date should be planned and recorded in advance to ensure antibiotic is not given beyond the recommended duration.

**• Step 8: Optimize PK-PD parameters**

- We cannot influence how a drug gets metabolized but we can influence drug administration for maximum efficacy.
- Age and co-morbidities like renal failure, sepsis and burns also influence the outcome of the patients.
- Overall, exposure of the infective agent to the unbound antibiotic drug fraction at the relevant effect site seems to be the most important factor.
- Optimizing Pk-PD parameters include loading doses when needed, therapeutic drug monitoring for toxicity and efficacy and optimization of drug infusion or administration.

- For concentration dependent antimicrobials: Ex. Loading dose of **Colistin** 9 million units stat and then followed by 3 million units q8H or 4.5 million units q12H [to target Colistin average steady state plasma concentration (Css, avg = 2-2.5 mg/L)]
- For Time dependent antimicrobials with significant post antibiotic effect: Ex. Inj **Vancomycin** is given as a loading dose of 20-35 mg/kg followed by a maintenance dose of 15-20 mg/kg q12h targeting an AUC/MIC between 400-600 mg h/L.
- For Time dependent antimicrobials: Ex. β-lactams, BL/BLI combinations and carbapenems are administered as prolonged infusions

Consider **Extended infusions for β-lactams** (Penicillins, Cephalosporins, and Carbapenems) for the following patients:

1. Critically ill patients
2. Patients with infections with organisms which have MICs close to breakpoints.
3. Patients who have large apparent volume of distribution (AVD)
4. Patients with normal or increased GFR.

***Extended infusion**[8]:

- **Cefepime** 2g IV 8h over 3 hours (for SDD breakpoints in Enterobacterales except Salmonella, Shigella)
- **Ceftazidime-avibactam** 2.5g IV 8h over 2 hours

(Enterobacterales except for Salmonella, Shigella)

- **Piperacillin-tazobactam** 4.5g IV 6h over 3hrs/ 4.5g IV 8h over 4hrs (for SDD breakpoints in Enterobacterales except Salmonella, Shigella)
- **Piperacillin-tazobactam** 4.5g IV 6h over 3hrs (*Pseudomonas aeruginosa*)
- **Ampicillin- sulbactam** 3g IV 6h over 3 hours (Acinetobacter species)
- **Carbapenem** 2g 8h over 3hrs (CRE in critically ill patients)

- Single daily dose of aminoglycosides is encouraged as it improves efficacy and decreases nephrotoxicity.
- Drugs which are incompatible with aminoglycosides should be reconstituted and administered separately.
- In case of drugs requiring loading dose, the loading dose should be given to all patients regardless of the patient's creatinine clearance. Maintenance dose should be based on the creatinine clearance.
- **Doxycycline** should be given with half a glass of water and patients advised to avoid recumbent postures for an hour afterwards to avoid esophagitis.
- Oral **fluoroquinolones** and **doxycycline** should not be given with milk or milk products/calcium supplements as food decreases the absorption.

## Key steps of establishing a health-care facility AMS programme[2, 23-26]

1. **Hospital Leadership commitment:** Hospital administrator should play a front role and remain committed to AMSP providing necessary funding and infrastructure support.
2. **Set up a Health care facility AMS team:** A committee responsible for framing, implementing and monitoring adherence to AMSP consisting of an ID physician, Hospital Infection Control Committee, Clinical microbiologist, Stewardship nurses trained in clinical aspects, Clinical pharmacologist, quality improvement/patient safety managers and officer in charge of pharmacy department.
3. **Laboratory Stewardship:** Guide discussions on the potential implementation of rapid diagnostic tests and new antibacterial susceptibility test interpretive criteria (e.g., antibiotic breakpoints) that might impact antibiotic use. Microbiology labs and stewardship programs can work together to optimize the use of such tests and the communication of results.
4. **Support from Information technology:** Availability of Hospital information management system including laboratory information.
5. **Support from Pharmacology Laboratory:** Therapeutic drug monitoring of antimicrobials (PK-PD) to mitigate the issue of developing resistance.

6. **Antimicrobial policy guidance:** Every hospital should frame their own hospital antibiotic policy in the form of an 'Antimicrobial stewardship guide' based on their institution specific antibiogram.
7. **Execute AMS Interventions:** Front-end strategies comprising of formulary restrictions with preauthorization of targeted antimicrobials, antibiotic cycling, antibiotic-stop orders, selective/cascade reporting along with Back-end strategies of prospective audits with timely feedback interventions and antibiotic time-outs should be consistently implemented.
8. **Monitoring the compliance to AMSP:** Measurement of compliance to AMSP is achieved by analyzing the adherence to institutional policy, appropriateness of antibiotic prescription, quantity of antibiotic usage, antimicrobial susceptibility & resistance patterns, clinical and financial outcome indicators.
9. **Educate and train:** Continuous education and training needed for stake holders, medical practitioners, pharmacists and nurses on AMSP. Rational use of antibiotics needs to be taught at all levels of medical school curriculum

- Antimicrobial stewardship is not just a strategy—it is a necessity. By ensuring responsible antibiotic use, we safeguard patient's health, protect communities, and combat the growing threat of antimicrobial resistance. The future of medicine depends on our actions today.

## 2. B. Principles of Antimicrobial Action [42, 43]

| | |
|---|---|
| **Inhibit Cell wall synthesis** | Beta-Lactams, Fosfomycin, Glycopeptides, Lipoglycopeptides |
| **Inhibitors of Cell membrane function** | Daptomycin, Polymyxin-B, Colistin |
| **Inhibitors of Protein Synthesis** | 30S- Aminoglycosides, Tetracyclines, Tigecycline<br>50S- Macrolides, Clindamycin, Chloramphenicol<br>50S&70S-Linezolid |
| **Inhibitors of DNA & RNA Synthesis** | Fluoroquinolones, Metronidazole, Rifampicin |
| **Inhibitors of Folic Acid Synthesis** | Sulphonamides, Trimethoprim, Nitrofurantoin |

## Types of Antimicrobial Resistance

1. **Biological Resistance:** to changes that result in observably reduced susceptibility of an organism to a particular antimicrobial agent.
2. **Environmental Mediated Resistance**:
   **a)** Reduced pH-diminishes Erythromycin, Aminoglycoside action
   **b)** Increased pH-diminishes Tetracycline action
   **c)** Anaerobic environment-diminishes Aminoglycoside action
   **d)** Cation-increased Mg & Ca ion **-**diminishes Aminoglycoside action
3. **Micro-organism mediated Resistance-**
   **a) Intrinsic Resistance-**Antimicrobial resistance resulting from the normal genetic, structural, or physiologic state of a microorganism

**(Ex)-**GPC-Aztreonam, Klebsiella Sp-Ampicillin, Proteus Sp-Colistin

**b) Acquired Resistance**- Bacteria can obtain the ability to resist the activity of a particular antimicrobial agent to which it was previously susceptible. Bacteria can acquire resistance through a **new genetic mutation** that helps the bacterium survive or by getting DNA from a bacterium that already is resistant. Unlike intrinsic resistance, acquired resistance may be a trait associated with specific strains of a particular organism group or species. Therefore, the presence of this type of resistance in any clinical isolate is unpredictable.

Bacterium DNA might change and alter the production of protein, leading to different bacterial components and receptors which render the bacteria unrecognized by the antibiotic. Bacteria sharing the environment might harbor intrinsic genetic determinants of resistance that would alter the genomics of the bacteria. An example is Escherichia coli (E. coli) and Haemophilus influenza resistance to trimethoprim.

**DNA Transfer**:

Bacteria can share genetic components with other bacteria and transfer the resistant DNA through a horizontal gene transfer. Usually, bacteria acquire external genetic material through three main stages:

Transformation (through naked DNA incorporation)

Transduction (through the process of phagocytosis)

Conjugation (through direct contact).

Staphylococcus aureus resistance to methicillin (MRSA) is one type following the DNA transfer mechanism

## Common Pathways of Antimicrobial Resistance

1. Enzymatic degradation or Modification of Antimicrobial agent
2. Decreased uptake or Accumulation of the Antimicrobial agent
3. Altered Antimicrobial target
4. Circumvention of the consequences of antimicrobial action
5. Uncoupling of Antimicrobial agent-target interactions and subsequent effects on bacterial metabolism

## Summary of Resistance mechanism of Antimicrobial class

1. **Beta-lactam**
   a) Enzymatic destruction-(ex) Staph-penicillinase, Enterobacterales- ESBL, Carbapenamses
   b) Altered target-(ex) Staph MRSA, Strep pneumoniae-penicillin resistance
   c) Decreased uptake-(ex) Pseudomonas aeruginosa-Imipenem
2. **Glycopeptide**
   a) Altered target-(ex) Stap aureus & Enterococcus resistance to Vancomycin
   b) Target over production-(ex) VISA
3. **Aminoglycoside**
   a) Enzymatic modification-(ex)-Many GPC, GNB resistance
   b) Decreased uptake-(ex)some GNB resistance to Aminoglycosides
   c) Altered target-(ex) Enterococci to Tobramycin
4. **Quinolones**
   a) Decreased uptake-(ex) GNB & Staph (efflux only)
   b) Altered Target-(ex) GPC, GNB resistance to Aminoglycosides

5. **Macrolides**
   a) Efflux-(ex) Streptococci& Staphylococci
   b) Altered Target-(ex) Streptococci& Staphylococci
6. **Tetracyclines**
   a) Decreased uptake
   b) Altered Target
   c) Enzymatic inactivation

## Mechanism of bacterial resistance

## Gram positive bacteria

MRSA is any strain of S. aureus that has developed (through natural selection) or acquired (through horizontal gene transfer) a multiple drug resistance to beta-lactam antibiotics. Beta-lactam (β-lactam) antibiotics are a broad-spectrum group that include some penams (penicillin derivatives such as methicillin and oxacillin) and cephems such as the cephalosporins

Staphylococcal cassette chromosome mec (SCCmec) is a genomic island of unknown origin containing the antibiotic resistance gene mecA. SCCmec contains additional genes beyond mecA, including the cytolysin gene psm-mec, which may suppress virulence in HA-acquired MRSA strains.

mecA encodes penicillin-binding protein 2a (PBP2a), which differs from other penicillin-binding proteins as its active site does not bind methicillin or other β-lactam antibiotics.

Enterococci showing resistance to aminoglycosides in two ways . Low level resistance is an inherent property, due to low uptake of drug and ribosomally mediated. High level resistance to aminoglycosides that is due to conjugative plasmids / transposons.

Resistance to Quinapristin – Dalfopristin due to *erm* genes (encoding 23SrRNA methyl transferase) – mediates macrolide-lincosamide- streptogramin B (MLSB). *vatD & vatE* genes (encodes virginiamycin acetyl transferase) - inactivate streptogramin A.

## Gram negative bacteria

Beta-lactamases (β-lactamases) are enzymes produced by bacteria that provide multi-resistance to beta-lactam antibiotics such as penicillins, cephalosporins, cephamycins, monobactams and carbapenems (ertapenem), although carbapenems are relatively resistant to beta-lactamase. Beta-lactamase provides antibiotic resistance by breaking the antibiotics' structure. β-lactamases (e.g., TEM-3, TEM-4, and SHV-2 which confer resistance to expanded-spectrum (extended-spectrum) cephalosporins.

Three major classes of enzymes are involved in carbapenem resistance: class A carbapenemases, class B metallo-β-lactamases (MBL), and class D β-lactamases (OXA)

# Chapter- 3: Empirical Therapy guidance for common infections including HAI & Anaerobic Infections

**Principles of Empiric Therapy[1]:**

**i.** No antibiotics are required for the majority of patients with acute febrile illness without an obvious focus of infection.

**ii.** Starting antibiotics for a presumed bacterial infection is not an emergency unless there is a suggestion of severe sepsis as per SEPSIS III consensus guidelines.

**iii.** Antibiotics, promptly, but adjust the drug's dosage and duration, switch to a new drug, or end antibiotic therapy when results do not support or justify the need to continue.

**iv.** Reassess the situation within 48 hours based on test results and patient status.

**v.** In patients with fever and thrombocytopenia, platelet transfusions are not recommended in general. Consider platelet transfusion when platelet counts are < 10,000 cu mm or in the presence of clinical bleeding in cases of dengue hemorrhagic fever

**vi.** Corticosteroids are not recommended in the treatment of acute undifferentiated fever.

**vii.** For patients with undifferentiated fever and negative rapid diagnostic tests for malaria and dengue- empirical treatment with Doxycycline is an option for the clinician.

**viii.** Supportive: Acetaminophen 650 mg every 6 hours round the clock is advisable, accompanied by tepid sponging for fever > $103^0$ F.

**ix.** Replace fluid and electrolytes as and when required either via parenteral or oral route as per clinical status as patients are prone for dyselectrolytemia and dehydration

## Avoid / Do not Use the following drugs in the respective infection site[8,9,10,11]

(Either they are not effective clinically in the respective infection site or not effective in vivo)

| | |
|---|---|
| **CSF** | • Agents administered by oral route only<br>• **First**- and **Second**-generation Cephalosporins and Cephamycins<br>• **Doripenem**, **Ertapenem**, and **Imipenem**<br>• **Clindamycin**, **Macrolides**, **Tetracyclines**<br>• **Fluoroquinolones** except **Moxifloxacin**<br>• BL/BLI combination drugs |
| **Respiratory Infection** | **Daptomycin** (inactivated by surfactant), Systemically administered **Colistin**, **Polymyxin B, Tigecycline** as stand alone therapy |
| **Infections other than UTI** | Mono therapy with Aminoglycosides |
| **Upper UTI** | **Nitrofurantoin**, **Oral Fosfomycin** |
| **UTI** | **Macrolides**, **Tetracyclines**, **Polymyxin B**, Echinocandins, Liposomal Amphotericin B |
| **Bacteremia** | **Tigecycline, Linezolid** and other Bacteriostatic drugs |
| **Ocular Infections** | Echinocandins |

## 3.1 Acute Undifferentiated Fever[1]

**Diagnostic Guidance**

**A. Day 1 or 2: Defer investigation** and **Anti-microbials**

Antibiotics can be considered in immunocompromised states, Febrile neutropenia, hemodynamically unstable patients with shock, asplenic patients**.**

**B. Day 3 or 4:** Complete Hemogram, Urine routine, Malaria - Peripheral smear / rapid diagnostic kits, may test for Dengue NS1 Ag.

**C. > 5 days:** As per (B) plus paired blood cultures, may test for Scrub typhus, Leptospirosis if suspicion is high, LFT, RFT, Urine Culture

**D.** X-ray chest for detecting ARDS in Scrub Typhus, Pleural Effusion in Dengue and USG abdomen to look for GB wall edema in Dengue fever and wherever necessary.

**Empirical Therapy Guidance for Acute Undifferentiated Fever[1,2,5,22]:**

| S. No | Type of Disease | Organisms | Initial Treatment / Preferred | Alternatives | Comments |
|---|---|---|---|---|---|
| 1 | **Typhoid fever**<br><br>**Duration of treatment**: 10-14 days. | Salmonella Typhi, Salmonella Paratyphi A | **Oral**:<br>**Trimethoprim-Sulfamethoxazole** 1 DS bid (or)<br>**Azithromycin** 1 G /Day/Oral<br>**Parenteral**:<br>**Ceftriaxone**-2g IV OD<br>**Paed:**<br>**Azithromycin** (o) 10mg/kg/OD/Day<br>**Ceftriaxone** IV 75 mg/Kg/OD/Day | **Cefixime** 20 mg/Kg/Day (or)<br>**Chloramphenicol** 500 mg qid (or)<br>**Amoxicillin-Clavulanate** 1.2 g IV tid | Change the empiric regimen based on susceptibility testing.<br>**>90% Salmonella Typhi is resistant to Fluoroquinolones. Avoid Fluoroquinolones for empirical treatment[27] .** |

| | | | | | |
|---|---|---|---|---|---|
| 2 | **Rickettsial infections**<br><br>**Duration of treatment:** 7days | Orientia tsutsugamushi, Rickettsia conorii, R. typhi | **Doxycycline** 100 mg bid PO/IV<br>**Paed:** **Doxycycline** (oral) 4.4 mg/kg/Day Div Bid | **Azithromycin** 500 mg OD **(or)** **Chloramphenicol** 500 mg qid<br>**Paed:** **Azithromycin** 10 mg/kg/Day od | **Parenteral Doxycycline is preferred in Scrub related ARDS, MODS, Pericarditis** |
| 3 | **Leptospirosis**<br><br>**Duration of treatment**: 7days | Leptospira sp | **Penicillin G** 1.5 MU IV /IM qid (or) **Ceftriaxone** 2 g IV OD<br>**Paed:** **Penicillin G** 250,000 U/kg/day IV div q6h, or **Ceftriaxone** 50 mg/kg/day IV, IM q24h, | **Doxycycline loading dose 200 mg IV stat followed by 100 mg IV BD**<br><br>**Paed:** **Doxycycline** (> 7 y) 4.4 mg/kg/day (max 200 mg/day) PO div bid or **Azithromycin** 20 mg/kg on day 1, 10 mg/kg on days 2 and 3 | **Mild Cases**-Oral<br><br>**Moderate & Severe Cases**-IV |

## 3.2 Sepsis[1,4]

### Diagnostic Guidance

**Sepsis** is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.

**Septic shock** is a subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone. Clinically they are identified by a vasopressor requirement to maintain mean arterial pressure of ≥ 65 mmHg and serum lactate level greater than 2 mmol/L (>18mg/dL) in absence of hypovolemia.

The organ dysfunction is represented by an acute increase in the Sequential [Sepsis-related] Organ Failure Assessment (**SOFA)** score of 2 points or more (with the baseline assumed to be 0 in patients without any known pre-existing organ dysfunction).

**SOFA Score predicts the mortality** due to organ dysfunction in sepsis. It includes organ systems like Respiratory, CVS, CNS, Liver, Renal and Hematological systems each system having scores 0-4

Score more than 11 predicts 90% mortality.0-6 points mortality is 10%. 7-9 points 20% mortality. 10-11 points predicts 50% mortality.

Adult patients with suspected infection can be quickly screened to identify which patients at risk for sepsis if they have at least 2 of the following 3 clinical criteria:

1. Respiratory rate of 22/minute or greater
2. Altered mentation
3. Systolic blood pressure of 100 mmHg or less.

These together constitute a bedside clinical score termed quick SOFA (**qSOFA**) useful for assessing and identifying the patients who may require more intensive monitoring and immediate intervention.

Then appropriate routine microbiologic cultures may include two sets of blood culture and wherever necessary respiratory secretions, urine, cerebrospinal fluid, wounds, and other body fluids should be obtained for cultures before initiation of empirical antimicrobial therapy.

## Empirical Therapy Guidance for Sepsis:

| Diagnosis | Preferred drug | Alternative | Remark |
|---|---|---|---|
| **Sepsis or septic shock with focus unclear**<br><br>**Rule out common tropical infections**<br><br>**Refer to appropriate sections for empirical antibiotic therapy for different sites of infection** | **Imipenem** 0.5 g IV qid<br>+/-<br>**Amikacin** 15 mg/kg/od<br><br>**+/-**<br><br>**Add MRSA or coverage against tropical infections or CR-GNB coverage or antifungals* in patients with appropriate risk factors.**<br><br>**Vancomycin**- 15 mg/kg/bd or tid<br>**Teicoplanin** 400 mg bid for 3 doses followed by 400 mg IV od<br>+/-<br>**Doxycycline** 100 mg bid IV<br><br>+/-<br><br>**Colistin** -9 mu IV stat, then 4.5 mu IV bid (or)<br>**Polymyxin B**<br>15-20 Lakh unit IV stat then 7.5 -10 lakh IV bid<br><br>+/-<br>Caspofungin 70 mg IV on day 1, then 50 mg IV OD (or) Micafungin 100 mg IV OD (or) Anidulafungin 200 mg IV stat, then 100 mg IV OD | **Meropenem** 1 g IV tid<br>or<br>**Cefoperazone – Sulbactam** 3 g IV bid<br><br>+/-<br>**Amikacin** 15 mg/kg/od<br><br>+/-<br><br>**Add MRSA or coverage against tropical infections or CR-GNB coverage or antifungals* in patients with appropriate risk factors.** | Septic shock patient must receive empiric combination therapy with at least two antibiotics of different antimicrobial classes.<br><br>Avoid **Piperacillin-Tazobactam** in septic shock till bacteremia with cephalosporin resistant organisms is excluded, as mortality increases (MERINO trial)<br><br>De-escalation of antimicrobials should be considered daily and at the earliest stage when the clinical situation permits/ once culture susceptibility reports are available**<br><br>Treatment duration of 7 to 10 days is adequate for most cases.<br><br>Longer courses appropriate in slow clinical response, undrainable foci of infection, bacteremia with *S. aureus*, some fungal and viral infections, or immunologic deficiencies.<br><br>Measurement of procalcitonin levels can be used to support shortening the duration of antimicrobial therapy. |

| |
|---|
| *__Risk factors for invasive Candida infections__ include immunocompromised status (neutropenia, chemotherapy, transplant, diabetes mellitus, chronic liver failure, chronic renal failure), prolonged invasive vascular devices (hemodialysis catheters, central venous catheters), total parenteral nutrition, necrotizing pancreatitis, recent major surgery (particularly abdominal), prolonged administration of broad-spectrum antibiotics, prolonged hospital/ICU admission, recent fungal infection, and multisite colonization. Triazoles are acceptable in hemodynamically stable, less ill patients who have not had previous triazole exposure and are not known to be colonized with azole-resistant species. |
| **If the infection is subsequently proven not to exist, then antimicrobials should be discontinued. De-escalation includes discontinuation of combination therapy within the first few days in response to clinical improvement and/or evidence of infection resolution |

## 3.3 Respiratory Tract Infections

### 3.3 A. Acute Pharyngitis[1]

| **Most Likely Pathogens[2]** | |
|---|---|
| **Viruses (>80 % of cases)** | Respiratory viruses (mostly)<br>Epstein barr virus (rarely) |
| **Bacteria** | Gr A Streptococcus<br>Streptococci ( Gr C & G)<br>Treponema pallidum<br>Neisseria gonorrhoeae<br>Corynebacterium diphtheriae |

## Diagnostic Guidance

Empirical antibiotic therapy is not indicated for viral infections with features like coryza, conjunctivitis, cough, hoarseness, diarrhoea, oral ulcerations and viral exanthema.

The **Centor score**[1,2]: (used to predict bacterial etiology)

1. Exudative pharyngitis,
2. Tender cervical lymphadenopathy,
3. Fever **(>38.0 C)** and
4. Absence of cough.

**Result:**

| Score | Group A Streptococcal Pharyngitis | Treatment |
|---|---|---|
| **0-2** | Unlikely | Symptomatic treatment only |
| **3-4** | Likely | Antibiotic treatment recommended |

**Empirical Therapy Guidance for Pharyngitis[1,5,22]:**

| Condition | Preferred drug | Alternative | Penicillin allergy |
|---|---|---|---|
| **Streptococcal pharyngitis** | **Penicillin V** (not easily available in India)-500 mg (8,00,000 IU) PO qid<br><br>**Penicillin G** not a substitute since oral absorption is -poor | **Amoxicillin-** 500-1000 mg PO tid,<br><br>(or)<br><br>**Benzathine Penicillin**<br>< 27 Kg-0.6 Mu IM single dose<br>≥ 27 Kg-1.2 Mu IM single dose | **Anaphylactic**: **Clindamycin**- 300 mg PO qid or 600 mg IV tid/ **Clarithromycin** 500 mg PO bid/ **Azithromycin**- 500 mg PO od<br>**Non-anaphylactic**: **Cephalexin** 750 mg bid PO/ **Cefadroxil**-1 gm once daily |
| **Paed Dosage: Penicillin V**-50-75mg/kg/Day PO div bid or tid,<br>**Amoxycillin- Standard Dose:** 50 mg/kg/Day div in tid, if those | | | |

| |
|---|
| who show poor response after 3 days course (or) history of antibiotic use in the past month then **Amoxycillin** **High Dose** 80-90 mg/Kg/Day PO div bid or tid, **Clindamycin** 30mg/kg/day PO div tid, **Clarithromycin** 7.5 mg/kg/Dose, **Azithromycin** 12 mg/kg od for 5 Days **(FDA Approved)** , **Cephalexin** 25mg/kg/dose, |
| **Antibiotic Duration:** [2]<br>**In India-High risk for Rheumatic fever-10 days** |

## 3.3 B. Acute Sinusitis[1,22]

| **Most Likely Pathogens**[2] | |
|---|---|
| **Viruses** | Influenza A & B<br>Rhino Virus<br>Corona Virus<br>Respiratory syncytial virus |
| **Bacteria** | Streptococcus pneumoniae<br>Hemophilus influenzae |

**Diagnostic Guidance**

Should be suspected in the following situations.

a) Persistence and non-improvement of symptoms and signs of acute rhinosinusitis beyond 10 days.

b) Worsening of symptoms or signs including new onset fever, headache or increase in nasal discharge following a typical viral URI that lasted 5-6 days and was initially improving (double sickening).

c) Acute onset of high fever **(>39.0 C )** with facial pain or purulent nasal discharge for at least 3-4 days.

## Empirical Therapy Guidance for Bacterial Sinusitis:

| Condition | Preferred drug | Alternative | Penicillin allergy |
|---|---|---|---|
| **Bacterial Sinusitis** | **Amoxicillin** 500-1000 mg PO tid / **Amoxicillin-Clavulanate** 625 mg PO tid | **Ceftriaxone**-2g IV OD / **Cefpodoxime**-200 mg PO bid (adults) | **Adults**: **Anaphylactic: Doxycycline** 100 mg bid / **Levoflox**-750mg PO od **Non-anaphylactic**: **Cefixime** 400 mg bid or **Clindamycin** 300 mg PO qid **Children**: **Anaphylactic**-**Levoflox**-10-15 mg /kg PO od **Non-anaphylactic**: **Cefixime** or **Clindamycin** |
| **Paed Dosage: Amoxicillin- Standard Dose:** 50 mg/kg/Day div in tid, if those who show poor response after 3 days course (or) history of antibiotic use in the past month then **Amoxicillin High Dose** 80-90 mg/Kg/Day PO div bid or tid with or without clavulanic acid, **Ceftriaxone** IM 50mg/kg/od, **Clindamycin** 30mg/kg/day PO div tid, **Clarithromycin** 7.5 mg/kg/Dose, **Cefixime** 8 mg/kg/Day bid | | | |
| **Antibiotic Duration-5 Days** | | | |

## 3.3 C. Acute Otitis Media (AOM)[1,22]

| Most Likely Pathogens[2] | |
|---|---|
| **Viruses (most cases)** | Influenza A & B<br>Rhino Virus<br>Corona Virus<br>Respiratory syncytial virus |
| **Bacteria (rarely bacterial superinfections can occur)** | Streptococcus pneumoniae<br>Hemophilus influenzae<br>Moraxella catarrhalis<br>Gr A Streptococcus |

**Diagnostic Guidance**

Antibiotic therapy is definitely indicated in any child with otorrhea (or) severe disease (or) bilateral AOM in children below the age of 24 months.

All other situations (children older than 24 months with non severe AOM whether unilateral or bilateral) (or) children between 6-24 months with non severe unilateral AOM can be managed with watchful waiting for 48-72 hours and antibiotics can be considered if there is failure to improve with conservative management.

**Empirical Therapy Guidance for Acute Otitis Media:**

| Condition | Preferred drug | Alternative | Penicillin allergy |
|---|---|---|---|
| **Acute Otitis Media** | **Amoxicillin** 500-1000 mg PO tid, **Amoxicillin Clavulanate** 625 mg PO tid | **Cefpodoxime**-200 mg PO bid (adults) / **Cefuroxime**-500 mg PO bid / **Ceftriaxone**-2g IV OD | **Anaphylactic: Azithromycin**-500 mg PO od / **Clarithromycin**--500 mg PO bid **Non-anaphylactic**: **Cefpodoxime, Cefuroxime** |

| |
|---|
| **Paed Dosage: Amoxicillin- Standard Dose:** 50 mg/kg/Day div in tid, if those who show poor response after 3 days course (or) history of antibiotic use in the past month then **Amoxicillin High Dose** 80-90 mg/Kg/Day PO div bid or tid with or without clavulanic acid, **Cefuroxime** 75-150 mg/Kg PO div bid, **Ceftriaxone** IM 75mg/kg/day, **Clarithromycin** 7.5 mg/kg/Dose, **Azithromycin** 10 mg/Kg on Day 1 followed by 5 mg/kg from day 2-5 |
| **Antibiotic Duration-5 Days** |

## 3.3 D. Acute Bronchitis[1]

| **Most Likely Pathogens[2]** | |
|---|---|
| **Viruses (most cases)** | Rhino Virus,<br>Influenza A & B<br>Parainfluenza virus,<br>Corona Virus,<br>Respiratory syncytial virus<br>Metapneumo virus & Adeno virus |

Acute tracheobronchitis is characterized by cough and phlegm production. The predominant etiology is viral. Antibiotics are not indicated even if sputum is purulent.

## 3.3.E. Community Acquired Pneumonia (CAP)[1,5]

| Most Likely Pathogens[2] | |
|---|---|
| **Bacteria** | Streptococcus pneumoniae (mostly)<br>Hemophilus influenzae (CLD, Smoking)<br>Moraxella catarrhalis (CLD, Smoking)<br>Staph aureus (associated with influenza)<br>Enterobacterales (CLD, Dementia, stroke)<br>Mycoplasma pneumoniae (young adults)<br>Chlamydia pneumoniae (young adults)<br>Legionella (exposure to cooling towers, hot tub, travel)<br>Coxiella burnetti (rural, live stock) |
| **Viruses** | Influenza A & B<br>Respiratory syncytial virus<br>Metapneumo virus<br>Parainfluenza virus<br>Corona Virus<br>Adeno virus<br>Rhino Virus<br>Other Respiratory viruses |
| **Special settings** | Burkholderia pseudomallei<br>Mycobacterium tuberculosis<br>Pneumocystis jirovecii |

## Diagnostic Guidance

Community Acquired Pneumonia is characterised as

a) Symptoms of an acute lower respiratory tract illness (cough with or without expectoration, shortness of breath, pleuritic chest pain) for less than 1 week.

b) At least one systemic feature (temperature >37.7°C, chills, and rigors, and/or severe malaise).

c) New focal chest signs on examination (bronchial breath sounds and/or crackles); with no other explanation for the illness.

d) When a chest X-Ray is available, CAP is defined as the above with new shadows on the X-Ray with no other defined cause.

All patients with CAP should be risk stratified for site of care as outpatients, or Inpatients non ICU and inpatients ICU based on scores such as CURB -65/ CRB-65, clinical assessment and pulse oximetry.

Blood cultures, Sputum cultures and CXR should be performed for inpatients. Periodical monitoring has to be done to identify early complication.

## Empirical Therapy Guidance for Adult Community Acquired Pneumonia[1,5]:

| Type of CAP | Preferred drug | Alternative | Comments |
|---|---|---|---|
| **Outpatients without co-morbidities (CURB Score-0-1)** | **Amoxicillin Clavulanate** | **Macrolide**** / **Cefuroxime** / **Cefpodoxime** | Beta lactam preferred over macrolides due to high prevalence of macrolide resistance in *S. pneumoniae* in India. **Doxycycline** monotherapy not recommended |
| **Outpatients with co-morbidities* or use of antimicrobial in 3 months (CURB Score-0-1)** | **Amoxicillin Clavulanate** and **Macrolide** / **Doxycycline** | **Cefuroxime** / **Cefpodoxime** and **Macrolide** / **Doxycycline** | |
| **Inpatient, Non-ICU (CURB Score-2)** | **Ceftriaxone** with **Macrolide** / **Doxycycline** | **Cefotaxime** / **Amoxicillin Clavulanate** and **Macrolide** / **Doxycycline** | If there is hypersensitivity to beta lactams: respiratory fluoroquinolones (exclude TB first) |
| **Inpatient ICU (CURB Score->3)** | **Ceftriaxone** with **Macrolide** / **Doxycycline** | **Cefotaxime, Piperacillin-Tazobactam** with **Macrolide** | |
| **Inpatient ICU with risk factors for *Pseudomonas aeruginosa*/ other Enteric Gram Neg Bacteria# (CURB Score->3)** | **Piperacillin-Tazobactam /Macrolide/ Doxycycline** | **Cefepime** / **Imipenem** / **Meropenem** with **Macrolide** / **Doxycycline** | The use of carbapenems is preferred over beta lactam beta lactamase inhibitor combinations in patients with septic shock |

| |
|---|
| **Dosage:**<br>**Amoxicillin Clavulanate** -625 mg PO tid / 1 g bid**, Macrolides (Azithromycin**-500 mg PO od or **Clarithromycin**--500 mg PO bid), **Doxycycline** 100 mg PO bid, **Cefuroxime** 500 mg PO bid, **Cefpodoxime** 200 mg PO bid, **Ceftriaxone** 2 gm IV od, **Cefotaxime** 2gm IV tid, **Piperacillin Tazobactam** 4.5 gm IV tid, **Cefepime** 2gm IV bid, **Imipenem** 500 mg IV qid |
| The empiric addition of oseltamivir in patients with CAP should be considered in the setting of an influenza outbreak |
| **If Community acquired MRSA## is suspected then:**<br>**Mild to moderate infection –Clindamycin IV or Doxycycline IV/PO or Trimethoprim-Sulfamethoxazole PO.**<br>**Severe infection – Vancomycin IV or Linezolid IV/PO.**<br>**If Hospital acquired MRSA### is suspected:**<br>**First line – Vancomycin IV or Linezolid IV/PO.**<br>**Second line – Ceftoroline IV** |
| * *Chronic heart, liver, renal or lung disease, diabetes mellitus, malignancies, alcoholism or use of immunosuppressive drugs*<br>** ***Azithromycin / Clarithromycin***<br># *Chronic respiratory disease (COPD, bronchiectasis, asthma, chronic bronchitis), neurologic disorders, enteral tube feeding and immunocompromised states.*<br>## *Preceding influenza, cavitary infiltrates with no underlying aspiration, shock, empyema*<br>**### if a hospitalized patient develops pneumonia symptoms (fever, cough, difficulty breathing, etc.) 48 hours or more after admission and if they have risk factors for MRSA [Patients with a history of hospitalization, contact with infected individuals or contaminated surfaces, or underlying medical conditions, invasive devices]** |

**CURB-65 Scoring: (1 score for each point present)**

**1). Confusion,**

**2). Urea: BUN (Blood Urea Nitrogen) > 10 mg/dL,**

**3). Respiratory Rate ≥ 30 /min,**

**4). Systolic BP < 90 or Diastolic BP ≤ 60 mm of Hg,**

**5). Age ≥ 65 Years**

## Empirical Therapy Guidance for Community Acquired Pneumonia in Paediatric Patients [1,5,22, 28, 29,30]

| **Outpatient treatment (oral therapy)** [28, 29,30] | | | |
|---|---|---|---|
| ***Age*** | ***First line*** | ***Second line*** | ***If Staphylococcus aureus suspected*** |
| **<3 months** | **Always admit and treat in the hospital** | | |
| **3 months to 5 years** | **Amoxicillin** (80 mg/ kg/d), BD for 5 days (in India, 40–50 mg/ kg/d is sufficient as penicillin-resistant pneumococci prevalence is <10%) | **Amoxicillin Clavulanate** (dose schedule same as that of **Amoxicillin**) *Or* **Cefpodoxime** (10 mg/kg/d), BD for 5 days *Or* **Cefuroxime** (30 mg/kg/d), BD for 5 days | **Amoxicillin Clavulanate** (dose schedule same as that of **Amoxicillin**) *Or* **Cefuroxime** (30 mg/kg/d), BD for 5 days *Or* **Linezolid*** (10 mg/kg/d), TID for 5 days |
| **>5 years** | Same as above and/or **Azithromycin** (10 mg/kg/d), OD for 5 days** | **Amoxicillin Clavulanate** or **Cefpodoxime** (as above) *and/or* **Azithromycin** (10 mg/kg/d), OD for 5 days** | Same as above |
| - Suspected influenza: Add oseltamivir -<15 kg -30 mg twice daily, 16-34 kg -45 mg twice daily, 35 -44 kg- 60 mg twice daily, 45 kg and more- 75 mg twice Daily | | | |

* **Linezolid** is a reserve drug for tuberculosis (TB), so the National Tuberculosis Elimination Programme (NTEP) has advised to use it with caution. **Add Macrolide only if clinical features suggestive of mycoplasma

| **Indications for admission or referral in Paediatric age group[28, 29,30]** | | |
|---|---|---|
| **Age < 3 months** | Oxygen saturation ($SpO_2$) < 92% | Marked tachypnea (e.g., 20 breath/min above the cutoff for that age) |
| **Severe malnutrition, not feeding/dehydrated** | Intermittent apnea and grunting | Failure of outpatient department (OPD) treatment |

| **Inpatient treatment (parenteral therapy) [28, 29,30]** | | | |
|---|---|---|---|
| ***Age*** | ***First line*** | ***Second line*** | ***Duration of Therapy*** |
| **<3 months** | **Cefotaxime ± Gentamicin** (5–7 mg/kg/d, OD) *Or* **Amikacin** (15 mg/kg/d, OD) *Or* **Ceftriaxone** (75–100 mg/kg/d), BD | **Piperacillin-tazobactam ± Gentamicin** or **Amikacin** *Or* **Cefoperazone-sulbactam ± Gentamicin** or **Amikacin** | 7-10 days (if no complications) *Or* 2-3 weeks (if complications) |
| **3 months to 5 years** | **Ampicillin** (100 mg/ kg/d, TID or QID)*** | **Amoxicillin Clavulanate** * *Or* **Cefotaxime** *Or* **Ceftriaxone** | 5-7 days (if no complications) *Or* 2–3 weeks (if complications) |
| **>5 years** | **Ampicillin** (dose same as above) and/or **Azithromycin** (10 mg/kg/d), OD for 5 days**** | **Amoxicillin Clavulanate** * Or **Cefotaxime** (150 mg/kg/d, TID) Or **Ceftriaxone** and/or **Azithromycin** (10 mg/kg/d), OD for 5 days**** | 5-7 days (if no complications) *Or* 2–3 weeks (if complications) |
| **When Methicillin sensitive Staphylococcus aureus suspected** | **Ceftriaxone** or **Cloxacillin** (50–100 mg/kg/d, QID) *Or* **Cefuroxime**/or **Amoxicillin Clavulanate** * + | **Ceftriaxone + vancomycin** (40–60 mg/kg/d, QID) or **linezolid**** (same as oral dose) | 10-14 days days (if no complications) *Or* 2–4 weeks (if complications) |

| | | | |
|---|---|---|---|
| | **Gentamicin** or **Amikacin** | | |
| **Methicillin-resistant *Staphylococcus aureus (CA - MRSA)*##** | **Clindamycin** IV or **Doxycycline** IV/PO or **Trimethoprim-Sulfamethoxazole** PO | **Vancomycin** IV or **Linezolid** IV/PO | 10-14 days days (if no complications) Or 2–4 weeks (if complications) |
| **Methicillin-resistant *Staphylococcus aureus (HA -*** *MRSA) ###* | B-lactam antibiotics + **Vancomycin**/ **Clindamycin** | **Linezolid*** *Or* **Clindamycin** | 10-14 days days (if no complications) Or 2–4 weeks (if complications) |
| **Inpatient ICU with risk factors for *Pseudomonas aeruginosa/* other Enteric Gram Negative Bacteria** | **Piperacillin Tazobactam** | **Cefepime / Imipenem / Meropenem** | 10-14 days days (if no complications) Or 2–3 weeks (if complications) |
| Suspected influenza: Add oseltamivir -<15 kg -30 mg twice daily, 16-34 kg -45 mg twice daily, 35 -44 kg- 60 mg twice daily, 45 kg and more- 75 mg twice Daily | | | |

* **Amoxicillin Clavulanate** injectable dose: 100 mg/kg/d, TID.
** **Linezolid** is a reserve drug for tuberculosis (TB), so the National Tuberculosis Elimination Programme (NTEP) has advised to use it with caution.
***Ampicillin** dose in severe infection: 200 mg/kg/d, TID or QID. .
****Add **Macrolide** only if clinical features suggestive of mycoplasma
## Preceding influenza, cavitary infiltrates with no underlying aspiration, shock, empyema
### if a hospitalized patient develops pneumonia symptoms (fever, cough, difficulty breathing, etc.) 48 hours or more after admission and if they have risk factors for MRSA [Patients with a history of hospitalization, contact with infected individuals or contaminated surfaces, or underlying medical conditions, invasive devices]

## 3.3 F Empyema[1]

**Diagnostic Guidance**

Empyema is a common complication of bacterial CAP. It should be suspected if there is persistent fever, leukocytosis and effusion on the CXR. Pleurocentesis and USG can be done to confirm the diagnosis.

The pleural fluid should be tapped and if it is purulent/ has organisms on the gram stain or culture, empyema is confirmed. It should also be suspected in complicated para-pneumonic effusions (pH < 7.0/ sugar <40 mg/dl/ LDH> 1000 IU/l/lactate > 45 mg/dl).

**Empirical Therapy Guidance for Empyema**

Drainage of the infected fluid is paramount and can be done by chest tube with or without fibrinolytics along with Empirical therapy for Community Acquired Pneumonia guidelines above.

## 3.4 Intra-Abdominal Infections[1]

### A. Primary or spontaneous peritonitis[1,5,22]

It refers to an extraperitoneal etiology, without an apparent source of contamination, in which the infectious bacteria enter the peritoneal cavity through the circulatory or lymphatic system and occurs commonly in patients with cirrhosis. Fever is the predominant symptom.

**Diagnostic Guidance**

Diagnosis requires an ascitic fluid absolute polymorphonuclear leukocyte (PMN) count> 250 cells/$mm^3$ and a positive ascitic fluid bacterial culture without an intra-abdominal surgically treatable source of infection.

Culture-negative neutrocytic ascites refers to patients who have a PMN count of at least 250 cells / $mm^3$ but with a negative bacterial culture in the absence of pancreatitis or recent receipt of antimicrobial therapy.

For an initial diagnostic paracentesis, other tests should be performed as clinically warranted on the remaining ascitic fluid which includes albumin, total protein, glucose, lactate dehydrogenase, amylase, and bilirubin.

**Prior to administering antibiotics, ascitic fluid (at least 10 ml) should be obtained and then directly inoculated into a blood culture bottle at the bedside, instead of sending the fluid to the laboratory in a syringe or container. The practice of immediate inoculation in blood culture bottles improves the yield on bacterial culture from approximately 65 to 90%**. Simultaneous blood cultures should be obtained, as up to 50% of patients with SBP have concomitant bacteremia.

## Empirical Therapy Guidance for Spontaneous Bacterial Peritonitis:

| Conditions | First Line | Alternative | Comments |
|---|---|---|---|
| **Commonly caused by gram negative organisms, *Escherichia coli* and *Klebsiella*. Occasionally *Staphylococcus, Enterococcus* or *Streptococcus* may be implicated.** | **Piperacillin Tazobactam** or **Cefoperazone-Sulbactam** | For severe cases and multi-drug resistant organism **Imipenem** or **Meropenem** may be more reasonable. | Antibiotics should be tailored as per the culture and sensitivity data. |
| **Dosage: Piperacillin-Tazobactam -**4.5 gm IV tid, **Cefoperazone-Sulbactam**-3 gm IV bid, **Imipenem**-500 mg IV qid, **Meropenem** -1 gm IV tid | | | |
| **Paed Dosage: Meropenem** 60 mg/kg/day IV div q8h **or Imipenem** 60 mg/kg/day IV div q6h**; or Piperacillin Tazobaactam** 240 mg pip/kg/day div q6h | | | |

## 3.4 B. Secondary peritonitis:

This most common etiology is the result of infectious bacteria from a source within the peritoneum as a result of spillage from an intra abdominal viscus. Pain is the predominant symptom.

## Empirical Therapy Guidance for Secondary Peritonitis:

| Conditions | First Line | Alternative | Comments |
|---|---|---|---|
| **Commonly caused by gram negative organisms, *Escherichia coli* and *Klebsiella and Anaerobes*** | **Imipenem** / **Meropenem** ± **Vancomycin** | **Colistin**, **Tigecycline**. | Antibiotics should be tailored as per the culture and sensitivity data. Add Echinocandins or fluconazole if risk factors for Candida. |
| **Dosage:** **Imipenem**-500 gm IV qid, **Meropenem** -1 gm IV tid, **Colistin**--9 mu IV stat, then 4.5 mu IV bid, **Tigecycline**-100mg IV stat followed by 50 mg 12 hourly, **Caspofungin** 70 mg IV on day 1, then 50 mg IV OD (or) **Micafungin** 100 mg IV OD (or) **Anidulafungin** 200 mg IV stat, then 100 mg IV OD | | | |
| **Paed Dosage:** **Meropenem** 60 mg/kg/day IV div q8h **or** **Imipenem** 60 mg/kg/day IV div q6h**; or** **Piperacillin Tazobactam** 240 mg pip/kg/day div q6h | | | |

## 3.4. C. Acute Diarrhoea[1,5]

**Diagnostic Guidance**

Vomiting is more suggestive of viral illness or illness caused by ingestion of a preformed bacterial toxin.

Symptoms more suggestive of invasive bacterial (inflammatory) diarrhoea include fever, tenesmus, and grossly bloody stool.

Most watery diarrhoea is self-limiting, testing is usually not indicated. If the patient has fever, tenesmus and bloody stool, stool microscopy and culture can be considered.

Routine microscopy of fresh stool is inexpensive and can identify the presence of numerous fecal leukocytes, suggesting an invasive bacterial infection.

**Pathogens causing Acute Diarrhoea[5]:**

| Mechanism | Illness | Stool findings | Causative agents |
|---|---|---|---|
| **Non-inflammatory (Enterotoxin)** | Watery diarrhoea | No fecal leucocytes,<br><br>Mild or No increase in fecal Lactoferrin | Vibrio cholerae, Enterotoxigenic Escherichia coli (LT & ST), Enteroaggregative E coli, Clostridium perfringens, Bacillus cereus, Staph aureus, Aeromonas hydrophilia, Pl.shigelloides, Norovirus, Rota virus, Enteric adeno virus, Giardia lamblia, Cryptosporidium sp, Cyclospora sp, Microsporidia |
| **Inflammatory (invasion or Cytotoxin)** | Dysentry | Fecal Polymorpho nuclear leucocytes, Substantial increase in fecal Lactoferrin | Shigella species, Salmonella Sp, Campylobacter jejuni, Enteroinvasive and Enterohemorrhagic E. coli, Yersinia enterocolitica, Listeria monocytogenes, Vibrio parahemolyticus, Clos.difficle, Entamoeba histolytica |

## Empirical Therapy Guidance for Acute Diarrhoea[1,5]:

| Cause | Treatment / Antibiotic |
|---|---|
| **Non-inflammatory** | Symptomatic treatment, Rehydration, Further evaluation if no resolution |
| **Suspected cause or based on stool direct examination & culture findings** | |
| ***V. Cholerae*** | **Doxycycline** 300mg once (Not recommended in children and pregnant women) **Azithromycin** 1 g as a single dose |
| **Shigella** | **Ceftriaxone** 2g i.v as single dose / **Cefixime** 400 mg bid for 5 days |
| **Amoebiasis** | **Metronidazole** 500 mg t.i.d for 5 days |
| **Giardiasis** | **Metronidazole** 500 mg t.i.d for 5 days |
| **Campylobacter** | **Azithromycin** 500 mg od for 3days |
| **Aeromonas** | **Cefixime** 400 mg bid for 5 days |
| **Ampicillin** or **Trimethoprim-Sulfamethoxazole** or **Fluroquinolones** are no longer drugs of choice in India in view of high resistance as per ICMR Annual Report 2023[27]. | |
| **Paed:** **Azithromycin** 10 mg/kg/day for 3 days or **Erythromycin** 40 mg/kg/day PO div qid for 5 days, **Cefixime** 8 mg/kg/day PO bd or tid, **Metronidazole** 30 mg/kg/day PO div qid | |

**Cautions and Considerations:**

- **Avoid Antibiotics in Certain Infections:** For suspected Shiga toxin–producing E. coli (STEC) infections, antibiotics should be avoided as they may increase the risk of hemolytic uremic syndrome.
- **Antimotility Agents:** Use with caution. While agents like loperamide can reduce stool frequency in traveler's diarrhea, they should be avoided in cases of dysentery or suspected C. difficile infection.
- **Probiotics**: Routine use is not recommended for acute diarrhea in adults, except in cases of post-antibiotic-associated illness.

## 3.5 Skin & Soft Tissue Infections[1, 22]

**Cellulitis:**

Cellulitis is an acute spreading infection that involves subcutaneous tissue; Clinically rapidly intensifying pain and redness is a common presentation. Fever and lymphadenopathy may be present. The borders in cellulitis are not well demarcated

**Furunculosis:**

Furunculosis is a deep infection of the hair follicle leading to abscess formation with an accumulation of pus and necrotic tissue. Furuncles appear as red, swollen, and tender nodules on hair-bearing parts of the body

**Carbuncle:**

It is a coalescence of several inflamed follicles into a single inflammatory mass with purulent drainage from multiple follicles

**Erysipelas:**

It is characterized by abrupt onset of fiery red swelling of the face or extremities. The distinctive features of erysipelas are well defined indurated margins, particularly along the naso-labial fold, rapid progression and intense pain.

**Necrotising Fascitis[1]:**

**a) Clinical signs which favour NF >Cellulitis:**

i) Symptoms; High grade fever, Delirium, Lethargy and Severe pain disproportionate to clinical signs

ii) General examination; Toxic look, Hypotension, Tachycardia, Pallor

iii) Limb examination; Skip areas (Areas of normal skin surrounded by infection) edema /tenderness extending beyond the cutaneous erythema, Dishwater-like pus discharge, Crepitus, Skin necrosis/ecchymoses, Probe sign* positive, Hypoesthesia over the skin, Bullous lesions, Wooden hard induration of subcutaneous tissue extending beyond the area of apparent skin involvement.

(Probe sign*: After infiltrating the involved area, a 2 cm incision is made down to the deep fascia. Gentle probing is performed with a blunt instrument or index finger and if the tissue dissects with minimal resistance, then probe test is considered to be positive).

**b) LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) (>6 favours NF):**

This score useful for the early operative debridement of necrotising fasciitis before it becomes clinically obvious.

| Parameter | Units/Score | Units/Score | Units/Score |
|---|---|---|---|
| CRP mg/dL | <150=0 | | ≥150 = 4 |
| WBC cells/$mm^3$ | <15000 =0 | 15000-25000 =1 | >25000 =2 |
| Hemoglobin g/dL | >13.5 = 0 | 11-13.5 = 1 | <11 = 2 |
| Sodium mmol/dL | ≥135= 0 | | <135 = 2 |
| Creatinine mg/dL | ≤1.6 = 0 | | >1.6 = 2 |
| Glucose mg/dL | ≤180= 0 | | >180 = 1 |

## 3.5 A. Empirical Therapy Guidance for Skin & Soft Tissue Infections

| Condition | Organism | Antibiotic | Duration | Comments |
|---|---|---|---|---|
| **Cellulitis** | *S.pyogenes*<br>*S.aureus* | **Cefazolin**<br>or<br>**Cephalexin**<br>or<br>**Amoxicillin-Clavulanate**<br>+/-<br>**Clindamycin** | 5-7 days (longer if clinically indicated) | -Obtain blood/ pus cultures before starting antibiotics<br>-Consider poly-microbial pathogens in diabetics<br>-Consider risk factors for MRSA and presence of TSS before using **Clindamycin** |
| **Necrotizing fasciitis** | *S. pyogenes*<br>*S.aureus*, anaerobes, Gram negative organisms (polymicrobial) | **Piperacillin-Tazobactam**<br>+<br>**Clindamycin**<br><br>**Alternative:**<br>**Meropenem**<br>+<br>**Clindamycin** | Generally, 14 days if adequate source control achieved | Early surgical debridement essential<br>Send blood and intraoperative specimens for bacterial cultures.<br>Consider use of IVIG for streptococcal NF/TSS |
| **Erysipelas** | *Propionibacterium acnes* /MSSA | **Amoxicillin-Clavulanate** | 5-7 days | |
| **Abscess** | *S. pyogenes, Oral anaerobes* | **Clindamycin or Ampicillin-sulbactum** | 5-7 days | |
| | *S.aureus*, facultative gram negative anaerobes | **Linezolid or Vancomycin**<br>+<br>**Ciprofloxacin** | Generally, 14 days | |
| **Dosage:** **Cefazolin**-1-2 g IV tid, **Cephalexin**-750 mg bid, 500 mg tid, **Amoxicillin Clavulanate**-1gm Po bid, 1.2 g IV bid, **Clindamycin**-300mg PO qid / 600 mg IV tid, **Piperacillin-Tazobatam**-4.5 gm IV tid, **Ampicillin-Sulbactam**-3 gm IV qid, **Linezolid**-600 mg PO bid, **Vancomycin**-15 mg/kg bid, **Ciprofloxacin**-400 mg IV bid | | | | |
| **Paed Dose :** **Cefazolin** 100 mg/kg/day IV div q8h**,** **Clindamycin** 30 mg/kg/day IV div q8h**,** **Vancomycin** 40 mg/kg/day IV q8h **Cephalexin** OR **Amoxicillin clavulanate** 45 mg/kg/day PO div tid, **Cefotaxime** 100–150 mg/kg/day IV div q8h OR **Ceftriaxone** 50 mg/kg/day IV, IM q24h | | | | |

## 3.5 B. Deep Neck Space Infections[1]:

## Empirical Therapy Guidance for Deep Neck Space Infections:

| Site of infection | Organisms | Immunocompetent | Immunosuppressed |
|---|---|---|---|
| **Peri-tonsillar abscess (Quinsy)** | *S.pyogenes, Oral anaerobes* | **Clindamycin or Ampicillin sulbactam or Amoxicillin-Clavulanate** | **Piperacillin-Tazobactam** |
| **Suppurative parotitis** | *Streptococci, oral anaerobes* | **Clindamycin or Ampicillin-sulbactam or Amoxicillin-Clavulanate** | **Piperacillin Tazobactam** plus **Clindamycin** |
| | | **Note:** Urgent ENT reference in case of obstructed salivary duct | |
| **Ludwig's angina** | *Streptococci, oral anaerobes* | **Clindamycin or Ampicillin-sulbactam or Amoxicillin-Clavulanate** | **Piperacillin-Tazobactam** Plus **Clindamycin** |
| **Odontogenic** | Viridians and other streptococci, *Peptostreptococcus* and other oral anaerobes | **Clindamycin or Ampicillin-sulbactam or Amoxicillin-Clavulanate** | **Piperacillin-Tazobactam** Plus **Clindamycin** |
| **Rhinogenic** | *S.pneumoniae, H.influenzae*, streptococci, anaerobes | **Ceftriaxone** + **linezolid** | **Piperacillin-Tazobactam** + **Clindamycin** |
| **Otologic** | *S.pneumoniae, H.influenzae*, streptococci, anaerobes | **Ceftriaxone** Plus **Metronidazole** | **Piperacillin-Tazobactam** + **Clindamycin** |
| **Prevertebral abscess** | *S.aureus*, facultative gram negative anaerobes | **Linezolid or Vancomycin** Plus **Ciprofloxacin** | **Piperacillin-Tazobactam** + **Clindamycin** |
| **Lemierre syndrome (Septic jugular thrombophlebitis)** | *Fusobacterium necrophorum*, *Streptococcus*, Anaerobes | **Piperacillin-Tazobactam** Plus **Clindamycin** | **Piperacillin-Tazobactam** Plus **Clindamycin** |

| |
|---|
| #Enterobacteriaceae must be considered as potential pathogens in immunosuppressed hosts (neutropenics, diabetics, critically ill, postoperative infections & trauma)<br>**Drainage of abscess/ collection where possible should be carried out |
| **Dosage:** **Cefazolin**-2 g IV tid, **Ceftriaxone**-2 gm IV od, **Amoxicillin Clavulanate**-1.2 g IV tid, **Clindamycin**-600 mg IV tid, **Piperacillin-Tazobactam**-4.5 gm IV tid, **Ampicillin-Sulbactam**-3 gm IV qid, **Linezolid**-600 mg PO /IV bid, **Vancomycin**-15 mg/kg bid, **Ciprofloxacin**-400 mg IV bid, **Metronidazole**-500 mg IV tid |

## 3.5 C Animal / Human Bite Infections

| Type / Organisms | Primary Agent | Alternative Agents | Comments |
|---|---|---|---|
| **Dog Bite:**<br>Pasteurella species, β-hemolytic streptococci, MSSA / MRSA, Staphylococcus intermedius, Neisseria species (commonly Neisseria weaveri) Eikenella corrodens, Capnocytophaga canimorsus. Actinomyces, Fusobacterium, Prevotella and Porphyromonas species. | **Amoxicillin Clavulanate** | **Cefotaxime + Clindamycin or Metronidazole**<br><br>**Severe bite/ Infection:**<br>**Ertapenem** | **Avoid Cloxacillin, Macrolides, First Generation Cephalosporins** |
| **Human Bite:**<br>Viridans streptococci, S. aureus, E.corrodens (which is particularly common in clenched-fist injury), Haemophilus influenzae, Anaerobic species including Fusobacterium nucleatum, Prevotella, Porphyromonas and Peptostreptococcus species | | | |

## 3.5 D Rabies PEP and PEP after Re-exposure[32]

**Animal transmitting Rabies in India**

| Frequent | Occasionally | Not Reported |
|---|---|---|
| Dogs<br><br>Cats | Monkeys<br>Mongoose, Shrew<br>Cows & Buffaloes<br>Foxes, Wolves & Jackels, Sheep & Goats, Beers, Pigs, Donkeys, Horses, Camels | Bats* Rodents* Birds Squirrel<br><br>* Bite by bats or rodents do not ordinarily necessitate rabies vaccination in India. However, bites by bats or rodents in unusual circumstances may be considered for vaccination in consultation with an expert in the field of rabies. |

**Category of Wound and Management**

| Category | Features | Wash | Vaccine / RIG |
|---|---|---|---|
| **Category-I** | Touching or feeding of animal<br><br>Licks on intact skin | Gently wash all scratches and wound with mild soap and running water for 15 min. Then apply Povidone-Iodine. | Vaccine & RIG Not indicated |
| **Category-II** | Nibbling of uncovered skin<br><br>Minor scratches or abrasions without bleeding | Gently wash all scratches and wound with mild soap and running water for 15 min. Then apply Povidone-Iodine. | Only Vaccine |
| **Category-III** | Single or multiple transdermal bites or scratches<br><br>Licks on broken skin<br><br>Contamination of mucous membrane with saliva | Gently wash all scratches and wound with mild soap and running water for 15 min. Then apply Povidone-Iodine. **Avoid Primary stitching until necessary** | Vaccine + RIG |

## Rabies -PEP-Post Exposure Prophylaxis

## Step 1-Management of wound

**Dos:**

- Washing of each wound(s) is/are desirable for up to 15 minutes and should be carried out as soon as possible.
- Gently clean wound/s with a detergent or any soap available.
- Apply available veridical topical preparation available antiseptic agent Preferably Povidone Iodine. If unavailable alcohol may be used

**Don'ts**:

- Do not apply irritants to the wound(s) like lime, chilli powder, turmeric, tobacco coffee powder, plant saps etc. as these will propel the virus deeper to cause nerve infection and ultimately leading to rabies encephalitis and death.
- Avoid bandage or covering of the wound (wherever practicable or as far as possible) and open dressing is recommended.
- Do not cauterize the animal bite wound(s).
- Avoid primary suturing of the wound. If needed, loose sutures can be done After proper RIG infiltration with only minimal suturing. In long run, it is always better to do secondary closure of wounds after two weeks to develop seroconversion on Day 14 i.e. 0.5IU/ml.

## Step 2-Active Immunization With Anti-Rabies Vaccines (ARV)

- The rabies vaccine is produced as one single IM dose with a potency of ≥ 2.5 IU Per IM dose for PEP and PrEP.
- Anti-Rabies Vaccine should be administered into the upper arm (deltoid region) in adults and into the anterolateral thigh region of young children and never

injected into to gluteal region. The gluteal region is not recommended because the fat present in this region retards the absorption of antigen and hence impairs the generation of the optimal immune response.

**i) Intradermal Route Of Vaccine (IDRV) Administration**

**Updated Thai Red Cross (TRC) regimen (2-2-2-0-2):**

- 0.1 ml of anti-rabies vaccine administered at 2 sites each on the deltoid area on days 0, 3, 7 & 28. There is no vaccine dose on day 14.
- WHO recommended a uniform ID dose of 0.1 mL for all CCVs having potency Equal to or greater than 2.5 IU per IM dose.
- With a 1 ml syringe, draw 0.2 ml (up to 8 units if the syringe is 40 units or 20 Units in 100 units syringe) of vaccine needed for one patient (i.e. 0.1 ml per ID site for 2 sites).

**ii) Intramuscular Route of Vaccine Administration**

**Essen regimen (1-1-1-1-1):**

One dose of anti-rabies vaccine administered intramuscularly on days 0, 3,7,14 & 28.

**Step-3 Passive Immunization With Rabies Immunoglobulin (RIG)**

- **Even the best of modern vaccines takes 10-14 days (or three injections Minimum on days 0,3 and 7) to elicit the protective antibody titre (or More than 0.5 IU/mL of serum) and thus RIG cover this vulnerable short Incubation (or window period) following exposures /severe wounds before it is physiologically possible for the victim to begin producing his/her antibodies**.
- Currently, two types of RIGs (ERIG & HRIG) (Equine Rabies Immunoglobulin, Human Rabies Immunoglobulin) are available for passive immunization
- However, RIGs alone (without vaccine) should never be used.

- **An infected bite wound is not a contraindication to the injection of RIG**.
- RIG is not indicated for bite victims that have ever received rabies vaccination (e.g. PrEP, PEP) beyond the seventh day after the first dose of the rabies vaccine, regardless of whether the doses were received on days 3 and 7, because an active antibody response to the rabies vaccine has already started, and this would represent a waste of RIG.
- It is preferable to use separate needles for infiltrating different wounds. Multiple needle injections into the wound should be avoided as far as possible.
- RIG should never be administered in the same syringe or at the same Anatomical site where the vaccine was administered.
- For mucosal exposure with no wound, rinsing with RIG can be considered.
- RIG must never be given intravenously

**It is advisable to also provide Inj. Tetanus Toxoid (TT) or Td (adult dT) vaccine 0.5 ml intramuscularly and course of antibiotics with analgesics if required.**

| Generic Name | Preparation available | Dose |
|---|---|---|
| **ERIG** | **300 IU per ml** | **40 IU per kg bodyweight** |
| **HRIG** | **150 IU per ml** | **20 IU per kg body weight** |

## Management of Rabies PEP During Re-Exposure For Previously Immunized People

a) For exposed or re-exposed patients who can document previous complete PrEP or PEP the following applies:
   - Wound washing (Good wound management)
   - One-Site Intradermal vaccine administration on days 0 and 3 or
   - One-site Intramuscular administration of an entire vaccine vial on days 0 and 3.
   - No RIG indicated

b) People, who cannot document previous PEP equivalent to PrEP or a complete PrEP , should receive a full PEP, including RIG if indicated.

c) If after completion of a complete course of PEP or PrEP, a re-exposure happens within 3 months then only thorough wound washing is to be done. The rabies vaccine is not required. If the duration of the last dose of the complete rabies vaccine regimen is more than 3 months then the Rabies vaccine is to be given as described in the schedule above.

## 3.6 Bone & Joint Infections[1]

## 3.6 A. Osteomyelitis[1]

**Diagnostic Guidance:**

**a) Radiology investigations:**

i) **X-ray should be first radiological investigation** for a suspected case of osteomyelitis even though is it insensitive test for acute osteomyelitis. However, X-ray finding will be positive in the majority of patients with chronic osteomyelitis.

Common finding includes osteopenia, periostitis and Brodie abscess.

ii) **Contrast enhanced MRI is the most sensitive** and specific radiological investigation for both acute and chronic osteomyelitis.

iii) Tracer scan with Tc99 or Gallium 67 citrate has high sensitivity for the diagnosis of acute osteomyelitis in non-traumatized bone.

iv) F-Fluorodeoxyglucose Positron emission tomography (PET) scan can be used if MRI is contraindicated as it has high diagnostic accuracy

**b) Blood investigations:**

Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are often abnormal.

White blood cell count can be normal or elevated and Anaemia can be a feature of chronic osteomyelitis.

Investigations directed towards identification of systemic illness like blood sugar, renal and liver function tests should be done.

**c) Cultures:**

Preferable to collect specimen prior to initiation of therapy.

Use standard techniques to collect sample.

**Swab cultures and sinus tract cultures may be unreliable and generally discouraged as they often grow skin colonizers.**

**Wound surface should be cleaned with normal saline before taking sample**

Samples should be collected using a syringe and needle.

A portion of the sample should also be placed in a sterile tube containing anaerobic medium like RCM if an anaerobic culture is required.

Blood culture-Blood culture should be obtained along with wound and bone culture for all patients presenting with acute Osteomyelitis.

## 3.6. B. Septic Arthritis[1]

**Diagnostic Guidance:**

i) Leucocytosis, high ESR and CRP are features of septic arthritis.

ii) Synovial fluid from the infected joint should send for WBC counts, gram stain, and culture before starting antibiotics.

iii) In septic arthritis synovial WBC counts are more 50000 cells /$mm^3$.

iv) Blood cultures should be obtained for all suspected cases of septic arthritis before starting antibiotics.

v) Radiology of infected joint in early stages will show periarticular soft tissue swelling, fat pad oedema with normal periarticular bone. As the infection worsens loss of joint space, periarticular osteoporosis and periosteal reaction will happen.

vi) CT and MRI are very sensitive techniques to pick up early changes of septic arthritis.

vii) Ultrasound is not only useful for assessing the amount of joint effusion but also to guide synovial fluid aspiration.

## 3.6. C. Prosthetic Joint Infection[1]

**Diagnostic Guidance:**

PJI is present when one of the following criteria is present:

a) Sinus tract communicating with a prosthesis

b) Presence of pus

c) Acute inflammation on histopathologic evaluation of periprosthetic tissue

d) Two or more positive cultures with the same organism like Coagulase negative Staphylococcus sp and Propionobacterium Sp. (intraoperatively and/ or preoperatively) or Single positive culture with the virulent organism like Staphylococcus aureus

**Investigations during –Preoperative:**

Total counts, ESR (>30) and CRP (>10). If ESR and CRP are normal PJI is unlikely.

Synovial fluid cell counts with predominant polymorphonuclear (PMN) Leucocyte and positive synovial culture have a high sensitivity and specificity for the diagnosis of Septic arthritis and PJI.

**Investigations during –Intra operative:**

At least 3 and optimally 5-6 samples of periprosthetic tissue must be obtained for:

**a**. Histopathology of periprosthetic tissue.

**b**. Periprosthetic tissue/pus culture.

**c**. Sonication of the prosthetic implant will detect biofilm organisms & improve microbiological yield especially in patients with prior receipt of antimicrobials.

Molecular methods and synovial fluid biomarkers are newer diagnostic modalities like especially **Interleukin 6** more than 7000 pg/ml in culture negative PJI.

## Empirical Therapy Guidance for Bone & Joint Infections [1,5,22]:

**Epidemiology of Osteomyelitis:** Staph aureus is the commonest agent**.**

After open fracture, contiguous long-bone osteomyelitis is typically caused by gram-negative bacilli or a polymicrobial mixture of organisms.

**Empiric therapy should target Staphylococcus aureus in case of hematogenous osteomyelitis and Gram negative bacteria in case of open fracture osteomyelitis.**

**Epidemiology of Prosthetic Joint Infection:**

About 50–70% of cases of PJI are caused by Staphylococci (S. aureus and coagulase-negative staphylococci), 6–10% by Streptococci, 4–10% by gram-negative bacilli, and the rest by other microorganisms.

**Empiric therapy should target Staphylococci Sp.**

| Suspected Organism | Drugs of Choice | Alternative Drugs | Remarks |
|---|---|---|---|
| **MSSA** | -**Cloxacillin**<br>-**Flucloxacillin**<br>-**Cefazolin** | -**Ceftriaxone**<br>-**Daptomycin** | **Rifampicin** 300-450mg PO/day may be added in presence of hardware.<br>Possible antagonism with Beta-lactams. Best results if along with FQN **(FQN use is unlikely in India due to widespread resistance)** |
| **MRSA** | -**Vancomycin**<br>-**Teicoplanin** | -**Daptomycin**<br>- **Linezolid**<br>-**Clindamycin**<br>- **Trimethoprim-Sulfamethoxazole** | -**Rifampicin** 300-450mg PO/day (as above)<br>-High dose of **Vancomycin** used 15-20mg/kg q8-12h (max. 2g/dose) Monitor trough levels, renal function |
| **B-hemolytic** *Streptococcus* | -**Penicillin G**<br>-**Ampicillin**<br>-**Ceftriaxone** | **Vancomycin** (if immediate hypersensitivity to Pen) | Monitor **Vancomycin** trough levels |

| | | | |
|---|---|---|---|
| ***Enterococcus spp.*** **Penicillin-susceptible** | -**Penicillin-G** -**Ampicillin** | -**Vancomycin** -**Teicoplanin** - | -Combination therapy with aminoglycoside not proven superior in PJI<br>-May use BLBLI (**Piperacillin-Tazobactam**) for BLase producers<br>- VRE to be treated as per individual susceptibility (**Daptomycin**, **linezolid**) are options |
| ***Enterococcus spp.*** **Penicillin resistant** | **Vancomycin** -**Teicoplanin** | **Daptomycin** - **Linezolid-** | |
| ***Pseudomonas spp.*** | **Ceftazidime** **Cefepime** **Ciprofloxacin** | -**Piperacillin Tazobactam** -**Meropenem** -**Polymyxin / Colistin** | **Ciprofloxacin** 750mg PO BD may be used upfront if susceptible (good penetration & bioavailability)<br>-Renal dose adjustment for **Colistin** only (Polymyxins have poor B&J penetration, use antibiotic laden spacer/ beads)** |
| ***Enterobacteriaceae*** | Beta-lactam based on in vitro susceptibility | **Meropenem** -**Polymyxin / Colistin** | **Ciprofloxacin** 750mg PO BD may be used upfront if susceptible (good penetration & bioavailability) -Renal dose adjustment for **Colistin** only (Polymyxins have poor B&J penetration, use antibiotic laden spacer/ beads)** |
| ***Propionibacterium acnes*** | **Ceftriaxone** | -**Vancomycin** -**Clindamycin** | Monitor **Vancomycin** trough levels<br>Higher risk of CDAD with **Clindamycin** prolonged use |
| **Gram- neg. Anaerobes** | **Metronidazole** | | **Metronidazole** need not be added for additional anaerobic cover in presence of BLBLI/ carbapenems |
| **Parenteral antibiotics are generally recommended for at least the 1st 2 weeks, may step down to oral antibiotics with good bioavailability if susceptible to complete the course of treatment* | | | |
| *** Antibiotic-impregnated cement spacers/beads must be considered in addition to systemic antibiotics especially in resistant infections with few drug options/ drugs which have poor B&J penetration/ drug toxicity.* | | | |
| **IV Dosage** : **Cloxacillin**-2 g IV qid, **Flucloxacillin**-2 g IV qid, **Cefazolin**-2 g IV bid, **Ceftriaxone**-2 g IV od, **Daptomycin**-8-10 mg/Kg/IV OD, **Vancomycin**-15 mg/kg IV bid, **Teicoplanin**-12 mg/kg q12h x 3 doses; foll. by 12 mg/kg/d, **Linezolid**-600 mg IV bid, **Penicillin G**-18-24 mu IV qid, **Ampicillin**-2 gm IV qid, **Ceftazidime**-2 gm IV tid, **Cefepime**-2 gm IV tid, **Piperacillin-Tazobatam-**4.5 gm IV tid, **Meropenem**-1 gmIV tid, **Polymyxin**-15L IV loading dose, 5L IV q8h, **Colistin**-9 mU loading dose, 4.5 mU IV bid, **Metronidazole**-500 mg Iv tid, | | | |

| | |
|---|---|
| **Trimethoprim-Sulfamethoxazole** -3.5 to 4 mg/kg/dose ,**Ciprofloxacin**- 400mg iv every 8 to 12 hrs, **Clindamycin** - 600mg iv every 6 hrs , **Rifampicin** - 600mg od<br><br>**Oral Dosage**: **Cloxacillin**-1g qid, **Flucloxacillin**-1g qid, **Linezolid**-600mg bid, **Metronidazole**-400 mg tid | |
| **Paed Dose: Cloxacillin** 100 mg/kg/ day div qid**, Clindamycin** 30 mg/kg/day IV div q8h**, Vancomycin** 40 mg/kg/day IV q8h, **Cefazolin** 100 mg/kg/day IV div q8h, **Ampicillin** 150 mg/kg/day IV div q6h, **Ceftriaxone**-50 mg/kg/day IV, IM q24h, **Cefepime** 150 mg/kg/day IV div q8h, **Meropenem** 60 mg/kg/day IV div q8h, **Ceftazidime** 150 mg/kg/day IV, IM div q8h, **Tobramycin** 6–7.5 mg/kg/day IM, IV div q8h, **Vancomycin** 40 mg/kg/day IV q8h, **Chronic**-**Cephalexin** 100 mg/kg/day PO div tid, **Dicloxacillin** 75–100 mg/kg/day PO div qid | |
| **Antibiotics with good Penetration into bone and Joint tissues** | Amoxicillin , Piperacillin -Tazobactam, Cloxacillin (2g IV Qid dose), Cephalosporins , Carbapenems , Aztreonam, Aminoglycosides , Fluroquinolones , Doxycycline , Vancomycin , Linezolid, Daptomycin , Clindamycin , Trimethoprim Sulfamethoxazole, Fosfomycin, Rifampicin , Dalbavancin and Oritavancin showed good penetration into bone and joint tissues reaching concentrations exceeding the MIC90 and / or MIC breakpoints of common bone and joint infections pathogens. |

## 3.7 Central Nervous System Infections

### 3.7. A. Acute Bacterial Meningitis[1]

**Diagnostic Guidance**

Differentiation of cause of ABM based on CSF analysis

| Parameter | ABM | Partially treated ABM | Viral | TBM |
|---|---|---|---|---|
| **CSF-TLC** | 1000-5000 (<100-10000) | 100-1000 | 10-1000 | 50-1000 |
| **CSF-DLC** | 80-95 % PMN | L > PMN | L > PMN<br>In acute stage PMN may predominate | L > PMN<br>In acute stage PMN may predominate |
| **CSF-Sugar** | < 40 in 50-60% | Low | Normal (except Mumps) | Ratio < 0.5 in 95% |
| **CSF-Protein mg%** | 100-500 elevated in all | 100-500 | 100-500 | 50-1000 |
| **CSF-Lactate** | Elevated | Elevated | Normal | - |

L-Lymphocytes PMN- Poly Morphonuclear Cells

a) The initial evaluation for a patient with suspected bacterial meningitis should include at least a complete blood count, two sets of blood cultures and if available CRP and PCT. CSF evaluation is a must. When a lumbar puncture cannot be done immediately, blood cultures should be drawn and empiric antibiotics administered.

b) The CSF should be sent for cell count, sugar and protein, gram stain and culture. An extra sample should be preserved for later tests that may be required. Samples should ideally be examined within 30- 60 minutes to increase positivity in CSF culture and for accurate assessment of cell counts. **If the delay is expected the samples should be kept at room temperature and never refrigerated.** The sensitivity of latex agglutination tests is kit dependent and variable.

c) Molecular tests have enhanced sensitivity as compared to cultures and can be requested if available.

d) Acute bacterial meningitis is a medical emergency. In children and adults presenting with suspected acute meningitis empirical intravenous antimicrobial treatment should be administered as early as possible. The "1 hour window" is generally regarded as the golden time period to initiate empirical antibiotic therapy. Any delay in diagnostic investigations should not delay therapy administration.

e) **Ceftriaxone** or **Cefotaxime** are equally recommended as first line agents for empiric treatment among acute bacterial meningitis. These drugs have adequate CSF penetration.

f) **Ampicillin** or **Amoxicillin** should be added to initial empiric antimicrobial regimen in the presence of any of the following risk factors for L.Monocytogenes infections.

- age over 60 years
- pregnancy
- immunosuppressive therapy
- organ transplantation
- malignancy
- advanced HIV disease
- DM
- End stage kidney disease
- Liver cirrhosis

g) In areas with known high prevalance of penicillin or cephalosporin resistance of S.pneumonia , Intravenous **vancomycin** would provide adequate antimicrobial coverage against resistant strains.

h) **Piperacillin Tazobactam**, **Cefazolin** have poor penetration in CSF. So don't use for CNS infections.

## Empiric therapy guidance for Community Acquired Acute Bacterial Meningitis[1,22]:

| | ***Likely pathogens*** | ***First line*** | ***Alternative*** |
|---|---|---|---|
| **Age < 1 month** | Gram negative (Klebsiella, E coli, Pseudomonas, Acinetobacter) Staphylococcus, Enterococcus, Pneumococcus, Candida | **Meropenem** (Add **Vancomycin** if risk of MRSA) | **Cefotaxime** and **Gentamicin** |
| **1 month – 50 years** | S. pneumoniae, Haemophilus influenzae, Meningococcus | **Ceftriaxone** and **Vancomycin** | **Cefotaxime** and **Vancomycin** |
| **>50 years, alcoholism or other diseases of impaired CMI** | S. pneumoniae, Meningococcus, Listeria, gram negative bacilli | **Ampicillin** and **Ceftriaxone** and **Vancomycin** | **Meropenem** and **Vancomycin** |
| **Meningitis-post neurosurgery or penetrating head trauma** | Staphyloccoccus epidermidis, staphylococcus aureus, propionibacterium acnes, pseudomonas aeruginosa, acinetobacter baumanii | **Meropenem 2gm iv 8 hourly and vancomycin 15mg/kg iv 8 hourly Based on cultures deescalate within 48hours-72hours** | **May need intra ventricular therapy in severe cases** |
| **Meningitis with basilar skull fractures** | S.pneumoniae, H.influenzae | **Ceftriaxone 2gm iv 12 hourly for 14 days** | |

| |
|---|
| **Dosage[5]:**<br>**Children**-**Penicillin G** 250,000 U/kg/day IV div q4h, **Ceftriaxone** 100 mg/kg/day IV q24h, **Cefotaxime** 200 mg/kg/day IV div q6h, **Meropenem**-120 mg/kg/Day in 3 divided doses, **Cefepime** 150 mg/kg/day IV div q8h, **Ampicillin**-200-400 mg/kg/Day in 4 divided doses, **Vancomycin**-45-60 mg/kg/Day in 3 divided doses,<br>**Adult**-**Meropenem**-6 g/Day in 3 divided doses, **Ceftriaxone**-4 g/Day in 2 divided doses, **Ampicillin**-12 g/Day in 6 divided doses, **Vancomycin**-45-60 mg/kg/Day in 2-4 divided doses |
| • The administration of dexamethasone 15- 20 minutes prior to giving the first dose of antibiotic has been found to be beneficial for pneumococcal meningitis in adults and Hemophilus influenza meningitis in children. The benefit of dexamethasone in childhood pneumococcal meningitis is debatable. The dose is 0.15 mg/kg every 6 hours for 48 hours -96 hours (10 mg 6 hourly in adults). A practical issue is that the turnaround time for confirmation of etiology of meningitis is at least 48 hours unless molecular tests are used.<br>Also in most suspected meningitis, the first dose of antibiotic is given soon after drawing blood cultures/ doing the lumbar puncture even before the basic CSF reports come in. Therefore it is acceptable to at least give one dexamethasone dose prior to the antibiotic in suspected meningitis. Further doses can be continued depending on the CSF reports. Steroids are not recommended for meningitis in neonates. |
| • If an organism is identified, therapy can be modified accordingly. If the organism is cephalosporin susceptible, **Vancomycin** can be stopped. |
| • In patients improving clinically, there is no need to repeat CSF analysis to demonstrate improvement or prior to stopping therapy. Repeat CSF should be done in cases of clinical non response at 48 hours, patients with penicillin/cephalosporin resistant strains who have received adjunctive dexamethasone, and in neonates to document sterilization of CSF. Causes of clinical non response in a case of bacterial meningitis include complications such as subdural empyema, cerebral abscess, ventriculitis etc or drug resistance. |
| • The duration of therapy for uncomplicated meningitis is generally 10-14 days. If a specific pathogen is identified then duration is pathogen dependent: 7 days for meningococcus and H. influenzae, 10-14 days for pneumococcus, 2-3 weeks for group B Streptococcus, 3-6 weeks for Listeria and 3 weeks for gram negative meningitis. |

## 3.7 B. Acute Febrile Encephalopathy/ Acute Encephalitis Syndrome[1]:

**Diagnostic Guidance:**

1) Think encephalitis if :

a) Altered mental status>24 hrs

b) Fever >38°c

c) Seizures or focal neurological signs

2) Use the encephalitis score :

a) Altered mental status >24 hrs→2

b) Seizures→3

c) CSF WBC > 5/mm→5

d) MRI abnormality → 9

Possible encephalitis : score >5 Sensitivity; 93% Specificity ; 51%

Probable encephalitis : score >8 Sensitivity ;51% Specificity ; 91%

3) CSF is king :

a) WBC>5/mm=best predictor

b) But 1 in 5 may have normal csf

c) Protein and glucose = non specific

4) Confirm the culprit:

a) HSV PCR =Gold standard

b) Repeat PCR if initial test is negative , but suspicion high

5) MRI helps, EEG supports:

a) MRI shows temporal lobe abnormality (HSV), thalamic signs (Arbo virus)

b) EEG: Lateralized periodic discharges (HSV) , delta Brush(Anti NMDAR or Autoimmune encephalitis)

6) Future tools:

mNGS : Broad, but costly

TIP:

Clinical clues + Smart testing =Best shot at diagnosis.

New tech is exciting, but clinical judgement still rules.

| Cause | Pointers to diagnosis | Diagnostic test |
|---|---|---|
| **Meningococcus** | Petechial rash, adrenal hemorrhage | Blood and CSF cultures<br>Latex/PCR in CSF for meningococcus |
| **Herpes simplex virus 1 and 2** | PLEDS on EEG, MRI showing temporal lobe involvement, CSF rbc | CSF HSV PCR for HSV-1 and II |
| **HHV6, HHV 7** | Rash | Specific PCR in CSF |
| **EBV** | Rash, generalized adenopathy, tonsillitis, organomegaly | EBV VCA IgM in blood<br>EBV PCR in CSF |
| **Varicella zoster** | Antecedent rash | Varicella IgM in blood<br>CSF varicella PCR |
| **HIV** | Fever, adenopathy, rash | HIV ELISA in blood<br>HIV PCR in blood |
| **Japanese encephalitis** | Epidemiology, dystonic and extrapyramidal movements<br>MRI shows changes in thalami, basal ganglia, substantia nigra | IgM antibody in serum and CSF |
| **Measles** | Antecedent or concurrent rash<br>History of vaccination | Measles IgM in blood and CSF |
| **Mumps** | Antecedent/ concurrent parotitis, high amylase,low sugar in CSF | Mumps IgM in blood<br>Mumps virus in CSF by PCR |
| **Influenza** | Respiratory prodrome, ongoing outbreak | Influenza PCR in throat swab |
| **Dengue** | Ongoing outbreak, rash, low WBC and platelets, biochemical hepatitis | Dengue specific PCR in CSF<br>Dengue IgM, NS1 antigen in blood |
| **Chikungunya** | Ongoing outbreak, Rash, severe joint pains | Chinkungunya PCR in CSF<br>Chinkungunya PCR in blood, IgM in blood |
| **Enterovirus** | Vesicular lesions in the mouth, GI symptoms, brain stem | Specific PCR in CSF |

| | | |
|---|---|---|
| | involvement | |
| **Rabies** | Epidemiology | Specific IgM antibody in CSF Nuchal skin biopsy/ conjunctival smears for direct fluorescent antibody Brain biopsy |
| **Chandipura** | Vesicular lesions in the mouth, GI symptoms, brain stem involvement | PCR in CSF, saliva/ IgM ELISA in CSF |
| **Nipah** | Epidemiology, contact with animals, fruit bats | PCR/ IgM ELISA in CSF |
| **Mycoplasma** | Respiratory illness, skin rash, haemolytic anemia | Mycoplasma IgM in blood<br>Mycoplasma PCR in throat swab |
| **Rickettsia** | Epidemiology, rash, eschar, multisystem involvement | IgM & IgG antibodies in serum Scrub typhus DNA in whole blood, buffy coat, eschar/skin rash |
| **Leptospirosis** | Icterus, myalgia, renal failure | Leptospira PCR in blood<br>Specific IgM in blood |
| **Enteric fever** | Protracted illness, hepatosplenomegaly | Blood cultures |
| **Cerebral malaria** | Pallor, splenomegaly | Smear or rapid antigen test for malaria |
| **Sepsis associated encephalopathy** | Infection at extra CNS site | Blood, urine cultures, CXR, chest and abdominal CT |

**Empiric therapy guidance for Acute Febrile Encephalopathy/ Acute Encephalitis Syndrome[1]:**

**Empirical Treatment (must be started immediately after drawing blood cultures)**

- **Ceftriaxone**-2 gm Iv bid
- **Acyclovir**[#] 10 mg /kg per dose tid (use in all suspected sporadic viral encephalitis)
- **Doxycyline** 100 mg bid
- All these drugs are empirical till alternate diagnosis is arrived.

| |
|---|
| * If the diagnosis of HSV is made a treat for 14-21 days. Stop acyclovir if alternative diagnosis made/ if MRI imaging does not suggest HSV/if two PCR 48 hours apart are negative. |
| * Imaging should be done before a lumbar puncture in patients with focal deficit, papilloedema, immune compromised hosts and those with features of raised ICP. Other contraindications for a lumbar puncture include respiratory/ cardiovascular compromise, platelet counts of less than 30,000 or infection at the site of the lumbar puncture. |
| # Prior to intravenous administration, acyclovir should be diluted to a concentration ≤7 mg/mL. (A 70-kg person would receive a dose of 700 mg, which would be diluted in a volume of 100 mL.) Each dose should be infused slowly over 1 h, rather than by rapid or bolus infusion, to minimize the risk of renal dysfunction. Care should be taken to avoid extravasation or intramuscular or subcutaneous administration. The alkaline pH of acyclovir can cause local inflammation and phlebitis (9%). Dose adjustment is required in patients with impaired renal glomerular filtration. Penetration into CSF is excellent, with average drug levels ~50% of serum levels[5] |

**Herpes simplex encephalitis :**

Dose of Acyclovir in patients with normal renal function is 10mg/kg intravenous every 8hours for 14 to 21 days.

Recently use of higher dose Acyclovir 20mg/kg intravenous every 8hours For 21days in neonates with herpes simplex encephalitis has decreased Mortality to 5% .

**Varicella Zoster encephalitis** :

Acyclovir 10-15mg/kg intravenous every 8hours for 10-14 days.

Alternative agent: Valacyclovir.

**Cytomegalo virus encephalitis:**

Combination of Ganciclovir 5mg/kg intravenous every 12hours and Foscarnet 60mg/kg intravenous every 8hours or 90mg/kg intravenous every 12hours for 3weeks.

**Auto immune encephalitis :**

Methyl prednisolone 1 gm intravenous OD for 5 days.

IVIG: 0.4 gm/kg/day for 5 days.

Plasmapheresis: 5 exchanges over 10-14 days.

## 3.7 C. Empiric therapy guidance for Brain Abscess[1]

| *Predisposing factor* | *Likely etiology* | *Empiric therapy* |
|---|---|---|
| **Hematogenous spread from cyanotic congenital heart disease/ lung infections/ endocarditis** | Aerobic/ microaerophilic Streptococci, S. aureus | **Ceftriaxone** and **Metronidazole** with/ without **Vancomycin** |
| **Contiguous spread from otitis media/mastoiditis/sinusitis/ dental infection** | Aerobic, microaerophilic, anaerobic streptococci, Anaerobic gram negative bacilli, S. aureus, Pseudomonas | **Ceftriaxone** and **Metronidazole** |
| **HIV** | Mycobacterium tuberculosis, Nocardia, Toxoplasma, Cryptococcus, Listeria | No empiric therapy |
| **Immunocompromised** | Nocardia, Mycobacterium, Toxoplasma, Mucorales, Aspergillus, Listeria, Cryptococcus, Candida | No empiric therapy |
| **Neonates** | Citrobacter/ Enterobacteriaceae, Candida | **Meropenem** |
| **Dosage[5]:**<br>**Children**-**Ceftriaxone** 100 mg/kg/day IV q24h, **Meropenem**-120 mg/kg/Day in 3 divided doses, **Vancomycin**-45-60 mg/kg/Day in 3 divided doses<br>**Metronidazole**-10 mg/Kg IV tid<br>**Adult**-**Meropenem**-6 g/kg/Day in 3 divided doses, **Ceftriaxone**-4 g/kg/Day in 2 divided doses, , **Vancomycin**-45-60 mg/kg/Day in 2-4 divided doses,<br>**Metronidazole**-400 mg IV tid | | |

## 3.8 Urinary Tract Infection[1,6]

**UTI Syndrome Classification**

| Syndrome | Features |
|---|---|
| **Asymptomatic Bacteriuria** | positive urine culture from an individual without symptoms or signs of UTI. |
| **Uncomplicated UTI** | Infection confined to bladder in afebrile men or women (Symptoms-Frequency, Urgency, Hesitancy, Suprapubic discomfort & sometime hematuria) |
| **Complicated UTI** | Infection beyond the bladder in men or women.<br>• Pyelonephritis<br>• Febrile or Bacteremic UTI<br>• Catheter Associated UTI<br>• Prostatitis |

**Diagnostic Guidance**:

**a.** **Urine microscopy** - the presence of 10 leukocytes/$mm^3$ of **uncentrifuged** urine or 10 leukocytes/hpf of the centrifuged sample, in a clinically suspected UTI, is important for diagnosis.

**b.** **Dipstick leukocyte esterase test** – This is a rapid screening test for UTI; a Negative test result does not rule out UTI.

**c.** **Urine culture** –This is most useful when collected from a patient with clinical features of UTI and should always be collected before the first dose of antibiotic. Usually, bacteriuria of $10^5$cfu/ml is associated with UTI.

However, **any colony count is significant in symptomatic young women and men with pyuria and bacteria grown from a suprapubic aspirate[6].**

d. Minimum sample volume of 10-20 ml. Collect Midstream clean catch urine. Supra-pubic aspiration especially in infants.

e. Collection procedure in a catheterized patient:

**If the catheter is in place<14days**, urine must be collected using a syringe and needle (No. 26) from the Foley's catheter after disinfecting the rubber surface with 70% ethyl alcohol.

**If the catheter is in place >14 days,** replace the old catheter before collection of urine for culture**.**

**Urine samples should not be obtained from catheter bags**.

f. **Storage & Transport**: Transport of the specimen and plating should be done within 1 hour. If delay, the urine sample must be refrigerated at 4ºC for a maximum of 6-8 hours.

g. **Blood cultures (two sets)** – Should be sent before the first dose of antibiotics if the patient is febrile, has suspected acute pyelonephritis or complicated UTI.

h. **Radiology** – Radiology should only facilitate the diagnosis of UTI.
Ultrasound of kidney, urinary tract and bladder is essential for all complicated and recurrent (more than 2 episodes) UTI.
CECT of kidney and the urinary system is indicated when pyelonephritis, perinephric abscess or intra-renal abscess are suspected.

**<u>Clinical features and investigations for different UTI syndromes</u>**:

| Conditions | Clinical symptoms | Routine Urine Analysis | Culture | Radiology |
|---|---|---|---|---|
| **Asymptomatic bacteriuria (ASB)** | Nil | May or may not have significant Pyuria and/or dipstick positive | Positive | Normal |
| **Uncomplicated UTI**<br>**-Acute Cystitis** | Fever with chills, Frequency, Urgency, dysuria, | significant Pyuria and/or dipstick positive | Positive | Bladder wall thickness |

| | | | | |
|---|---|---|---|---|
| | suprapubic tenderness | | | |
| **Complicated UTI**<br>**-Acute Pyelonephritis** | In addition to cystitis – Vomiting, Flank pain, renal angle tenderness | significant Pyuria and/or dipstick positive | Positive | -USG-Renal swelling -CECT if performed-Renomegaly, decreased opacification of affected area, perinephric fat stranding, congenital anomalies -DMSA if performed-Photopenic area |
| **Acute Epididymo-orchitis** | Acute onset unilateral scrotal pain with/without swelling. **Torsion should be ruled out** | significant Pyuria and/or dipstick positive | -Urethral swab for N.gono culture -MSU for culture -First pass urine / urethral swab for NAAT for N.gono, C.trachomatis & M.genitalia if available | -Colour Doppler USG for testicular vascularity assessment to differentiate between epididymo-orchitis and testicular torsion |

## Empiric treatment regimens for Urinary Tract Infections[1,5,19]:

| Urinary syndrome | Drug of choice | Alternative choice | Comments |
|---|---|---|---|
| **ASB** | Not required | | Only in Pregnancy and urological procedures treatment indicated. |
| **Uncomplicated UTI**<br>**-Acute cystitis** | **Nitrofurantoin**, **Fosfomycin** | **Trimethoprim-Sulfamethoxazole** **Amikacin** -Single dose | Dosage adjustment as per eGFR.<br><br>**Fosfomycin** and **Nitrofurantoin** should be avoided when there is suspicion |

| | | | |
|---|---|---|---|
| | | | of pyelonephritis or prostatitis / presence of systemic features of infection.<br><br>**Fosfomycin** susceptibility to being requested for, and used only for Gram-negative MDR organisms. |
| **Adult Dosage**: **Nitrofurantoin**-100 mg bid 5-7 days, **Fosfomycin**-3 g single dose, **Trimethoprim-Sulfamethoxazole** -1 DS bid-3 days, **Amikacin-**15 mg/kg single dose<br>**Paed Dosage: For mild disease: Trimethoprim-Sulfamethoxazole-**8 mg/kg/day of TMP PO div bid for 3 days, **Nitrofurantoin** 5-7 mg/kg/24 hr in 3-4 divided doses, **For moderate to severe disease: Cefixime** 8 mg/kg/ day PO qd, **Ceftriaxone** 50 mg/kg IM q24h for 3–5 days<br>**Alternative: Amoxicillin** 30 mg/kg/dose PO div tid in **Amoxicillin clavulanate** PO | | | |
| **Complicated UTI**<br>**-Acute Pyelo-nephritis** | **Ertapenem** | **Imipenem**<br>**Meropenem**<br>**Amikacin** | Dosage adjustment as per eGFR.<br><br>Treatment is for a minimum of 7 days.<br>The total duration of treatment is 14 days in children.<br><br>Same treatment regimen to be used for complicated UTI except the duration is extended (7-14 days).<br><br>Avoid **Piperacillin-Tazobactam** in septic shock till bacteremia with cephalosporin resistant organisms is excluded, as mortality increases (MERINO trial) |
| **Dosage: Ertapenem**-1 g IV od for 7-10 days, **Imipenem**-500 mg IV qid, **Meropenem**-1 gm IV tid, **Amikacin-**15 mg/kg od for 7 days<br>**Paed Dosage: Ertapenem** 30mg/Kg/Day div bid**, Meropenem** 60 mg/kg/day tid**, Imipenem** 60-100 mg/kg/day qid | | | |
| **Complicated UTI**<br>**-Acute Prostatitis** | **Ertapenem** | **Piperacillin-Tazobactam**,<br>**Imipenem**,<br>**Meropenem**,<br>**Trimethoprim-Sulfamethoxazole** | Urine and prostatic massage specimen for cultures to be collected before antibiotics. Prostatitis requires a minimum of 21 days antibiotics.<br>**Aminopenicillin &** |

| | | | |
|---|---|---|---|
| | | | **Glycopeptide have very poor Prostate penetration[5]** |
| **Chronic Prostatitis** | **Trimethoprim-Sulfamethoxazole 1 DS bid for 2-3 months** | **Fosfomycin 3 g od for 2-3 months Azithromycin 500 mg od for 3 weeks** | |
| **Dosage:** Ertapenem-1 g IV od, Imipenem-500 mg IV qid, Meropenem-1 gm IV tid, Piperacillin Tazobactam-4.5 g IV qid, Trimethoprim-Sulfamethoxazole -1 DS bid | | | |
| **Epididymo-orchitis (High risk of sexually transmitted)** | **Ceftriaxone + Doxycycline** | **Levofloxacin** | |
| **Dosage:** Ceftriaxone-500 mg IM single dose followed by Doxycycline 100 mg bid for 10 days, Levoflox-500 mg od for 10 days | | | |
| **Epididymo-orchitis (Low risk of sexually transmitted; likely due to enteric or urinary organisms)** | **Cotrimoxazole**, **Ciprofloxacin** | | |
| **Dosage**: Trimethoprim-Sulfamethoxazole -1 DS bid, Ciprofloxacin-500 mg bid | | | |
| *Note: -*<br>*Local antimicrobial resistance patterns should be the basis for empiric treatment.*<br>*For acute pyelonephritis, three strategies may be employed: hospital admission, completely outpatient parenteral antibiotic therapy (OPAT) or single dose of parenteral antibiotic and supportive care in emergency room before home discharge with subsequent OPAT.*<br>*Antibiotics should be changed based on susceptibility results as soon as they are available.*<br>*Intravenous antibiotics must be reviewed at 48 hours, and stepping down to oral antibiotics should be considered.*<br>***Post-treatment urine cultures in asymptomatic patients are not indicated routinely.***<br>*UTIs in males are usually complicated and uncommon in the absence of obstructive pathology.*<br>***No antibiotic treatment is required when there is the presence of pus cells in urine, along with negative culture results or in those with asymptomatic bacteriuria**. If the pyuria persists, causes for sterile pyuria should be investigated.* | | | |

## Empirical Treatment Regimens For Urinary Tract Infections In Paediatric Age Group

| Urinary syndrome | Drug of choice | Alternative choice | Comments |
|---|---|---|---|
| **Uncomplicated UTI** | **Trimethoprim-Sulfamethoxazole** -8-10 mg/kg/ day PO BID for 7 to 10 days | **Cefixime**- 8-10 mg/kg/day PO BID | |
| **Complicated UTI** | **Cefotaxime**- 8-10 mg/kg/day PO BID | **Amikacin-** 15 mg/kg/ day IV Single dose for 10 to 14 days | |
| | **Ceftriaxone**- 100 mg/kg/ day IV OD for 10 to 14 days | | |

### ANTIBIOTICS AND PEDIATRIC DOSAGE

| Antibiotics | Pediatric Dosage |
|---|---|
| **Amoxicillin** | 80 – 90 mg/kg/day PO in 2 divided doses |
| **Azithromycin** | 12 mg/kg PO OD |
| **Cefepime** | 150 mg/kg/ day in 3 divided doses |
| **Ceftriaxone** (< 2 months of age) | 60 mg/kg/ day in 2 divided doses |
| **Ceftriaxone** ( > 2 months of age) | 100 mg/kg/ day in 2 divided doses |
| **Ertapenem** (≥ 3 months to < 12 years) | 15 mg/kg/dose IV/IM BID |
| **Fosfomycin** (< 10 kg) | 200-300 mg/kg/ day IV in 3 divided doses |
| **Fosfomycin** (≥ 10 to < 40kg) | 200-400 mg/kg/ day IV in 3 divided doses |
| **Fosfomycin** (≥ 40 kg) | 12-16 g IV in 3 divided doses |

| | |
|---|---|
| **Fosfomycin** (≥ 4 weeks to < 1 year of age) | 1 g PO Single dose |
| **Fosfomycin** (≥ 1 year to < 12 years of age) | 2 g PO Single dose |
| **Fosfomycin** (≥ 12 years of age) | 3 g PO Single dose |
| **Meropenem** (< 2 months of age) | 20 mg/kg/ dose TID |
| **Meropenem** (> 2 months of age) | 120 mg/kg/ day in 3 divided doses |
| **Piperacillin – tazobactam** | 90 mg/kg/ dose QID |
| **Trimethoprim-Sulfamethoxazole** | 8 – 10 mg/kg/ day |

## 3.9 Pelvic Infections[1]

**Diagnostic Guidance:**

1. **Puerperal sepsis**: Defined as "Infection of the genital tract occurring between rupture of membranes or labour and the 42nd day postpartum with 2 or more of the following":
   * Pelvic pain
   * Pyrexia *i.e.* oral temperature 38.5°C or higher on any occasion
   * Abnormal vaginal discharge, *e.g.* presence of pus or discharge with a foul odour
   * Delay in the rate of reduction of the size of the uterus (<2cm/day during the first 8 days)

2. **Pelvic inflammatory disease (PID):** Comprises inflammatory disorders of the upper genital tract, including endometritis, salpingitis, tubo-ovarian abscess, or pelvic peritonitis. The symptoms include fever, pelvic pain, dyspareunia and abnormal vaginal discharge. The diagnosis of PID would be likely in the presence of features listed below:

   * Sexually active young women
   * Symptoms of pelvic or lower abdominal pain
   * Presence of cervical motion tenderness or uterine tenderness or adnexal tenderness on clinical examination
   * No other cause identified for the above symptoms and signs

3. **Vaginitis & cervicitis**: It comprises a spectrum of inflammatory disorders of the lower female genital tract characterized by vaginal discharge, odour, pruritus, and dyspareunia.

Blood cultures and other samples such as mid-stream urine, vaginal swab, cervical swab, throat swab, placental swabs, sputum, cerebrospinal fluid, epidural site swab, caesarean section or episiotomy site, wound swabs should be obtained prior to starting antibiotics.

Antibiotics should be given as soon as possible. Results of laboratory tests should be checked and the microbiologist consulted to ensure optimum antimicrobial therapy.

## Empiric Therapy Guidance for Pelvic Infections [1,5,19]:

| S. no. | Clinical condition / procedure | Common pathogens | Preferred AMA | Alternate AMA | Comments |
|---|---|---|---|---|---|
| 1. | **Puerperal sepsis / Septic abortion / Chorio amnionitis** | Gram positive: Streptococci (A, B, D), S.aureus<br>Gram negative: E.coli, Enterobacteriaceae including Klebsiella, Enterobacter, Citrobacter, Pseudomonas aeruginosa, Proteus mirabilis, Gardnerella vaginalis, Bacteroides, Clostridium perfringens, Anaerobes | **Piperacillin-Tazobactam** | **Clindamycin + Gentamicin**<br>If the patient is in septic shock, consider **Imipenem** / **Meropenem** with or without **Amikacin** plus **Vancomycin**, or **Teicoplanin** to cover MRSA | Usually polymicrobial. Antibiotics should be started within one hour of diagnosis of sepsis. |
| **Dosage**: **Piperacillin-Tazobactam** 4.5 g IVqid, **Clindamycin** 600-900 mg IV + **Gentamicin**-60 mg IV tid, **Imipenem**-500 mg qid, **Meropenem**-1 g tid, **Amikacin**-15 mg/kg IV OD, **Vancomycin**- 15 mg/kg/bd or tid, **Teicoplanin** 400 mg bid for 3 doses followed by 400 mg IV od | | | | | |
| 2. | **Pelvic Inflammatory disease (mild to moderate)** | *N. gonorrhoeae*, *C. trachomatis* and anaerobes. *E. coli, Bacteroides* GBS, GAS, *S. aureus* | **NACO based**:<br>Tab. **Cefixime**<br>PLUS<br>Tab. **Metronidazole**<br>PLUS<br>Cap. **Doxycycline** | **CDC based**:<br>**Levofloxacin** with **Metronidazole** or **Ceftriaxone** plus **Doxycycline** with or without **Metronidazole** | |
| **Dosage**: **Cefixime** (400 mg orally STAT) + **Metronidazole** (400 mg tds X 14D) + **Doxycycline** (100 mg bd X 14 D),<br>**Levofloxacin** (500 mg OD X 14 days) with **Metronidazole** (400 mg tds X 14days),<br>**Ceftriaxone** (250 mg IM single dose) +**Doxycycline** (orally 100 mg BD X 14 days) with **Metronidazole** (400 mg BD X 14 days) | | | | | |
| 3. | **Pelvic Inflammatory disease (severe) eg turbo-ovarian abscess, pelvic abscess** | | **Ceftriaxone** PLUS **Doxycycline** | **Clindamycin** PLUS **Gentamicin** or **Piperacillin-Tazobactam** / **Imipenem** (for severely ill patients) | An attempt should be made to obtain cultures and de-escalate based on that. Duration is two weeks but can be extended depending upon the clinical situation. Antibiotics may be altered after obtaining culture reports of pus/or blood |

| | | | | | |
|---|---|---|---|---|---|
| **Dosage**: **Ceftriaxone** (2 g IV OD) + **Doxy** (100 mg orally or IV BD)<br>**Clindamycin** (900 mg IV every 8 hours) + **Genta** IV or IM (2 mg/kg), followed by a maintenance dose (1.5 mg/kg) every 8 hours. Single daily dosing (3–5 mg/kg) can be substituted<br>**Piperacillin-Tazobactam** 4.5 g IV qid, **Imipenem**-500 mg IV qid | | | | | |
| 4. | **Vulvo Vaginal Candidiasis** | *C. albicans,*<br>*C. glabrata,*<br>*C. tropicalis* | Fluconazole<br>or<br>local<br>Clotrimazole | Miconazole | Treat for 7 days in pregnancy, diabetes<br>Recurrent infections: 150 mg Fluconazole on day 1,4,7 then weekly for 6 months |
| **Dosage: Fluconazole**-150 mg single dose, **Clotrimazole**-500 mg vaginal tablet single dose,<br>**Miconazole**-100 mg Vaginal suppository daily for 7 days | | | | | |
| 5. | **Vaginal Trichomoniasis** | *T. vaginalis* | **Secnidazole**<br>or<br>**Tinidazole**<br>**or**<br>**Metronidazole** | | Alcohol to be avoided during treatment and 24 hours after **Metronidazole** or 72 hours after completion of **Tinidazole** to reduce the possibility of a disulfiram-like reaction.<br>Partner treatment essential. |
| **Dosage: Secnidazole-**2 g PO Single dose, **Tinidazole**-500 mg bid -5 days,<br>**Metronidazole**-400 mg bid for 7 days | | | | | |
| 6. | **Bacterial Vaginosis** | Overgrowth of anaerobes *(Gardnerella vaginalis, Mobiluncus)* | **Metronidazole**<br>or<br>**Metronidazole**<br>gel<br>or<br>**Clindamycin**<br>Cream | **Secnidazole**<br>or<br>**Tinidazole**<br>or<br>**Clindamycin**<br>or<br>**Clindamycin**<br>ovules | Refrain from sexual activity or use condoms during the treatment.<br>**Clindamycin** cream is oil-based and might weaken latex condoms |
| **Dosage: Secnidazole**-2 g PO Single dose, **Tinidazole**-500 mg bid -5 days,<br>**Metronidazole**-400 mg bid for 7 days, **Metronidazole** gel- 0.75%, one applicator (5 g) intravaginal x 5 days, **Clindamycin Cream**- 2%, one applicator (5 g) intravaginal x 7 days,<br>**Clindamycin**-300 mg bid -7 Days, **Clindamycin ovules**- 100 mg intravaginally OD HS for 3 days | | | | | |

## 3.10 Infective Endocarditis[1,5]

**Diagnostic Guidance**:

As blood culture data is crucial in antibiotic selection, in stable patients with recent antibiotic exposure it is reasonable to stop all antibiotics and draw blood cultures after an antibiotic free interval. Three sets of blood cultures should be drawn at 30 minutes interval before the initiation of antibiotics.

**Table: Modified Duke's Criteria for the Diagnosis of IE-2023 Update**

| Criteria | Features |
|---|---|
| **Major Criteria** | 1. **Positive Blood Culture:**<br>Typical microorganisms consistent with IE from 2 separate blood cultures:<br>Viridans streptococci, Streptococcus bovis, HACEK group, Staphylococcus aureus; or community-acquired enterococci in the absence of a primary focus,<br>**(or)**<br>persistently positive blood culture, defined as recovery of microorganism consistent with infective Endocarditis from: at least 2 positive cultures of blood samples drawn >12 h apart or all 3 or a majority of ≥4 separate cultures of blood (with first and last sample drawn at least 1 h a part)<br>**(or)**<br>Single positive blood culture for Coxiella burnetii or anti–phase 1 IgG antibody titer ≥1:800<br>**(or)**<br>PCR or other nucleic acid based technique for Coxiella burnetii, bartonella species, or Tropheryma whipplei from blood<br>**(Or)**<br>Indirect immunofluorescence assays for detection of Igm and IgG antibodies to bartonella henselae or Bartonella quintana with immunoglobulin G (IgG) titre more than or equal to 1:800<br><br>2. **Imaging Citeria**-Evidence of endocardial involvement<br>(1) Echocardiography and cardiac computed CT imaging<br><br>1. Echocardigraphy and cardiac CT showing vegetation ,valvular /leaflet perforation ,valvular /leaflet aneurysm ,abscess,psuedoaneurysm,or intracardiac fistula.<br>**OR**<br>Significant new valvular regurgitation on echocardiography as compared with previous imaging.Worsening or changing of preexisting regurgitation is not suffivient.<br>**OR**<br>New partial dehiscence of prosthetic valve as compared with previous imaging |

| | |
|---|---|
| | 2. Positron emission computed tomography with 18F -flurodeoxyglucose (18F) FDG PET CT imaging) Abnormal metabolic activity involving native or prosthetic valve ,ascending aortic graft (with concomitant evidence of valve involvement) intracardiac device leads or other prosthetic material.<br><br>**3.Surgical criteria**<br>Evidence of IE documented by direct evidence during heart surgery neither Major imaging criteria nor subsequent histological or microbiological confirmation |
| **Minor criteria** | 1. Predisposition, predisposing heart condition, or IDU, Endovascular intracardiac implantable electronic device, previous history of IE,<br>2. Fever, temperature >38°C or 100.4 °F<br>3. Vascular phenomena, major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages & Janeway lesions<br>4. Immunological phenomena glomerulonephritis, Osler nodes, Roth spots, and rheumatoid factor<br>5. Microbiological evidence: positive blood culture but does not meet a major criterion as noted above (excludes single positive cultures for coagulase negative staphylococci and organisms that do not cause endocarditis) or serological evidence of active infection with organism consistent with IE |
| **Definitive IE**- Two Major criteria or One Major and at least 3 Minor criteria or 5 Minor Criteria<br><br>**Possible IE**- 1 Major and 1 or 2 minor criteria, 3-4 minor criteria | |

**Empirical Therapy Guidance for Antimicrobial therapy for IE[1,31]:**

| Native Valve IE | Etiologies (usual) | Suggested Regimens (Primary) | Adjunct Diagnostic or Therapeutic Measures or comments |
|---|---|---|---|
| **Empirical Treatment-awaiting cultures (No h/o skin/soft tissue infection or abscesses, no h/o IV drug abuse, no h/o CVC line or recent cardiac/prosthetic valve replacement)** | VGS, Enterococci, NVS, Streptococcus gallolyticus | **Ceftriaxone** 2 g IV q24h plus **Vancomycin** 1 gm 8hrly (40mg/kg/day in two divided doses) or **Ampicillin-sulbactam** 3g q6h (**Ampicillin-** 150mg/kg/day or **Sulbactam** 50 mg/kg/day ) in 4 divided doses or **Ampicillin** 2 g IV in q4h Or 200 mg/kg/day in six divided doses<br><br>**Paed** :<br>**Peniciilin G**- 200,000–300,000 U/kg/24 hr IV given every 4 hr up to 12–24 million U/day **(or)**<br>**Ceftriaxone-**100 mg/kg/24 hr IV given every 12 hr or 80 mg/kg/24 hr IV given every 24 hr up to 4 g/day (if total amount is over 2 g/day then dosing should be every 12 hr) **(or)**<br>**Vancomycin-**40 mg/kg/24 hr IV given every 8–12 hr up to 2 g/day | **Gentamicin** used for synergy, peak levels need not exceed 4 mcg/ml.<br>• Advantage of **Ampicillin-sulbactam** (AS) over **CP/Ampicillin**: AS Covers β-lactamase producing Enterococci & HACEK Group of organisms<br>• Combination of **Ceftriaxone** with **Gentamicin** does not cover Enterococcus, Nutritionally variant **Streptococci (Abiotrophica & Granulicatella)** |

| | | | |
|---|---|---|---|
| **Native Valve IE (Risk factors for S. aureus)** | MSSA<br><br>CA-MRSA, HA-MRSA*** | **Flucloxacillin** (200 -300 mg/kg/day in 4-6 equally divided doses) **(or)**<br>**Cefazolin-** 100 mg/kg/24 hr IV given every 8 hr up to 12 g/day<br>in three divided doses for 6 weeks<br>**Vancomycin**: 40-60 mg/kg/24 hr IV given every 8-12 hr up to 2 g/day<br>**Alternative Therapy:**<br>**Daptomycin**<br>6 mg/kg q24h (for Right-sided IE)<br>Or<br>8-10 mg/kg q24h (For left- sided IE) | **Vancomycin** trough levels -1 hour before the 4rth dose of **Vancomycin** Recommended **Vancomycin**. Trough levels in serious MRSA infections- 15-20 µg/ml. **Nephrotoxicity** (0-12%) which is associated with **Vancomycin** trough levels greater than or equal to 15 µg/mL, in those receiving high dose **Vancomycin** (greater or equal to 4 / day), **concomitant use of nephrotoxic agents** |
| **PVE pending blood cultures or with negative blood cultures** | | **Ceftriaxone** 2 g IV q24h<br>Paed Dose: 100mg/kg/day in two divided doses<br>AND<br>**Vancomycin** (25 mg/kg loading dose followed by 30-60 mg/kg per 24 h IV)<br>AND<br>**Gentamicin** 1mg/kg q12h<br>AND<br>**Rifampicin** 450-900 mg od po/IV | Use lower dose of **Rifampicin** in severe renal impairment. |

- *NVS–Nutrionally Variant Streptococci
- **CP-Crystalline Penicillin
- VGS-Viridans Group Streptococcus
- ***MSSA-Methicillin Sensitive Staphylococcus aureus,
- CA-MRSA-Community-Acquired Methicillin Resistant Staphylococcus aureus,
- HA-MRSA-Hospital Acquired Methicillin Resistant Staphylococcus aureus.

## 3.11 Health Care Associated Infections[1]

### 3.11 A) SSI-Surgical Site Infection:

Surgical site infections (SSIs) are a major concern, affecting about 2-5% of surgical patients.

**Do not report following conditions as SSI:**

Stitch abscess (minimal inflammation and discharge confined to the points of suture penetration).

Episiotomy infection site

Newborn circumcision infection site.

Infected burn wound.

**Note:** Specific criteria are used for identifying infected episiotomy and circumcision sites and burn wounds.

**Diagnostic Guidance:**

**Superficial Incisional SSI**

Infection occurs within 30 days after the operation and infection involves only skin or subcutaneous tissue of the incision and at least one of the following:

Purulent drainage from the superficial incision with or without laboratory confirmation.

Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision.

At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat and the superficial incision are deliberately opened by the surgeon unless incision is culture-negative. Diagnosis of superficial incisional SSI can be made by the surgeon or attending physician.

**Deep Incisional SSI**:

- Infection occurs within 30 days after the operation if no implant is left in place or within 1 year if implant is in place and the infection appears to be related to the operation and
- infection involves deep soft tissues (e.g., fascial and muscle layers) of the incision and at least one of the following:

1. Purulent drainage from the deep incision and not from the organ/space.
2. A deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms: Fever (>38 ºC), localized pain or tenderness unless the site is culture-negative.
3. An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination.
4. Diagnosis of a deep incisional SSI can be made by a surgeon or attending physician.

Notes:

Report infection that involves both superficial and deep incision sites as deep incisional SSI.

Report an organ/space SSI that drains through the incision as a deep incisional SSI.

**Organ/Space SSI:**

Infection occurs within 30 days after the operation if no implant is left in place or within 1 year if implant is in place and the infection appears to be related to the operation and infection involves any part of the

anatomy (e.g., organs or spaces), other than the incision, which was opened or manipulated during an operation and at least one of the following:

1. Purulent drainage from a drain that is placed through a stab wound into the organ/space.
2. Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space.
3. An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination.
4. Diagnosis of an organ/space SSI can be made by a surgeon or attending physician

**Investigations** :

Pus for Bacterial Culture, Fungal culture if appropriate.

**Empirical Therapy Guidance for Incisional Surgical Site Infection[1]:**

| | ***Single-drug regimens*** | ***Combination regimens*** |
|---|---|---|
| **Surgery of Intestinal or Genitourinary Tract** | **Piperacillin-Tazobactam** - 4.5 g every 8 h IV | **Ceftriaxone** 1-2 g every 24 h + **Metronidazole** 500 mg every 8 h IV |
| | **Imipenem**- 500 mg every 6 h IV / **Meropenem**-1 g every 8 h IV | **Ciprofloxacin** 400 mg IV every 12 h or 750 mg po x 12 h + **Metronidazole** 500 mg every 8 h IV |
| **Surgery of trunk or extremity away from axilla or perineum** | **Cloxacillin** or **Flucloxacillin**- 200 -300 mg/kg/day in 6 equally divided dose | |
| | **Cefazolin** 1-2 g every 8 h IV | |
| **Surgery of axilla or perineum** | | **Ciprofloxacin** 400 mg IV every 12 h or 750 mg po x 12 h + **Metronidazole** 500 mg every 8 h IV |

**Preventive measures :**

These can be categorized into pre-procedural, perioperative, and intraoperative phases. Key pre-procedural considerations include optimizing chronic health issues such as glucose control, medication assessment, addressing chronic wounds/infections, and smoking cessation. Perioperative steps may entail preoperative showers, hair clipping, administering operation-specific antibiotics, and appropriate skin preparation. Additionally, maintaining optimal intraoperative conditions, including temperature, air circulation, and sterility, is imperative for preventing wound infections.

## 3.11 B. Central Line Associated Blood Stream Infection (CLABSI)

CLABSI should be suspected in patients with:

a) Fever in a patient with a central venous catheter with no other apparent source

b) Erythema, induration or tenderness within 2 cm of the catheter exit site

c) Clinical signs of sepsis that start abruptly after catheter infusion

**Diagnostic Guidance**:

CLABSI is a surveillance definition used by the CDC and defined as the recovery of a pathogen from a blood culture (a single blood culture for an organism not commonly present on the skin and 2 or more blood cultures for organism commonly present on the skin) in a patient who had a central line at the time of infection or within 48 hours before the development of infection. The infection cannot be related to any other infection the patient might have and must not have been present or incubating when the patient was admitted to the facility.

Confirmation of CLABSI requires both a positive blood culture and a collaborative clinical and microbiological review of the patient. Blood culture should be obtained prior to initiation of antibiotic therapy.

Paired blood samples, drawn from the catheter and a peripheral vein, should be sent for culture, and the bottles should be appropriately marked to reflect the site from which the samples were obtained. If a blood sample cannot be drawn from a peripheral vein, it is recommended that 2 blood samples should be drawn through different catheter lumens.

**The case definition for BSI (must meet one of two criteria):**

**Criterion 1:**

Patient has a recognized pathogen cultured from one or more blood cultures AND

Organism cultured from blood is not related to an infection at another site

**Criterion 2:**

Patient has at least one of the following signs or symptoms:

fever (>38°C) or hypotension AND organism cultured from blood is not related to an infection at another site.

Common skin contaminant is cultured from two or more blood cultures drawn on separate occasions.

Establishing diagnosis of CRBSI requires the presence of BSI and demonstrating that the infection is related to the catheter. The catheter tip should be cultured and growth of >15 colony-forming units (CFU) from a 5-cm segment tip by semiquantitative (roll-plate) culture, or growth of > $10^2$cfu by quantitative (sonication) broth culture of the same pathogen as in peripheral blood culture supports the diagnosis of CRBSI.

## Empirical Therapy Guidance for CLABSI[1]

Catheter removal is essential.

**Systemic antibiotic therapy is usually NOT required if:**

1. Positive catheter tip culture in absence of clinical signs of infection.
2. Positive blood cultures from the catheter with negative cultures through the peripheral vein, in absence of clinical signs of infection.
3. Phlebitis in absence of signs of infection

| Aetiology | Preferred Regimen | Alternative | Remarks |
|---|---|---|---|
| **Gram-negative (*Klebsiella Pneumoniae, Acinetobacter* spp.) more common than Gram positive** | **Imipenem- Cilastatin** 500 mg IV q6h<br><br>**Add MRSA in patients with appropriate risk factors**.<br><br>**Vancomycin**- 15 mg/kg/bd or tid / **Teicoplanin** 400 mg bid for 3 doses followed by 400 mg IV od<br><br>**Paed Dose:**<br>**Imipenem**-15-25 mg/kg/dose IV 6 Hrly<br>**Teicoplanin** (250mg/m' IV over 30min stat, then 125mg/m IV or IM daily | **Cefoperazone–Sulbactam** (3g IV BD)<br><br>**Add MRSA in patients with appropriate risk factors**<br><br>**Paed Dose:**<br>**Cefoperazone-sulbactam**-25-60 mg/kg/dose IV 6 Hrly | Duration of therapy for uncomplicated bacteraemia- 10 to 14days from the day the culture was negative.<br><br>Persistent bacteraemia after 72 hours of catheter removal- treat for 4- 6 weeks |
| ***Candida species*** | Micafungin100mg IV daily<br>or<br>Anidulafungin loading dose 200mg, then100 mg daily<br>or<br>Caspofungin loading dose 70 mg, then 50 mg daily<br>or<br>Fluconazole 800-mg loading dose, then400 mg daily | Amphotericin-B (lipid) 3–5 mg/kg daily<br>or<br>Amphotericin B deoxycholate-0.5–1 mg/kg daily<br>or<br>Voriconazole 400mg (6mg/kg) q 12h for 2 doses then 200 | Fluconazole may be used as a preferred agent/ step down agent after 5-7 days of initial echinocandin therapy if the isolate is susceptible; the patient has no |

| | | | |
|---|---|---|---|
| | **Paed Dose :**<br>**Micafungin**-Infant 10mg/kg, child 8mg/kg,<br>**Anidulafungin** 2-4mg/kg IV day 1, then 1-2mg/kg<br>**Caspofungin** 70mg/m2 day 1, then <3mo 25 mg/m2, ≥3mo 50mg/m' (max 50mg) daily IV over 1hr. | mg (3 mg/kg ) q12h | previous azole exposure and is not critically ill. |

**Preventing CLABSI : Keystone Bundle Intervention**:

- Hand hygiene prior to catheter insertion
- Use of maximal sterile barrier precautions.
- Use of alcohol-containing chlorhexidine for skin antisepsis before insertion
- Avoidance of the femoral site
- Removal of unnecessary catheters as soon as possible

## 3.11 C Hospital Acquired Pneumonia (HAP) / Ventilator Associated Pneumonia (VAP)[1]

**Diagnostic Guidance:**

When a patient who is hospitalized/on mechanical ventilation for > 48 hours develops new or progressive infiltrates on chest radiography and has at least 2 of the following features:

a) Fever> 100.4 °F.

b) Leucocytosis (>12000/µl) or leucopenia (<4000/ µl).

c) Altered mental status with no other recognizable cause in the elderly.

d) New onset purulent sputum or change in sputum character.

e) Worsening gas exchange (i.e. increased FiO2 requirement).

f) New onset or worsening cough or dyspnea.

g) Rales or bronchial breathing.

Microbiological criteria:

and at least one of the following:

a) positive growth in blood culture not related to another source of infection
b) positive growth in culture or pleural field
c) positive quantitative culture from bronchoalveolar lavage (> $10^4$) or protected specimen brushing (> $10^3$)
d) histopathological evidence of pneumonia

**HAP:** Respiratory samples should be obtained by spontaneous expectoration, sputum induction or nasotracheal suctioning and subjected to semi- quantitative cultures.

**VAP:** The preferred method for lower respiratory tract sample collection - endotracheal aspirate either blind or bronchoscopic method.

**Empiric Therapy Guidance for VAP[1]:**

| | **Preferred / Early onset / Minimum prior antibiotic exposure** | **Alternative / Late onset / Prior antibiotic exposure** | |
|---|---|---|---|
| **Empiric (VAP/HAP)** | **Cefoperazone – Sulbactam** or **Piperacillin-Tazobactam**<br><br>**Plus**<br>**Amikacin** 15-20mg/Kg IV OD | **Meropenem / Imipenem-Cilastatin**<br><br>In settings where carbapenem resistance is >20%- **Ceftazidime-Avibactam** + **Aztreonam** (or) **Colistin/polymyxin B** | **Levofloxacin** (750 mg IV q24h) may be used as an alternative to **Amikacin** as a second anti-pseudomonal agent. Empirical therapy for MRSA recommended if prevalence >10-20% in the setting |

**Dosage:** **Cefoperazone Sulbactam**- 3 g IV bid, **Pip Taz**-4.5 g IV tid, **Imipenem-Cilastatin**-500 mg IV qid, **Meropenem**-1 g IV tid, **Colistin** -9 mu IV stat, then 4.5 mu IV bid (or) **Polymyxin B** -15-20 Lakh unit IV stat then 7.5 -10 lakh IV bid, **Ceftazidime-avibactam**: 2.5 g IV q8h, infused over 3 hours **PLUS** **Aztreonam:** 2 g IV q8h, infused over 3 hours, administered at the same time as **Ceftazidime-avibactam**

***General comments***

1. De-escalation should be done once the culture reports are available.
2. Recommended duration of therapy: 7 days if there is a good clinical response or longer if clinically indicated (immunodeficiency, empyema, lung abscess, cavitations, necrotising pneumonia, etc)
3. Clinical picture and procalcitonin levels may be used to guide discontinuation of antibiotics.
4. In susceptible cases, **Levofloxacin** may be used as an oral step-down therapy.
5. **Faropenem** should not be used as a step-down therapy in VAP/HAP susceptible to Carbapenems.
6. **Tigecycline** is not recommended routinely in the treatment of VAP.
7. If a patient with suspected VAP has septic shock and rapidly deteriorating status, empiric coverage for MRSA and carbapenem resistant GNB can be added along with antipseudomonal bta-lactam.
8. Antibiotic doses should be adjusted according to GFR and ideal body weight except in those with morbid obesity where the dose is calculated using this formula = (actual body weight + ideal body weight)/2

## 3.11 D. Catheter Associated Urinary Tract Infection-CAUTI[1]

**Diagnostic Guidance**:

Patient must meet 1, 2, and 3 below:

1. Patient had an indwelling urinary catheter that had been in place for

   More than 2 consecutive days in an inpatient location on the date of event AND

   was either:

   Present for any portion of the calendar day on the date of event,

   OR

   Removed the day before the date of event

2. Patient has at least one of the following signs or symptoms:

   fever (>38.0°C)

   suprapubic tenderness

   costovertebral angle pain or tenderness

   urinary urgency

   urinary frequency

   dysuria

3. Patient has a urine culture with no more than two species of organisms

   identified, at least one of which is a bacterium of $\geq 10^5$ CFU/ml

**Note:**

In patients with spinal cord injury, increased spasticity, autonomic dysreflexia, or sense of unease are also compatible with CA-UTI.

Indwelling urinary catheters are generally considered

**Short term** if they are in-situ for < 30 days

**Chronic or long term** when in-situ for ≥ 30 days

## Empirical Therapy Guidance for CA UTI[1]:

The two important considerations in the management of CA-UTI

- Removal of the indwelling catheter (7 days or longer)
- Antimicrobial chemotherapy (type and duration of therapy)

Because of the possibility of biofilm formation on the catheter surface, it may be reasonable to replace the catheter before the therapy if it has been in place for >7 days

| Category | Treatment | Comments |
|---|---|---|
| **Asymptomatic CA-ASB** | Not recommended | Only recommended in the following circumstances -Before urologic surgery or implantation of prosthesis in the urinary tract -In pregnancy |
| **Symptomatic CA-UTI** | **Levofloxacin** 750 mg PO daily **Ciprofloxacin** 500 mg PO BID<br>**Amikacin** 15 mg/kg single dose | Patients with CA-UTI who are severely ill<br>-**Piperacillin/tazobactam** 4.5 g IV q6hr<br>-**Ertapenem** 1 g IV q24hr<br>-**Meropenem** 1 g IV q8hr*<br>* preferably used in patients with sepsis and septic shock |
| **Candiduria – Indication Symptomatic Neutropenia (rule out candidemia) urological surgery** | Fluconazole-150 mg x 14 days for Susceptible strains<br>Flucytosine –2.5 g od for 14 days for<br>Candida glabrata<br>and Candida krusei | -Isolation of Candida in urine usually suggest a colonization<br>-Always rule out obstructive uropathy with imaging if symptomatic candidal urinary infection is suspected |
| **Post-op infections following solid organ transplant with CA-UTI (kidney, liver, heart, lung)** | **Piperacillin-Tazobactam** 4.5 g IV q6h<br>or **Cefoperazone-sulbactam** 3 g IVq12h<br>**Imipenem- Cilastatin** 500 mg IV q6h or<br>**Ertapenam** 1 g IV q24hr /**Meropenem** 1g IV q8h | -Obtain blood and urine cultures before starting antibiotics<br>-De-escalate to narrow spectrum agent on receipt of sensitivities |

Targeted therapy should be initiated according to urine culture result and tailored according to the susceptibility report. For multidrug resistant organisms, **Colistin** may be necessary; its empiric use is preferably avoided.

## 3.11 E. Clostridium difficile Infection (CDI)[1]

**Diagnostic Guidance:**

Clostridioides difficile formerly Clostridium difficile is a gram positive spore forming bacterium. Clostridium difficile infection (CDI) in adults is associated with increased morbidity, additional length of hospital stay and an increase in healthcare costs.

The available literature suggests that the prevalence of CDI is ranging between 4%- 34% across various centers in India. The increasing prevalence is related to the increasing use of antibiotics across specialities. Management and prevention of CDI require an early suspicion, rapid and accurate diagnosis and measures for appropriate use of antibiotics.

Antimicrobial stewardship programmes need to be emphasized for reducing incidence and morbidity associated with CDI.

Tests should not be performed for asymptomatic patients & do not perform repeat testing (within 7 days) during the same episode of diarrhoea.

## Sensitivity and specificity of the diagnostic methods for CDI :

| Approach | Description | Advantages | Disadvantages | Interpretation |
|---|---|---|---|---|
| **Preferred approaches (two-tiered approach that includes an initial highly sensitive test followed by a highly specific test)** | | | | |
| NAAT followed by toxin EIA test | NAAT (highly sensitive) is performed first, followed by the toxin EIA (highly specific) if the NAAT is positive | ▪ High sensitivity<br>▪ Helps distinguish between colonization and true infection | ▪ Toxin EIA can be falsely negative | **+NAAT, +Toxin EIA:** CDI<br>**+NAAT, –Toxin EIA:** Asymptomatic carriage or CDI with falsely negative toxin EIA*<br>**–NAAT:** No CDI and no asymptomatic carriage |
| GDH antigen test followed by toxin EIA test | GDH (highly sensitive) is performed first, followed by toxin EIA (highly specific) if GDH is positive | ▪ High sensitivity | ▪ Toxin EIA could be a false negative | **–GDH:** No CDI<br>**+GDH, +Toxin EIA:** CDI<br>**+GDH, –Toxin EIA:** Asymptomatic carriage or CDI with falsely negative toxin EIA* |
| GDH antigen and toxin EIA tests (followed by NAAT if discrepant results) | GDH and toxin EIA are both performed first, followed by NAAT if there is a discrepancy in GDH and toxin EIA results | ▪ High sensitivity<br>▪ Combination of all three tests increases specificity | ▪ Resource-intensive<br>▪ A positive NAAT test in the setting of discrepant GDH and Toxin EIA results still does not completely distinguish between true CDI | **+GDH, +Toxin EIA:** CDI<br>**+GDH, –Toxin EIA, +NAAT:** CDI or asymptomatic carriage*<br>**+GDH, –Toxin EIA, –NAAT:** No CDI and no asymptomatic carriage<br>**–GDH, +Toxin EIA:** Technical error, |

| | | | | |
|---|---|---|---|---|
| | | | and asymptomatic carriage. | repeat testing<br>**–GDH, –Toxin EIA:** No CDI and no asymptomatic carriage |
| **Alternative approaches** | | | | |
| NAAT only | NAAT/PCR that detects toxin gene | ▪ High sensitivity<br>▪ Rapid results | ▪ Low specificity<br>▪ Cannot distinguish true infection from colonization | **(+) NAAT:** CDI or asymptomatic carriage*<br>**(–) NAAT:** No CDI and no asymptomatic carriage |
| GDH antigen test followed by NAAT | GDH is performed first, followed by the NAAT if GDH is positive | ▪ High sensitivity<br>▪ Rapid results<br>▪ Inexpensive | ▪ Low specificity<br>▪ Uses two tests with high sensitivity but both with low specificity<br>▪ Cannot distinguish true infection from colonization | |

## Recommendations for the Treatment of Clostridium difficile Infection in Adults[1,31]

| Etiology | Primary Regimen | Alternate Regimen |
|---|---|---|
| **Initial episode, non-severe:** Leukocytosis with a white blood cell (WBC) count of ≤15 000 cells/mL and a serum creatinine level <1.5 mg/dL | **VAN** 125 mg given 4 times daily by mouth for 10 days<br><br>**Paed: Metronidazole** 7.5 mg/kg/dose (max 500 mg/dose) PO tid × 10 days **(OR)** **Vancomycin** 10 mg/kg/dose (max 125 mg/dose) PO qid × 10 days | Oral **Vancomycin** is not available - **Metronidazole**, 400 mg 3 times per day by mouth for 10 days |

| | | |
|---|---|---|
| **Initial episode, severe:** Leukocytosis with a WBC of ≥15 000cells/mL or a serum creatinine level >1.5 mg/dL | **VAN**, 125 mg 4 times per day by mouth for 10 days | |
| **Initial episode, fulminant:** Hypotension or shock, ileus, megacolon | **VAN,** 500 mg 4 times per day by mouth or by nasogastric tube. If ileus, consider adding rectal instillation of VAN. Intravenously administered **Metronidazole** (500 mg every 8 hours) should be administered together with oral or rectal VAN, particularly if ileus is present | |
| **First recurrence** | • **VAN** 125 mg given 4 times daily for 10 days if **Metronidazole** was used for the initial episode. | Use a prolonged tapered and pulsed **VAN** regimen if a standard regimen was used for the initial episode (eg, 125 mg 4 times per day for 10–14 days, 2 times per day for a week, once per day for a week, and then every 2 or 3 days for 2–8 weeks). |
| **Second or subsequent recurrence** | **VAN** in a tapered and pulsed regimen<br>• **VAN**, 125 mg 4 times per day by mouth for 10 days followed by rifaximin 400 mg 3 times daily for 20 days.<br><br>**Paed: Vancomycin** in a tapered and pulsed regimen* (OR) **Vancomycin** 10 mg/kg/dose (max 125 mg/dose) PO qid × 10 days followed by **rifaximin** 10 mg/kg/dose (max 400 mg/dose) PO tid × 20 days (OR) **Fidaxomicin** 16 mg/kg/dose (max 200 mg/dose) PO bid × 10 days | • Faecal microbiota transplantation |

| | | |
|---|---|---|
| **Severe/Fulminant (first or Recurrent Episode)** | **Paed : Vancomycin** 10 mg/kg/dose (max 500 mg/dose) PO qid × 10 days If critically ill, consider adding **metronidazole** 7.5 mg/kg/dose (max 500 mg/dose) IV tid × 10 days | |

1. All randomized trials have compared 10-day treatment courses, but some patients (particularly those treated with **Metronidazole**) may have delayed response to treatment and clinicians should consider extending treatment duration to 14 days in those circumstances.
2. The opinion of the panel is that appropriate antibiotic treatment for at least 2 recurrences (ie, 3 CDI episodes) should be tried prior to offering faecal microbiota transplantation.
3. For children with an initial episode of severe CDI, oral **Vancomycin** is recommended over **Metronidazole**. There are insufficient data at this time to recommend the administration of probiotics for primary prevention of CDI outside of clinical trials
4. Bezlotoxumab, a recently approved monoclonal antibody targeting C. Difficile toxin has shown promising results in managing recurrent infections

## 3.12 Anaerobic Bacterial Infection[5,7]

The physician must consider several points when approaching the patient with a possible infection due to anaerobic bacteria.

1. For anaerobes to cause tissue infection, they must spread beyond the normal mucosal barriers.

2. Conditions favoring the propagation of anaerobic bacteria, particularly a lowered oxidation-reduction potential, are necessary. These conditions exist at sites of trauma, tissue destruction, compromised vascular supply, and necrosis.
3. Frequently, a complex array of infecting microbes can be found, occasionally with >10 different species isolated from a suppurative site.
4. Anaerobic organisms tend to be found in abscess cavities or in necrotic tissue.
5. The failure of an abscess to yield organisms on routine culture is a clue that the abscess is likely to contain anaerobic bacteria. Often smears of this "sterile pus" are found to be teeming with bacteria when Gram stain is applied.
6. Gas is found in many anaerobic infections of deep tissues but is not diagnostic because it can be produced by aerobic bacteria as well.
7. Although a putrid-smelling infection site or discharge is considered diagnostic for anaerobic infection, this manifestation usually develops late in the course and is present in only 30–50%of cases.
8. Some species (the best example being the B. fragilis group) require specific therapy. However, many synergistic infections can be cured with antibiotics directed at some but not all of the organisms involved. Antibiotic therapy, combined with debridement and drainage, disrupts the interdependent relationship among the bacteria, and some species that are resistant to the antibiotic do not survive without the co-infecting organisms.

9. Manifestations of severe sepsis and disseminated intravascular coagulation are unusual in patients with purely anaerobic infection.

## Empirical Therapy for Anaerobic Infection[5,7]

**Antibiotics that are no useful activity against anaerobes** includes

- Aminoglycosides,
- Monobactams, and
- Trimethoprim-sulfamethoxazole.

| Site of Infection | Type of Organisms | Empirical Therapy | Alternate therapy |
|---|---|---|---|
| **Infections above the Diaphragm** | Prevotella, Porphyromonas, Fusobacterium and Bacteroides species other than the B. fragilis group along with Streptococci (Aerophilic & Micro aerophilic) | 1.β-lactam/β-lactamase inhibitor combinations (**Ampicillin-sulbactam**, **Ticarcillin–clavulanic acid**, **Piperacillin-Tazobactam**), 2. **Clindamycin** or 3. **Metronidazole** with **Penicillin** | |
| **Infections below the Diaphragm** | Bacteroides species, including B. fragilis | 1.β-lactam/β-lactamase inhibitor combinations ( **Ticarcillin–clavulanic acid**, **Piperacillin-Tazobactam**), 2. **Carbapenem** 3. **Moxifloxacin** **Not recommended: (Clindamycin, Ampicillin-sulbactam)** | A two-drug regimen is an alternative, with one drug active against anaerobes and the other against coliforms (e.g., **Metronidazole** with either a Cephalosporin or a **Fluoroquinolone**). |
| **CNS Infections** | | **Carbapenem**, **Metronidazole** | |

**Tetanus**[5,31]

1. **Metronidazole-**500 mg IV every 6 h for 7 days is preferred for antibiotic therapy.
2. An alternative is **penicillin** (100,000–200,000 IU/ kg per day)
3. Antitoxin should be given early in an attempt to deactivate any circulating tetanus toxin and prevent its uptake into the nervous system.
4. Two preparations are available: human tetanus immune globulin (TIG) and equine antitoxin. TIG is the preparation of choice, as it is less likely to be associated with anaphylactoid reactions. A single IM dose (500–5000 IU) is given, with a portion injected around the wound. Equine-derived antitoxin -after hypersensitivity testing, 10,000–20,000 U is administered IM as a single dose or as divided doses.

   **Paed Dose :**

   i) Oral (or intravenous) **metronidazole** (30 mg/kg per day, given at 6-hour intervals; maximum dose, 4 g/day) decreases the number of vegetative forms of C tetani and is currently considered the antibiotic of choice.

   ii) **Parenteral penicillin G** (100,000 U/kg per day, administered at 4 to 6 hour intervals, with a daily maximum of 12 million U) is an alternative treatment.

**Clostridium Botulism:**

1) Antibiotic therapy is not part of the treatment of uncomplicated infant or food-borne botulism, because the toxin is primarily an intracellular molecule that is released into the intestinal lumen with vegetative bacterial cell death and lysis.

2) Indeed, there is a theoretical concern that antibiotics with clostridiocidal activity may increase the amount of free toxin in the large bowel and actually worsen an infant's clinical status.

3) Antibiotic use in infant botulism patients is indicated only for the treatment of secondary infections. In these patients, aminoglycosides in particular should be avoided, because this class of antibiotics can potentiate the action of botulinum toxin at the neuromuscular junction.

4) Wound botulism requires aggressive treatment with antibiotics and antitoxin in a manner analogous to that for tetanus and may require wound debridement to remove the source of the toxin.

# Chapter – 4 : Definitive Therapy Guidance

## "Definitive Therapy guidance will guide which antibiotics to choose when Organism identified / Culture & Sensitivity report available in hand"

### 4. 1 A) Definitive Therapy Enterobacterales-(Ecoli/klebsiella): Third generation cephalosporins resistant (cefotaxime, ceftriaxone, ceftazidime, and cefoperazone): [9,10,11,19]

| Name of the Syndrome | Preferred Agent | Alternative options | Do not use |
|---|---|---|---|
| **Uncomplicated cystitis** | **1. Nitrofurantoin**<br>**2. Trimethoprim-sulfamethoxazole** if susceptibility demonstrated | **1. Amoxicillin-clavulanate**,<br>**2.** Single-dose Aminoglycosides and<br>**3.** oral **Fosfomycin** (only for E coli) | 1.**Doxycycline** (intestinal excretion),<br>2.**Fosfomycin** (for organisms other than E coli) |
| **Pyelonephritis and complicated urinary tract infections** | **1. Carbapenem-Ertapenem, Meropenem, Imipenem-Cilastatin,**<br>**2. Cefepime-Enmetazobactam** | **1.** Once-daily Aminoglycosides<br>**2. Ciprofloxacin, Levofloxacin,** or **Trimethoprim-sulfamethoxazole**- if susceptibility demonstrated<br>**3. Piperacillin tazobactum and cefoperazone sulbactum (if susceptible and without bacteremia)** | **1. Nitrofurantoin**<br>**2.** oral **Fosfomycin** (do not achieve adequate concentrations in the renal parenchyma) |
| **Infections outside of the urinary tract** | **Carbapenem-Ertapenem, Meropenem, Imipenem-Cilastatin** | **1. Piperacillin tazobactum and cefoperazone sulbactum (if susceptible and without bacteremia)**<br>**2. Cefepime-Enmetazobactam**<br>**3.** After appropriate clinical response is achieved, transitioning to<br>a) oral **Fluoroquinolones** or<br>b) **Trimethoprim-sulfamethoxazole** | oral step-down to<br>**1. Nitrofurantoin**,<br>**2. Fosfomycin** (poor serum concentrations),<br>**3. Amoxicillin Clavulanate**,<br>**4. Doxycycline** (unreliable serum concentration) for ESBL-E bloodstream infections.<br>**5.Piperacillin-Tazobactam** is not recommended for the treatment of bacteremia caused by ESBL-E, even if susceptibility is demonstrated |

| | | | |
|---|---|---|---|
| **Chronic Prostatitis** | 1. **Carbapenems (Ertapenem, meropenem, imipenem-cilastin)** (if there is a concomitant pyelonephritis)<br>2. **Fosfomycin**, dosed at 3 g orally daily for one week, followed by 3 g orally every 48 hours for 6 to 12 weeks<br>3. **TMP-SMX DS** 1 tab BD for 6 weeks | 1. **Minocycline** 100mg BD for 6 weeks | 1. **Nitrofurantoin** (does not achieve adequate levels in the prostate)<br>2. **Fosfomycin** should be avoided for prostatitis caused by Gram-negative organisms other than E. coli |

## 4. 1 B) Definitive Therapy - Carbapenem Resistant Enterobacterales- (Ertapenem, Meropenem-Resistant)[9,10,11]

| Name of the Syndrome | Preferred Agent | Alternative options | Do not use |
|---|---|---|---|
| **Uncomplicated cystitis** | 1. **Fosfomycin** (only for Ecoli)<br>2. Single-dose Aminoglycosides*<br>3. **Nitrofurantoin**<br>4. **Ciprofloxacin* & Levofloxacin***,<br>5. **Trimethoprim Sulfamethoxazole**<br>*** if susceptibility demonstrated** | 1. **Colistin** (Single dose) | 1. **Doxycycline**,<br>2. **Polymyxin -B** (Non renal clearance),<br>3. **Fosfomycin** (for K. pneumoniae and several other gram-negative organisms which frequently carry fosA hydrolase genes that may lead to clinical failure) |
| **Pyelonephritis and complicated urinary tract infections** | 1. **Aztreonam plus Avibactam** (or) **Ceftazidime-Avibactam**<br>2. **Colistin** | 1. Once-daily Aminoglycosides<br>2. **Ceftazidime-avibactam** (KPC, Oxa 48)<br>3. **Ceftazidime-avibactam** and **Aztreonam** (over 3 hours) for MBL<br>4. **Ciprofloxacin**, **Levofloxacin**, or **Trimethoprim-sulfamethoxazole** (if susceptibility demonstrated) | 1. **Nitrofurantoin**<br>2. oral **Fosfomycin** (do not achieve adequate concentrations in the renal parenchyma)<br>3. **Polymyxin-B** |

| | | | |
|---|---|---|---|
| **Infections outside of the urinary tract-** | 1. **Aztreonam plus Avibactam** (or) **Ceftazidime-Avibactam**<br>2. **Polymyxin-B** | 1. **Tigecycline** (can be considered in intra-abdominal infections, skin and soft tissue infections and osteomyelitis)<br>2. **Colistin**<br>3. **Polymyxin** plus other agent to which organism has demonstrated susceptible MIC (like **tigecycline**, aminoglycosides, IV **Fosfomycin**) | 1. Extended-infusion **Meropenem** + **Colistin**/Aminoglycoside<br>2. **Tigecycline**-For Blood & Urine as a single agent |

## 4.2. Treatment option for Pseudomonas aeruginosa with Difficult to Resistance (DTR-Pseudomonas aeruginosa)-DTR is defined as P. aeruginosa exhibiting non-susceptibility to all of the following: Piperacillin-Tazobactam, Ceftazidime, Cefepime, Aztreonam, Meropenem, Imipenem-Cilastatin, Ciprofloxacin, and Levofloxacin[9,10,11,19]

| Name of the Syndrome | Preferred Agent | Alternative options | Do not use |
|---|---|---|---|
| **Uncomplicated cystitis** | 1. Single-dose aminoglycosides | 1. **Colistin**<br>2. **Ceftazidime-Avibactam Plus Aztreonam** | 1. **Polymyxin -B** (Non renal clearance),<br>2. **Fosfomycin** (-fos-A intrinsic resistance) |
| **Pyelonephritis and complicated urinary tract infections** | 1.**Colistin**<br>2.**Ceftazidime-Avibactam Plus Aztreonam (if Synergy)** | 1. once-daily aminoglycosides | |
| **Infections outside of the urinary tract-** | 1.**Polymyxin-B** | 1. **Colistin**,<br>2. Aminoglycosides<br>3. **Ceftazidime-Avibactam Plus Aztreonam (if Synergy)** | Nebulised Antibiotics-lack of benefit & Broncho constriction |

## 4.3. Treatment option for Carbapenem Resistant Acinetobacter baumanii[9,10,11,19]

| Name of the Syndrome | Preferred Agent | Alternative options | Do not use |
|---|---|---|---|
| **Bacteremia / VAP** | 1. **Polymyxin B plus Minocycline**<br>2. **Polymyxin B plus Tigecycline**<br>3. **Polymyxin B plus high dose sulbactam**<br>4. **Polymyxin B** | 1. High dose- **sulbactam**<br>2. **Colistin** | **Fosfomycin** not for combination therapy. |

**4.1,4.2, 4.3 -Suggested Dosage Regimens[5,7,9,10,11,12]:**

| Drug | Suggested Dosage |
|---|---|
| **Fosfomycin** | 3 grams PO as a single dose |
| **Amikacin** | 15 mg/Kg IV every 24 hours |
| **Ampicillin-sulbactam** | Total daily dose of 6-9 gm of **Sulbactam**<br>i) 2 gm of Ampicillin + 1 gm **Sulbactam** every 4 hourly-infuse over 3o min<br>ii)6 gm of Ampicillin + 3 gm **Sulbactam** every 8 hourly-infuse over 4 hrs |
| **Ceftazidime-Avibactam** | 2.5 grams IV every 8 hours, infused over 3 hours |
| **Ceftazidime-Avibactam + Aztreonam** | 2.5 grams IV every 8 hours, infused over 3 hours Plus **Aztreonam** 2 gm IV every 8 hrs-Infuse simultaneously |
| **Avibactam + Aztreonam** | Loading dose 2gm Aztreonam plus 0.5gm Avibactam followed by 1.5 gms of Aztreonam every 6 hourly infused over 3 hours plus 0.5gms of Avibactam every 6 hourly infused over 3 hours simultaneously |
| **Cefepime enmetazobactam** | 2.5 grams (2 grams cefepime and 0.5 grams enmetazobactam) every 8 hourly |
| **Ciprofloxacin** | 400 mg IV bid/tid, 500 mg / 750 mg PO bid |
| **Ertapenem** | 1 gm every 24 hours infused over 30 min |
| **Imipenem-Cilastatin** | 500 mg every 6 hours infused over 30 min or 3 hours |
| **Levofloxacin** | 750 mg IV /PO every 24 Hours |
| **Meropenem** | 1 gm IV every 8 hours infused over 30 min, Meningitis-2 gm every 8 hours infused over 3 hours |
| **Minocycline** | 200 mg IV /PO every 12 hours |
| **Nitrofurantoin** | 100 mg PO bid |
| **Tigecycline** | 200 mg IV as a single dose, then 100 mg IV every 12 hours |
| **Trimethoprim Sulfamethoxazole** | 160 mg (trimethoprim component) IV/PO every 12 hours (consider maximum dose of 960 mg trimethoprim component per day) |
| **Colistin** | 9 mu IV stat, then 4.5 mu IV bid |
| **Polymyxin-B** | 15-20 Lakh unit IV stat then 7.5 -10 lakh IV bid |

**Note:** Nebulised Antibiotics-lack of benefit & Broncho constriction[10]

## 4.4 Treatment option for Staphylococcus aureus-MSSA, MRSA[5,7,19]

| Sensitivity of the isolate | Preferred Agent | Alternative options | Comments |
|---|---|---|---|
| **Sensitive to Methicillin & Resistant to Penicillin (MSSA)** | 1. **Cefazolin-** (2 g q8h),<br>2. **Cloxacillin-**(2g q4h) | **Flucloxacillin-2 gm 6th Hrly** | **Vancomycin** is a less effective option than a β-lactam. |
| | **Oral Therapy for Skin infection:**<br>1. **Clindamycin** (300 mg tid),<br>2. **Trimethoprim Sulfamethoxazole** (2 DS tablets bid),<br>3. **Cephalexin** (500 mg qid),<br>4. **Minocycline** or **Doxycycline** (100 mg q12hb), or<br>5. **Cefadroxil** (1gm q12h) | **Dicloxacillin** (500 mg qid) | All collections should be drained, and drainage should be cultured |
| **Resistant to Methicillin & Sensitive to Vancomycin (MRSA)** | **For Bacteremia, Endocarditis:**<br>1. **Vancomycin** (15–20 mg/kg q8–12hb),<br>2. **Daptomycin** (6–10 mg/kg IV q24h) | **Ceftaroline** (600 mg IV q8–12h) | For the treatment of prosthetic valve endocarditis, the addition of gentamicin (1mg/kg q8h) and rifampin 300mg (PO q8h) is recommended. |
| | **Osteomyelitis and Complicated skin Infection:**<br>1. **Vancomycin** (15–20 mg/kg q8–12hb),<br>2. **Daptomycin** (6-10mg/kg IV q24h) | 1. **Linezolid** (600 mg q12h PO or IV)<br>2. **Ceftaroline** (600 mg IV q8–12h),<br>3. **Trimethoprim Sulfamethoxazole** (5 mg [based on TMP]/kg IV q8–12h) | Sensitivity testing is necessary before an alternative drug is selected.<br>To obtain vancomycin trough level 15-20ug/ml or target AUC 24 / MIC of 400-600<br><br>Daptomycin cannot be used for the treatment of pneumonia |
| | **Oral Therapy for Skin infection:**<br>1. **Clindamycin** (300–450 mg tid),<br>2. **Trimethoprim Sulfamethoxazole** (1 or 2 DS tablets bid),<br>3. **Minocycline** or **Doxycycline** (100 mg q12h),<br>4. **Linezolid** (600 mg bid) | | All collections should be drained, and drainage should be cultured |

| | | | |
|---|---|---|---|
| **Intermediate Resistant or Complete resistance to Vancomycin (VISA, VRSA)** | **Daptomycin** (6–10 mg/kg IV q24h) for bacteremia, endocarditis, osteomyelitis, and complicated skin infections | 1. **Linezolid-** (600mg q12h PO or IV)<br>2. **Ceftaroline** (600 mg IV q8–12h),<br>3. **Trimethoprim Sulfamethoxazole** (5 mg [based on TMP]/kg IV q8–12h) | Sensitivity testing is necessary before an alternative drug is selected. **Ceftaroline** is used either alone or in combination with **Daptomycin** |

## 4.5. Treatment option for Enterococcus fecalis / Vancomycin Resistant Enterococcus faecium[5,7,19]:

| Name of the Syndrome | Enterococcus fecalis | Vancomycin & Ampicillin Resistant Enterococcus faecium |
|---|---|---|
| **Endovascular infections (including endocarditis)** | **Ampicillin Sensitive:**<br>• **Ampicillin** plus **Ceftriaxone**<br>• **Ampicillin** plus **Gentamicin** **(if HLAR-Sensitive)**<br>**Ampicillin Resistant:**<br>• **Vancomycin** plus **Gentamicin** **(if HLAR-Sensitive)**<br>**Vancomycin Resistant:**<br>• High-dose **Daptomycin** (single agent for bacteremia) plus linezolid/ gentamicin/tigecycline (for endocarditis) | •High-dose **Daptomycin(10-12mg/kg)** plus **linezolid**/ **gentamicin**/**tigecycline**<br>•**Tigecycline and linezolid cannot be given as a single agent in endocarditis.** |
| **Meningitis** | • **Ampicillin** plus **Ceftriaxone** and consider **Gentamicin**<br>• **Vancomycin** plus **Gentamicin**<br>• High-dose **Daptomycin** (plus Intra thecal **Daptomycin**) ± another active agent- **Linezolid** can be considered | • High-dose **Daptomycin** (plus Intra ventricular **Daptomycin**) ± another CSF-penetrating active agent (**linezolid**/**ampicillin** to be considered)<br>• **Linezolid** ± another CSF penetrating active agent |
| **Urinary tract infections** (uncomplicated) | • **Fosfomycin** (3 g PO, one dose)<br>• **Amoxicillin** (500 mg IV or PO q6h)<br>• **Nitrofurantoin** (100 mg PO q6h) | • **Linezolid**<br>• **Nitrofurantoin** (100 mg PO q6h)<br>• **Fosfomycin** (3 g PO, one dose) |
| a-Potentially active agents may include an aminoglycoside (if HLR is not detected**),** **Ampicillin**, **ceftaroline, tigecycline**, or a fluoroquinolone (which, if the isolate is susceptible, may be favored in meningitis). | | |
| ***HLAR**-High Level Aminoglycoside Resistant | | |
| **Dosage:** **Ampicillin** -12 g/d IV in divided doses q4h, **High dose** **Ampicillin**-30 g per day, **Ceftriaxone** -2 g IV q12h, **Penicillin - G**-18–30 mU/d IV in divided doses q4h, **Vancomycin** -15 mg/kg IV per dose, **Gentamicin**-1–1.5 mg/kg IV q8h, **Daptomycin**-10-12 mg/Kg per day, **Linezolid** -600 mg IV q12h,<br>**Meningitis**: **Ampicillin** -20-24 g/d IV in divided doses q4h, **Ceftriaxone** -2 g IV q12h, **Penicillin - G**-24 mU/d IV in divided doses q4h, **Vancomycin** -500-750 mg IV 6 hrly, **Gentamicin**-1–1.5 mg/kg IV q8h, **Daptomycin**-10-12mg/Kg per day, **Linezolid** -600 mg IV q12h | | |

## 4.6 A. Definitive antimicrobial treatment for IE [5,7,41]

Antibiotic therapy for native valve Infective Endocarditis[a] due to VGS and group D streptococci, *Streptococcus gallolyticus* (Formerly Known as *Streptococcus bovis*), *Abiotrophia defective* and Granulicatella Species

| ORGANISM(S) | DRUG (DOSE, DURATION) | COMMENTS |
|---|---|---|
| Streptococci | | For PVE 6-week regimens are preferred. |
| **Penicillin**-susceptible streptococci, *S. gallolyticus* MIC ≤0.12 µg/mL[b]) | **Penicillin G** (2–3 mU IV q4h for 4 weeks) or | Can use **Ampicillin** or **Amoxicillin** (2 g IV q4h) if **penicillin** is unavailable. |
| | **Ceftriaxone** (2 g daily as a single dose for 4 weeks) or | Can use **Ceftriaxone** in patients with non-immediate penicillin allergy. |
| | **Vancomycin**[c] (15 mg/kg IV q12h for 4 weeks) or | Use **Vancomycin**[c] for patients with immediate (urticarial) or severe penicillin allergy. |
| | **Penicillin G** (2–3 mU IV q4h) *or* **Ceftriaxone** (2 g IV daily) for 2 weeks *plus* **Gentamicin**[d] (3 mg/kg daily IV or IM, as a single dose[e] or divided into equal doses q8h for 2 weeks) | Avoid 2-week regimen when risk of aminoglycoside toxicity is increased and in prosthetic-valve or complicated endocarditis. Can use **Ampicillin** or **Amoxicillin** (2 g IV q4h) if **Penicillin** is unavailable. |
| Relatively **Penicillin**-resistant streptococci, *S. gallolyticus*(MIC >0.12 µg/mL and <0.5 µg/mL[f]) | **Penicillin G** (4 mU IV q4h) *or* **Ceftriaxone** (2 g IV daily) for 4 weeks *plus* **Gentamicin**[d] (3 mg/kg daily IV or IM, as a single dose[e] or divided into equal doses q8h for 2 weeks) or | Can use **Ampicillin** or **Amoxicillin** (2 g IV q4h) if **Penicillin** is unavailable. **Penicillin** alone at this dose for 6 weeks or with **Gentamicin** during the initial 2 weeks is preferred for PVE caused by streptococci with **Penicillin** MICs of ≤0.12 µg/mL. |
| | **Vancomycin**[c] as noted above for 6 weeks | Use **Vancomycin**[c] for patients with immediate (urticarial) or severe penicillin allergy. Obtain allergy consultation for further evaluation including role of β-lactam desensitization. **Ceftriaxone** alone or with **Gentamicin** can be used in patients with non-immediate β-lactam allergy. |
| Moderately **Penicillin**-resistant streptococci (MIC, ≥0.5 µg/mLand <8 µg/mL[g]); *Granulicatella*, *Abiotrophia*, or *Gemella* spp. | **Penicillin G** (4–5 mU IV q4h) *or* **Ceftriaxone** (2 g IV daily) for 6 weeks *plus* **Gentamicin**[d] (3 mg/kg daily IV or IM as a single Dose[e] *or* divided into equal doses q8h for 6 weeks) or | Preferred for PVE caused by streptococci with **Penicillin** MICs of >0.12 µg/mL. Can use **Ampicillin** or **Amoxicillin** (2 g IV q4h) if **Penicillin** is unavailable. |
| | **Vancomycin**[c] as noted above for 6 weeks | Regimen is preferred by some. |
| Enterococci[h] | | For PVE 6-week regimens are preferred. |
| | **Penicillin G** (4–5 mU IV q4h) *plus* **Gentamicin**[d] (1 mg/ kg IV q8h), both for 4–6 weeks or | Can treat NVE for 4 weeks if symptoms last <3 months. Treat NVE with >3 months of symptoms for 6 weeks. Can abbreviate **Gentamicin** course in some patients (see text). |
| | **Ampicillin** (2 g IV q4h) *plus* **Gentamicin**[d] (1 mg/kg IV q8h), both for 4–6 weeks or | Can use IV **Amoxicillin** in lieu of **Ampicillin** (same dose). Can abbreviate **Gentamicin** course in some patients (see text). |
| | **Vancomycin**[c] (15 mg/kg IV q12h) *plus* | Use **Vancomycin** plus **Gentamicin** only for |

| | | |
|---|---|---|
| | **Gentamicin**[d] (1 mg/kg IV q8h), both for 6 weeks or | penicillin-allergic patients (preferable to desensitize to penicillin if immediate (urticarial) allergy; consult allergy) and for isolates resistant to **Penicillin**/**Ampicillin**. |
| Staphylococci (S. aureus and coagulase-negative) | | |
| MSSA infecting native valves (no foreign devices) including complicated right-sided and left sided endocarditis. | **Flucloxacillin** (2 g IV q4h for 6 weeks) or | Addition of **Gentamicin** is not recommended. For uncomplicated right sided endocarditis a 2-week course may be effective. |
| | **Cefazolin** (2 g IV q8h for 6 weeks) or | Can use **Cefazolin** regimen for patients with non-immediate **Penicillin** allergy; see text regarding **Cefazolin** vs anti staphylococcal penicillin as primary therapy. Addition of **Gentamicin** not recommended. |
| | **Vancomycin**[c] (15 mg/kg IV q12h for 6 weeks) | Only use **Vancomycin** for patients with immediate (urticarial) or severe **Penicillin** allergy until allergy consultation can be obtained for β-lactam desensitization evaluation; addition of **Gentamicin** not recommended. |
| MRSA infecting native valves (no foreign devices) | **Vancomycin**[c] (15 mg/kg IV q8–12h) or **Daptomycin** (8–10 mg/kg daily) for 6 weeks | No role for routine use of **rifampin**. |
| MSSA infecting prosthetic valves | **Flucloxacillin** (2 g IV q4h for 6–8 weeks) *plus* **Gentamicin**[d] (1 mg/kg IM or IV q8h for 2 weeks) *plus* **Rifampicin** 300 mg PO tid for 6-8 weeks | Use **Gentamicin** during initial 2 weeks; determine **Gentamicin** susceptibility and await blood culture clearance ; if patient is highly allergic to **Penicillin**, use regimen for MRSA and obtain allergy consultation; if β-lactam allergy is of the minor nonimmediate type, **Cefazolin** can be substituted for oxacillin, nafcillin, or **Flucloxacillin**. |
| MRSA infecting prosthetic valves | **Vancomycin**[c] (15 mg/kg IV q12h for 6–8 weeks) *plus* **Gentamicin**[d] (1 mg/kg IM or IV q8h for 2 weeks) *plus* **Rifampicin** 300 mg PO tid for 6-8 weeks | Use **Gentamicin** during initial 2 weeks; determine **Gentamicin** susceptibility and await blood culture clearance. **Daptomycin** (8–10 mg/kg daily) could be considered as an alternative to **Vancomycin** but data are limited. |
| HACEK Organisms | | For PVE 6-week regimens are preferred. |
| | **Ceftriaxone** (2 g/d IV as a single dose for 4 weeks) | Can use another third-generation cephalosporin at comparable dose. |
| | **Ampicillin/sulbactam** (3 g IV q6h for 4 weeks) | Use **Ampicillin** only if β-lactamase production can be excluded. If the isolate is susceptible, **Ciprofloxacin** (400 mg IV q12h) can be used. |
| Coxiella burnetii[d] | **Doxycycline** (100 mg PO q12h) *plus* hydroxychloroquine (200 mg PO q8h), both for at least 18 (native valve) or 24 (prosthetic valve) months | Follow serology to monitor response during treatment (antiphase I IgG and IgA decreased 4-fold and Ig antiphase II negative) and thereafter for relapse. |

a. Regimens adapted from the guidelines of the American Heart Association and the European Society of Cardiology (ESC). Doses of **Gentamicin**, **Vancomycin**, and **Daptomycin** must be adjusted for reduced renal function. .

b. MIC ≤0.125 μg/mL per ESC.

c. **Vancomycin** dose is based on actual body weight. Adjust for trough level of 10–15 μg/mL for streptococcal and enterococcal infections and 15–20 μg/mL for staphylococcal infections.

d. Aminoglycosides should not be administered as single daily doses for enterococcal endocarditis and should be introduced as part of the initial treatment. Target peak and trough serum concentrations of divided-dose **Gentamicin**1 h after a 20- to 30-min infusion or IM injection are ~3.5 μg/mL and ≤1 μg/mL, respectively;

e. **Netilmicin** (4 mg/kg qd, as a single dose) can be used in lieu of **Gentamicin** for streptococcal infection only.

f. MIC>0.125 μg/mL and ≤2.0 μg/mL per ESC.

g. MIC>2.0 μg/mL per ESC; treat with regimen for enterococci (BSAC).

h. Antimicrobial susceptibility must be evaluated; see text.

i. **Rifampicin** increases warfarin and dicumarol requirements for anticoagulation

j. Outpatient oral antibiotic treatment—using dual therapy with agents such as dicloxacillin, moxifloxacin, linezolid, rifampicin, or amoxicillin—may be considered in select patients with left-sided infective endocarditis (IE) due to Streptococcus spp., Enterococcus faecalis, Staphylococcus aureus, or coagulase-negative staphylococci (CoNS) if all the following criteria are met- Completed at least 10 days of appropriate intravenous (i.v.) antibiotic therapy, or at least 7 days post-cardiac surgery, clinically stable, with resolution or significant improvement of infection signs and symptoms, no evidence of abscess formation or other complications on

transoesophageal echocardiography (TOE), and no valve abnormalities requiring surgical intervention.

**Ampicillin** 200mg/kg/day in six divided doses (Max dose-2g IV in q4h).

**4-wk therapy** recommended for patients with symptoms of illness <3mo;

**6-wk therapy** recommended for native valve symptoms>3mo and for pts with prosthetic valve & material. Recommended for patients with creatinine clearance >50 mL/min.

## 4.6 B. Definitive Therapy for Fungal IE[1]:

| Etiology | Suggested regimens | | Remarks |
|---|---|---|---|
| | **Preferred** | **Alternative** | |
| **Candida species (unspeciated) / C.albicans, C.tropicalis / C.parapsilosis** | Micafungin100mg IV daily<br>or<br>Anidulafungin loading dose 200mg, then100 mg daily<br>or<br>Caspofungin loading dose 70 mg, then 50 mg daily<br>or<br>Fluconazole 800-mg loading dose, then 400 mg daily | Amphotericin B (lipid) 3–5 mg/kg daily<br>or<br>Amphotericin B deoxycholate-0.5–1 mg/kg daily<br>or<br>Voriconazole 400mg (6mg/kg) q 12 h for 2 doses then 200mg (3 mg/kg) q12h | Fluconazole may be used as a preferred agent/ step down agent after 5-7 days of initial echinocandin therapy if the isolate is susceptible; the patient has no previous azole exposure and is not critically ill. |
| **C.auris / C.haemulonii / C.krusei** | Micafungin100mg daily;<br>Or<br>Anidulafungin loading dose 200 mg, then100 mg daily | Voriconazole 400mg (6mg/kg) bid for 2 Doses then 200 mg (3 mg/kg) bid | |

| | | | |
|---|---|---|---|
| **C.glabrata** | Voriconazole 400mg (6mg/kg) bid for 2 Doses then 200 mg (3 mg/kg ) bid<br>or<br>Micafungin100mg daily;<br>or<br>Anidulafungin loading dose 200mg, then100 mg daily | Fluconazole (step down) 800mg daily Or Amphotericin B (lipid) | Fluconazole maybe given as step down therapy in high dose if MIC favourable. |

## 4.6 C. Indication for surgery in Infective Endocarditis patient with associated condition[1]

| **Indication for surgery** | **Timing** |
|---|---|
| Heart failure | |
| Aortic / Mitral IE with severe regurgitation /valve obstruction causing Pulmonary oedema or cardiogenic shock | Emergency |
| Aortic / Mitral IE with fistula into cardiac chamber or pericardium causing Refractory pulmonary oedema or shock | Emergency |
| Aortic / Mitral IE with severe acute regurgitation or valve obstruction and Persisting heart failure or echo cardiographic signs of poor hemodynamic tolerance | Urgent |
| Aortic / Mitral IE with severe regurgitation and no HF | Elective |
| Uncontrolled Infection | |
| Locally uncontrolled infection (abscess / aneurysm / fistula / enlarging vegetation) | Urgent |
| Persisting fever and positive blood culture >7-10days | Urgent |
| Infection caused by fungi or multi resistant organism | Urgent |
| Prevention of Embolism | |
| Aortic / Mitral IE with large vegetation (>10mm) following episode of Embolism despite appropriate antibiotic therapy | Urgent |
| Aortic / Mitral IE with large vegetation (>10mm) and predictor of a Complicated course | Urgent |
| Isolated very large vegetation (>15mm) | Urgent |

## 4.7 Definitive Therapy for Sexually Transmitted Infections[44]

| STI | Drug of Choice | Alternative Choice | Comments |
|---|---|---|---|
| **Gonococcal Urethritis, Cervicitis, Pharyngitis, Ano rectal discharge** | **Ceftriaxone-** 500mg IM Single dose | **Cefixime** 800 mg PO Single dose **(or) Gentamicin** 240 mg IM Single Dose **plus Azithromycin** 2 g PO Single dose | For Pregnant women- **Ceftriaxone-**500mg IM Single dose **(or) Cefixime** 800 mg PO Single dose |
| **Chlamydia trachomatis- Urethritis, Cervicitis, Pharyngitis, Ano rectal discharge** | **Doxycycline** 100 mg PO BID for 7 days | **Azithromycin** 1 gm Single dose (or) **Erythromycin** 500 mg qid -7 days (or) **Ofloxacin** 200-400 mg bid 7 days | For Pregnant women- **Azithromycin** 1 gm Single dose (or) **Erythromycin** 500 mg qid -7 days (or) **Amoxycillin** 500 mg tid 7 days |
| **Mycoplasma genitalium- Non- gonococcal urethritis, Cervicitis, PID** | **Doxycycline** 100 mg PO BID for 7 days **+ Azithromycin 1** g PO day 1, followed by 500mg PO for 3 days. | **Doxycycline** 100 mg PO BID for 7 days **+ Moxifloxacin** 400mg once daily for 7 days. | |
| **Trichomoniasis** | **Metronidazole** 2 gm Single dose (or) **Metronidazole** 400 mg bid -7 days | **Tinidazole** 2 g Single dose **(or) Secnidazole** 2g Single dose **(or) Tinidazole 500** mg bid-5 days | |
| **Vaginal Candidiasis** | **Fluconazole** 150mg PO Single dose | **Clotrimazole** Vaginal tablet 100 mg HS 7 days (or) **Miconazole** vaginal pessaries 200 mg HS 3 days | |
| **Syphilis-** Primary / Secondary / Early latent < 1 Yr | **Inj.Benzathine Penicillin** 2.4 MU IM Single dose | **Doxycycline** 100 mg PO BID for 14 days **(or) Erythromycin** 500mg qid 14 days **(or) Ceftriaxone** 1-2 g OD -14 days. | |
| **Syphilis-** Late latent > 1 Yr / Tertiary / Syphilis of unknown duration | **Inj.Benzathine Penicillin** 2.4 MU IM once a week for 3 weeks | **Doxycycline** 100 mg PO BID for 30 days (or) **Procaine Penicillin** 1.2MU IM OD 20 days | |
| **Genital Ulcer Disease- Herpetic** | **Acyclovir** 400 mg tid for 7 days | **Valaciclovir** 500 mg bid 7 days | |

# Chapter – 5: Intrinsic Resistance / Expected Resistance

| Organism | Intrinsic Resistance / Expected Resistance[8,12] |
|---|---|
| **Enterobacterales:** | |
| Escherichia coli | There is no intrinsic resistance to Beta Lactam |
| Klebsiella pneumonia / oxytoca | **Ampicillin** |
| Citrobacter koseri | **Ampicillin** |
| Citrobacter freundii | **Ampicillin, Amoxicillin Clavulanate, Ampi-Sulbactam, 1st, 2nd Gen Cephalosporins, Cephamycins** |
| Enterobacter cloacae & Klebsiella aerogenes | **Ampicillin, Amoxicillin Clavulanate, Ampi-Sulbactam, 1st Gen Cephalosporins, Cephamycins** |
| Proteus mirabilis | **Tetracycline, Tigecycline, Nitrofurantoin, Colistin / Polymyxin-B** |
| Proteus vulgaris and Proteus penneri | **Ampicillin, 1st, 2nd Gen Cephalosporins, Tetracycline, Tigecycline, Nitrofurantoin, Colistin / Polymyxin-B** |
| Morganella morganii | **Ampicillin, Amoxicillin Clavulanate, 1st, 2nd Gen Cephalosporins, Tigecycline, Nitrofurantoin, Colistin / Polymyxin-B** |
| Providencia rettgeri and Providencia stuartii | **Ampicillin, Amoxicillin Clavulanate, 1st Cephalosporins, Tetracycline, Tigecycline, Nitrofurantoin, Colistin / Polymyxin-B** |
| Salmonella & Shigella Sp | **Aminoglycosides, 1st, 2nd Gen Cephalosporins** |
| Serratia marcescens | **Ampicillin, Amoxicillin Clavulanate, Ampi-Sulbactam, 1st, 2nd Gen Cephalosporins, Cephamycins, Nitrofurantoin, Colistin / Polymyxin-B** |
| Yersinia enterocolitica | **Ampicillin, Amoxicillin Clavulanate, 1st Gen Cephalosporins** |

Enterobacterales are also intrinsically resistant to **Clindamycin**, **Daptomycin**, **Fusidic acid, Vancomycin, Lipoglycopeptides** (**Oritavancin, Teicoplanin, Telavancin**), **Linezolid, Tedizolid, Quinupristin-dalfopristin**, **Rifampin**, and **Macrolides** (**Erythromycin, Clarithromycin** & **Azithromycin**- Except- Salmonella and Shigella spp. with **Azithromycin**).

| **Non-Fermentors GNB:** | |
|---|---|
| Acinetobacter baumanii / calcoaceticus complex | **Ampicillin, Amoxicillin Clavulanate, Aztreonam, Chloramphenicol, Fosfomycin, Ertapenem, Tetracycline** and **Doxycycline**. But to a lesser degree to **Minocycline** and **Tigecycline**. |
| Burkholderia cepacia complex | **Ampicillin, Amoxicillin Clavulanate, Ampi-Sulbactam, Piperacillin, Ertapenem, Colistin / Polymyxin-B, Fosfomycin** |
| Pseudomonas aeruginosa | **Ampicillin, Amoxicillin Clavulanate, Ampi-Sulbactam, Cefotaxime, Ceftriaxone, Tetracycline, Tigecycline, Cotrimoxazole, Chloramphenicol, Ertapenem** |
| Stenotrophomonas maltophilia | **Ampicillin, Amoxicillin Clavulanate, Ampi-Sulbactam, Piperacillin- Tazobactam, Aztreonam, Cefotaxime, Ceftriaxone, Tetracycline, Ertapenem, Imipenem, Meropenem,** Aminoglycosides |

These non fermentative gram-negative bacteria are also intrinsically resistant to penicillin (ie, **Benzylpenicillin**), cephalosporins I (**Cephalothin, Cefazolin**) , cephalosporin II (**Cefuroxime**), cephamycins (**Cefoxitin, Cefotetan**), **Clindamycin**, **Daptomycin**, fusidic acid, glycopeptides (**Vancomycin**), **Linezolid**, macrolides (**Erythromycin, Azithromycin, Clarithromycin**), **Quinupristin-dalfopristin and Rifampin**

| Organism | Intrinsic Resistance / Expected Resistance |
|---|---|
| **Staphylococci** | |
| S.saprophyticus | **Fosfomycin**, Fusidic Acid and Novobiocin (used for organism identification purpose) |
| S.capitis | **Fosfomycin** |
| S.cohnii / S.xylosus | Novobiocin |
| Staphylococci species are intrinsically resistant to **Aztreonam**, **Polymyxin B/ Colistin**, and Nalidixic acid. | |
| **Enterococcus Sp** | |
| Enterococcus fecalis | Cephalosporins, **Clindamycin**, Aminoglycosides, **Trimethoprim Sulfamethoxazole,** Fusidic Acid, **Quinipristin-Dalfopristin** |
| Enterococcus faecium | Cephalosporins, **Clindamycin**, Aminoglycosides, **Trimethoprim Sulfamethoxazole,** Fusidic Acid |
| Enterococcus gallinarum / casseliflavus | Cephalosporins, **Clindamycin**, Aminoglycosides, **Trimethoprim Sulfamethoxazole,**, Fusidic Acid, **Quinipristin-Dalfopristin**, **Vancomycin** |
| Enterococci are also intrinsically resistant to **Aztreonam**, **Polymyxin B/Colistin**, and Nalidixic acid | |

# Chapter – 6 : Antibiotic activity spectrum

## 6.A) Antibiotic activity Spectrum -Gram Positive Cocci[7,8,12,19]

| Pathogen | Penicillins–Acid labile & Acid Stable Penicillin | Penicillinase Stable Penicillins | BL /BLI Combinations | Carbapenems | Cipro/Ofloxacin | Levo /Moxifloxacin | Cefazolin/Cefuroxime/Cefotaxime | Cefoxitin /Oxacillin | Aminoglycosides-Gentamicin only |
|---|---|---|---|---|---|---|---|---|---|
| Enterococcus fecalis (S) | | | | A | | | | | |
| E. faecium (S) | | | | | | | | | |
| E. faecalis (VRE) | | | | | | | | | |
| E. faecium (VRE) | | | | | | | | | |
| Staph. aureus MSSA | | | | | | | | | |
| S. aureus MRSA | | | | | | | | | |
| Staph coag-neg (MS) | | | | | | | | | |
| Staph coag-neg (MR) | | | | | | | | | |
| Strep. Pneumonia | | | | | | | | | |
| Strep.Viridans | | | | | | | | | |

**(a-Imipenem only)**

| Pathogen | Erythromycin / Azithromycin | Clindamycin | Tetra/Doxycycline | Daptomycin | Vancomycin | Teicoplanin | Linezolid | CoT | Nitrofurantoin | Fosfomycin (o) |
|---|---|---|---|---|---|---|---|---|---|---|
| Enterococcus fecalis (S) | | | | | | | | | | |
| E. faecium (S) | | | | | | | | | | |
| E. faecalis (VRE) | | | | | | | | | | |
| E. faecium (VRE) | | | | | | | | | | |
| Staph. aureus MSSA | | | | | | | | | | |
| S. aureus MRSA | | | | | | | | | | |
| Staph coag-neg (MS) | | | | | | | | | | |
| Staph coag-neg (MR) | | | | | | | | | | |
| Strep. Pneumonia | | | | | | | | | | |
| Strep.Viridans | | | | | | | | | | |

## 6.B) Antibiotic activity Spectrum -Enterobacterales[7,8,12,19]

| Pathogen | Penicillin –Acid labile &Stable Penicillin | Penicillinase Stable Penicillin | BL /BLI Combinations | Carbapenems | Cipro/Ofloxacin | Levo /Moxifloxacin | Cefazolin/Cefuroxime | Cefotaxime/Ceftriaxone | Aminoglycosides-Gentamicin /Amikacin |
|---|---|---|---|---|---|---|---|---|---|
| Citrobacter freundii | | | | | | | | | |
| Citrobacter koseri | | | a | | | | | | |
| Enterobacter cloacae/ K.aerogenes | | | | | | | | | |
| E. coli (S) | | | | | | | | | |
| GNB (ESBL) | | | b | | | | | | |
| GNB (KPC) | | | | | | | | | |
| GNB (MBL) | | | | | | | | | |
| Klebsiella pneumonia/oxytoca | | | | | | | | | |
| P.mirabilis | | | | C | | | | | |
| P.vulgaris | | | | C | | | | | |
| Salmonella Sp | | | | | | | | | |
| Shigella Sp | | | | | | | | | |

| Pathogen | Erythromycin / Azithromycin | Clindamycin | Tetra/Doxycycline | Tigecycline | Polymyxin B / Colistin | Chloramphenicol | CoT | Nitrofurantoin | Fosfomycin (o) |
|---|---|---|---|---|---|---|---|---|---|
| Citrobacter freundii | | | | | | | | | |
| Citrobacter koseri | | | | | | | | | |
| Enterobacter cloacae/ K.aerogenes | | | | | | | | | |
| E. coli (S) | | | | | | | | | |
| GNB (ESBL) | | | | | | | | | |
| GNB (KPC) | | | | | | | | | |
| GNB (MBL) | | | | | | | | | |
| Klebsiella pneumonia/oxytoca | | | | | | | | | |
| P.mirabilis | | | | | | | | | |
| P.vulgaris | | | | | | | | | |
| Salmonella Sp | d | | | | | | | | |
| Shigella Sp | d | | | | | | | | |

a. AmoxClav, Amp Sul only, **Pip-Taz** may sensitive,

b. used for mild infection & uncomplicated cystitis only,

c. **Imipenem** MICs for Proteus spp., Providencia spp., and Morganella morganii tend to be higher (eg, MICs in the intermediate or resistant range) than **Meropenem** or **Doripenem**

d. **Azithromycin** only

## 6.C) Antibiotic activity Spectrum- Non Fermenting Gram Negative Bacilli[7,8,12,19]

| Pathogen | Penicillin –Acid labile &Stable Penicillin | Penicillinase Stable Penicillin | Amoxy Clav | Ampi-Sulbctam | Pip-Taz | Ertapenem | Imipenem/ Meropenem | Cipro/Ofloxacin | Levo /Moxifloxacin |
|---|---|---|---|---|---|---|---|---|---|
| Acinetobacter baumannii | | | | | | | | | |
| Pseudomonas aeruginosa | | | | | | | | | |
| Stenotrophomonas maltophilia | | | | | | | | | |

| Pathogen | Cefazolin/Cefuroxime / Cefotaxime/Ceftriaxone | Aminoglycosides- Gentamicin /Amikacin | Tetra/Doxycycline | Tigecycline | Polymyxin B /Colistin | Chloramphenicol | CoT | Nitrofurantoin | Fosfomycin (o) |
|---|---|---|---|---|---|---|---|---|---|
| Acinetobacter baumannii | | | | | | | | | |
| Pseudomonas aeruginosa | | | | | | | | | |
| Stenotrophomonas maltophilia | | | | | | | | | |

| | |
|---|---|
| | **Clinically effective** |
| | **Potential alternative agent** |
| | **Clinically effective in some settings or should be used in combination with another agent** |
| | **Not Recommended** |

| | |
|---|---|
| **Penicillin –Acid labile** | **Penicillin G, Benzathine & Procaine penicillin** |
| **Penicillin –Acid Stable** | **Ampicillin, Amoxicillin, Pen V** |
| **Penicillinase Stable Penicillin** | **Cloxacillin, Dicloxacillin** |
| **BL /BLI Combinations** | **Amoxicillin Clavulanate, Ampicillin Sulbactam, Piperacillin Tazobactam, Cefoperazone Sulbactam** |

# Chapter – 7 : Tables on Dosage, Duration, Drug Interaction and Administration

## 7.A. Antibacterial Drugs[1]

| SL. No | Name | Daily Dose | Maximum daily dose | Dose modification with CrCl (ml/min) | Available | Recon-stitute | Further Dilution | Incompatibility | Infusion time (mins) | Additional comments |
|---|---|---|---|---|---|---|---|---|---|---|
| 1. | **Benzylpenic - illin** Inj | **Low Dose** 0.6 to 1.2 MU q4 hrs IM per day<br><br>**High Dose** 20-40 lac Units IV q 4 hourly (for meningococcal meningitis, the administration should be be done q 2h )<br><br>**Paed dose:** Penicillin G 200,000-300,000 U/kg/24hrs every 4-6hrs/divided doses | 24 Million Units | 10.50, decrease dose by 25% <10% decrease dose by 50%, post HD | 5 lacs/10 lacs | 3 ml of WFI | 100 ml of N.S. | IV incompatibilities include dobutamine, dopamine, norepinephrine, **Gentamicin**, **vancomycin**, **Cefazolin**, **Erythromycin**, lidocaine morphine, - | 30 min | Cross sensitivity to most cephalosporins, B lactams. No cross sensitivity to **Aztreonam**. Probenecid indomethacin, sul fonamides, thiazides. Salicy lates may increase its level due to inhibition of tubular secretion potassium chloride IMU of **Penicillin G** Potassium contains 0.3 mEq of Na and 1.68 mEq of K. Caution should be exercised when given in high doses. |
| 2. | **Cloxacillin** Inj | **Most infections** : 1-2 gm IV Q6H<br><br>**Serious infections**: 2 gm IV Q4H | 12g | NC | 250/500mg | | 500mg in 10ml of NS or 5% dextrose | Blood products or with lipid emulsions. A list of 19 durgs have been | Inject slowly over 3-4 minutes | Bactericidal for methicillin sensitive S aureus (MSSA) Potential to interact with probinecid, methotrexate and warfarin |

| SL. No | Name | Daily Dose | Maximum daily dose | Dose modification with CrCl (ml/min) | Available | Recon-stitute | Further Dilution | Incompatibility | Infusion time (mins) | Additional comments |
|---|---|---|---|---|---|---|---|---|---|---|
| | | **Paed dose:** 100-200mg/kg/ 24hrs divided q6H | | | | | | shown to be incompatible with **Cloxacillin** in some studies although these are not listed in prescribing information | | |
| 3. | **Ampicillin** Inj. | 2 g 4hourly ( total 12 g/day)<br><br>IV:1-2gm Q4H-Q6H<br><br>Oral:250-500mg P/O Q6H<br><br>**Paed dose:** 100-150mg/kg/ 24hrs divided q6H | 12 g | <10-20:0.5-1 g 8 hourly HD: 1 g 2 hourly; 1 g post HD | 500 mg | 5 ml of WFI | 100 ml of N.S. | | 30-60min | Prolonged infusion In creased incidence of rashes with allopuinol |
| 4. | **Amoxicillin sodium & clavulanate potassium** ( each 30 mg contains 25 mg Amoxicillin 5 mg clavulanate) | Usual dose:1.2 g 8 hourly Sever infections 1.2 g 6 hourly<br>**Paed dose:**<br>**Standard dose:** 25-50mg/kg/24h divided q8h<br>**High Dose:** | | <10.20:1.2 g IV stat followed by 600 mg 12 hourly<br><br><10: 1.2 IV stat followed by 600 mg OD | 300 mg / 600 mg/ 1.2 g<br><br>300 mg / 600 mg/ 1.2 g | 5 ml of WFI per 300 mg<br><br>5 ml of WFI per 300 mg | None<br><br>50 – 100 ml NS (50 ml of NS per 600 mg Augment in) | Aminoglycosides blood products glucose, dextran. Bicarbonate iv lipid emulsions | 4 min (BOLUS) 30-40 min (INFUSION) | Prolonged infusion* potential to interact with acenocoumarol, warfarin and probenecid |

| SL. No | Name | Daily Dose | Maximum daily dose | Dose modification with CrCl (ml/min) | Available | Recon-stitute | Further Dilution | Incompatibility | Infusion time (mins) | Additional comments |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 80-90mg/kg/24h divided q8h | | | | | | | | |
| 5. | **Ampicillin & Sulbactam Inj** | Usual:1.5-3 g6 hourly 3gm IV Q6H<br><br>For Acinetobacter:<br><br>ampicillin6gm/sulbactam 3 g iv q 4 hourly<br><br>**Paed dose:**<br>**Mild /moderate infection:** 100-200mg/kg/24h for Ampicillin divided q6h<br>**Severe infections:** 200-400mg/kg/24h for Ampicillin divided q6h | **Ampicillin** 12 g<br><br>**Sulbactam** :4 g | <30:1.5-3 g 12 hourly<br><br><15:1.5-3 g OD | 1.5g/0.75 g<br><br>1.5g/0.75 g | 5 ml WFI<br><br>2 ml of WFI per 0.75 g | None<br><br>25 ml of N.S/ 0.75 g | Aminoglycosides | 5 min (BOLUS) 30-40 min (INFUSION) | Prolonged infusion* Probenecid may impair its excretion |
| 6. | **Piperacillin sodium & Tazobactam** | 4.5 g 8 hourly Severe infections and anti- | **Piperacillin 16 g/ tazobacta** | 20-40:3.375g,q6h; <20-2.25gq 6h, | 2.25g/4.5g | 5 ml of WFI per gm of | 100 ml of N.S. | RL, blood products albumin, | 30min | L vial (4.5 g of **Piperacillin-Tazobactam**) has 12 meq of sodium |

| SL. No | Name | Daily Dose | Maximum daily dose | Dose modification with CrCl (ml/min) | Available | Recon-stitute | Further Dilution | Incompatibility | Infusion time (mins) | Additional comments |
|---|---|---|---|---|---|---|---|---|---|---|
| | Inj | Pseudomonal coverage: 4.5 g 6 hourly<br><br>**Paed dose:** 300mg/kg/24h divided q6h | **m 2 g** | HD, 2.25g q 8h. Loading dose must always be given irrespective of status of clearance An additional dose of 7.5 g piperacillin – tazobactam should be administered following each hemodiaysis session | | Piperacillin (20 ml for 4.5 gm of **Piperacillin Tazobactam** | | hydrolystates, aminoglycosides, | | Prolonged infusion*<br><br>Potential for interaction with warfarin, heparin and methotrexate. May Prolong neuromuscular blockade of vecuronium<br><br>Increased nephrotozicity if combined with vancomycin |
| 7. | **Ticarcillin & Clavulanic acid** | 50 mg/kg/day<br><br><60kg;IV 200-300mg ticarcillin/kg/day divided Q4H-Q6H<br><br>≥60kg:IV 3gm ticarcillin Q4H-Q6H<br><br>Usual dose:3.1g 6 hourly<br>Severe infections | | 30-60: 2 g 4 hourly 10-30:2 g 8 hourly <10:2 g 12 hourly<br>10 with hepatic dysfunction: 2 g OD Patients on peritoneal dialysis: 3.1 g 12 hourly Patients on HD:2 g 12 | 3.1 g | 13ml of WFI | 50 ml of N.S. | Sodium bicarbonate, aminoglycoside | 30 min | Prolonged Infusion* Probenecid may decrease its elimination |

| SL. No | Name | Daily Dose | Maximum daily dose | Dose modification with CrCl (ml/min) | Available | Recon-stitute | Further Dilution | Incompatibility | Infusion time (mins) | Additional comments |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 3.1 g 4 hourly<br><br>**Paed dose:** 200-300mg/kg/24h divided q4-6h for ticarcillin | | hourly, with 3.1 g post HD | | | | | | |
| 8. | **Cefazolin** Sodium Inj | 50 mg/kg/day in three divided doses<br><br>Usual dose: 1 g 8 hourly<br>For severe infections: 2 g 6- 8 hourly<br>**Paed dose:** 100-150mg/kg/ 24h q6-8h | 8 g | 35-54: Full doses at 8 hourly interval, 11-34- half the usual dose every 12h, less than 10- half the usual dose every 24h:0 | 500 mg/1 g | 10 ml of WFI | 30 ml of NS | - | 10 min | Do not give as prolonged infusion for preoperative prophylaxis probenecid may decrease renal tubular secretion |
| 9. | **Cefuroxime** Sodium Inj | 750 mg hourly<br>**Serious infections**: 1.5 g 8 hourly Q6H-Q8H<br>**Paed dose:**<br>**IV:** 100-150mg/ kg/ 24h divided q8h<br>**oral :** 20-30mg/ | - | 10-20:750 mg 12 hourly<br><br><10:750 mg OD | 250 mg/ 750 mg/ 1.5 g<br><br>250 mg/ 750 mg/ 1.5 g | 2/6/15 ml of WFI<br><br>2/6/15 ml of WFI | None<br><br>50-100 ml of NS | Aminoglycosides sodium bicarbonate | 5 min (BOLUS)<br><br>15-30 min (INFUSION) | Do not give as prolonged infusion for preoperative prophylaxis |

| SL. No | Name | Daily Dose | Maximum daily dose | Dose modification with CrCl (ml/min) | Available | Recon-stitute | Further Dilution | Incompatibility | Infusion time (mins) | Additional comments |
|---|---|---|---|---|---|---|---|---|---|---|
| | | kg/24h divided q8-12h | | | | | | | | |
| 10. | Cefotaxime Sodium Inj | **Usual dose:** 1 g 8 hourly **Severe infections:** 2g q4h- **q8h** **Paed dose:** 100-200mg/kg /24h divided q6h | 12 g | <50-10:2g 12 hourly <10: 2 g OD | 250mg/lg | 5ml of WFI | 20 ml of NS | Aminoglycosides | 10 min | prolonged infusion |
| 11. | Ceftriaxone | **Usual dose:** 2 gm OD **Meningitis synergistic treatment for enterococcal endocarditis**: 2g 12 hourly **Paed dose:** 100mg/kg/24h divided OD/q12h | 4g | NC | 250mg/1g | 10 ml of WFI | 50 ml of NS | Aminoglycosides, **Vancomycin**, fluconazole calcium-containing IV solutions like RL, TPN | 30min | CI in hyperbilirubinemia |
| 12 | Ceftazidime inJ.BOLUS Ceftazidime Inj: INFUSION | **Usual dose**: 2g Q8H-Q12H **Severe infections**: 2g 6-8 hourly **Paed dose:** 100-150mg/kg/ | 8g | <50-30 1g iv bd 30-10:1g iv OD <10:500 mg OD | 250/500/1g/ 2g 250mg/500 mg/1g/2g | 2.5 ml of WFI/250 mg 2.5 ml of WFI 250 mg | None 50 ml of N.S. | Sodium bicarbonate aminoglycosides, **Vancomycin** | 5 min 15-30 min | Nephrotoxicity with concomitantaly administered nephrotoxic agents such as aminoglycosides..or potent diuretic such as furosemide Contains |

| SL. No | Name | Daily Dose | Maximum daily dose | Dose modification with CrCl (ml/min) | Available | Recon-stitute | Further Dilution | Incompatibility | Infusion time (mins) | Additional comments |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 24h divided q8h | | | | | | | | 2.3mEq of Na per gram of **Ceftazidime** |
| 13 | **Cefoperazone** (CPZ) sodium inj.BOLUS<br><br>**Cefoperazone** sodium Inj.INFUSION | 40-80 mg/kg/day<br><br>Usual dose: 1-2g 12 hourly (4g/day)<br>Severe infections: 2-4gm Q8H-Q12H<br><br>**Paed dose:**<br>50-200mg/kg/24h divided q8-12h<br>Note: q12h for <8 days | 8g | NC | 1g/2g<br><br>1g/2g | 1ml WFI/100 mg<br><br>5 ml of WFI/g | None<br><br>20-100 ml of N.S/g | Sodium bicarbonate aminoglycosides | 5 min<br><br>15-60 min | Concomitant severe hepatic & renal dysfunction: Not more than 2g/day<br><br>Prolonged infusion* |
| 14 | **Sulbactam (SBT) & Cefoperazone (CPZ) sodium** Inj.(1:1)<br><br>**Sulbactam (SBT) & Cefoperazone (CPZ)** | **Usual dose:**<br>3g 12 hourly<br>Serious<br>3-6gm Q12H<br><br>**Paed dose:**<br>SBT/CPZ (1:1): 40-80mg/kg/24h divided q6-8h | SBT/CPZ (1:1): 8g (i.e. SBT 4g/CPZ 4g/CPZ 4g)<br><br>SBT/CPZ (1:2):12g (i.e.SBT 4g/CPZ | **Sulbactam** requires renal dose modification<br><30-15: 1g 12 hourly (max 2g/day)<br><15:500 mg 12 hourly (max 1g/day) | 1g: (Cefoperazone 0.5 g + **sulbactam** 0.5g)<br><br>1.5 g: (Cefoperazone 1g+ **sulbactam** | 3.4 ml of WFI per 1g vial<br><br>3.2 ml of WFI per 1g vial | 100ml of RL | Sodium bicarbonate aminoglycosides | 15-20 min | RL should not be used for the initial reconstitution as the mixture is incompatible<br><br>Prolonged infusion* |

| SL. No | Name | Daily Dose | Maximum daily dose | Dose modification with CrCl (ml/min) | Available | Recon-stitute | Further Dilution | Incompatibility | Infusion time (mins) | Additional comments |
|---|---|---|---|---|---|---|---|---|---|---|
| | **sodium (1:2)** | SBT/CPZ (1:2) 60-120mg/kg/24h divided q6-8h | 8g)<br><br>Max dose of | <30-15 :Inj cefoperazone/**sulbactam** (1:2) 1.5 g 8 hrly<br><br>Infections: 6g 12 hourly | 0.5g) 3g: | | | | | |
| 15 | **Cefepime** Inj. | **Usual dose**:<br>2 g-12 hrly<br>**Severe infections:**<br>2 g 8-12 Hrly<br>**Paed dose:**<br>100-150mg/kg/ 24h divided q8h | 6 g | < 50-10: 1 g OD<br>< 10: 0.5-1 g OD<br>Hemodialysis patients: 1 g on day 1 then 500 mg everyday | 250 / 500 / 1 g | 2.5 ml of WFI / 250 mg | 50 – 100 ml of N.S. | | 30 min | Prolonged infusion*<br>High doses may cause encephalopathy if creatinine clearance reduced |
| 16 | **Cefpirome sulphate** Inj | **Usual dose**:<br>1 g 12 hourly<br>**Severe infections:**<br>2 g 12 hourly<br>**Paed Dose:**<br>**Dosing safety and efficacy not established** | 2 g | 2 g loading dose followed by<br>< 50-20 : 1 gm 12 hourly<br>20-5 : 1 gm OD | 1 g<br><br>1 g | 10 ml of WFI<br><br>10 ml of WFI | None<br><br>100 ml of NS per g | Sodium bicarbonate | 4 min (BOLUS)<br>20 – 30 min (INFUSION) | Avoid with nephrotoxic agents<br>( aminoglycosides, loop diuretics)<br>Not recommended in Children |
| 17 | **Imipenem & Cilastatin** Sodium Inj. | **For most infections**<br>500 mg 6 hourly<br>**Severe infections :**<br>1 g q 8 hourly | 4 g | If initial dose is 500 mg 6 hourly, then | 500 mg | 20 ml of WFI | 100 ml of N.S. per 500 mg | Lactate and diluents containing lactates | 30 min | Risk of seizures if renal dysfunction, CNS infection (meningitis, SOL) and |

| SL. No | Name | Daily Dose | Maximum daily dose | Dose modification with CrCl (ml/min) | Available | Recon-stitute | Further Dilution | Incompatibility | Infusion time (mins) | Additional comments |
|---|---|---|---|---|---|---|---|---|---|---|
| | | **Paed dose:**<br>**<3 months age and <1.5kg** :<br>25mg/kg/dose q12h for **age**<1 week, q8h for **ages** 1-4 weeks, q6h for 4 weeks-3 months age.<br>**<3 months - 12 years of age**:<br>15-25mg/kg/dose q6h<br>**<12 years:**<br>10-15mg/kg/dose q6h | | Loading dose of 500 mg IV stat followed by<br>< 70-41: 500 mg 8 hourly<br><40-21: 500 mg 12 hourly<br>< 20 or HD : 250 mg OD<br><5: do not give until HD is initiated within 48 hrs<br>Patients on hemodialysis should receive **Imipenem** after Dialysis | | | | | | Gancyclovi Patients receiving valproic acid concomitantly may require measurement of valproic acid levels<br>Prolonged infusion* |
| 18 | **Meropenem**<br>Inj. | **Usual dose:**<br>1 g 8 hourly<br>**Meningitis or treatment of resistant gram** | 6 g | <50: Loading dose of 1 gm IV stat followed by maintenance | 500 mg / 1 g | 5 ml of WFI per 250 mg | 50 ml of N.S. | Should not be added to or mixed with other drugs | 15 – 30 min | Prolonged infusion* |

| SL. No | Name | Daily Dose | Maximum daily dose | Dose modification with CrCl (ml/min) | Available | Recon-stitute | Further Dilution | Incompatibility | Infusion time (mins) | Additional comments |
|---|---|---|---|---|---|---|---|---|---|---|
| | | **negatives :**<br>2 g 8 hourly<br>**Paed dose:**<br>60-120mg/kg/24h divided q8h | | dose as follows<br>26-50, 12 hourly<br>10-25, half of the dose at 12 hourly interval<br><10, half dose at 24 hr interval | | | | | | |
| 19 | Vancomycin hydrochloride Inj. | Loading dose:25-30 mg/kg of actual body wt followed by maintenance dose of<br>**Usual dose**:<br>15 mg/kg Q8-2 hourly<br>**Meningitis**:<br>15-20 mg/kg Q8H-Q12H<br><br>**Adults (60 kgs with normal CrCL):** | Not to exceed 2 g/dose | Dose mg /day:<br>15.4 mg X CrCL<br>HD: 1 g q48h (after HD | 500 mg / 1 g | 10 ml of WFI per 500 mg | 100 ml of 0.9 % N.S. or 5% dextrose per 500 mg<br>Concentrations of no more than 5 mg/mL is recommended in adults | Alkaline solutions, β - lactam antibiotics | Infusion rate not exceeding 15 mg/min<br>Usual infusion rate:<br>1 g in 200 ml 0.9% NS over 60 min &<br>500 mg in 100 ml 0.9% NS over 30 min | **Vancomycin** trough levels to be drawn1 hour before the 5th dose of **Vancomycin**<br>Recommended trough levels is 10-15 µg/ml in mild-moderate and 15-20 µg/ml in serious infections-.<br>Nephrotoxicity (0-12%) is associated with **Vancomycin** trough levels greater than or equal to 15 µg/mL, high dose **Vancomycin** ( greater or equal to 4 |

| SL. No | Name | Daily Dose | Maximum daily dose | Dose modification with CrCl (ml/min) | Available | Recon-stitute | Further Dilution | Incompatibility | Infusion time (mins) | Additional comments |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 1.5 g (loading dose) followed by 1 g 12 hourly<br><br>**Paed dose:** 40-60mg/kg/24h divided q6h | | | | | In selected patients in need of fluid restriction, a concentration up to 10 mg/mL may be used | | 0 to 500 mg in 100 ml ( 30 minutes ) 501-1250 mg in 250 ml ( 60 minutes ) 1251-1750mg in 500ml ( 90 minutes ) 1751-2250mg in 500 ml ( 120 minutes ) If red-man syndrome- Infusion can be increased over 3 hours | g/day), concomitant use of nephrotoxic agents and piperacillintazobactam, and duration of **Vancomycin** therapy Concomitant use of opioids may increase the potential for redman |
| 20 | Teicoplanin Inj. BOLUS | **Loading dose** of 6 mg/kg 12 | - | < 60-40 or on HD, | 200 mg / 400 mg | 1.5 ml of WFI per | none | Aminoglycosides | 1 min | Bone marrow suppression- Monitor |

| SL. No | Name | Daily Dose | Maximum daily dose | Dose modification with CrCl (ml/min) | Available | Recon-stitute | Further Dilution | Incompatibility | Infusion time (mins) | Additional comments |
|---|---|---|---|---|---|---|---|---|---|---|
| | Teicoplanin Inj. INFUSION | hourly for first 3 doses followed by 6 mg/kg OD **Usual dose** : 400 mg IV 12 hourly for 3 doses followed by 400 mg OD **For more serious Infections** (Endocarditis dose bone and joint infection) 12 mg/kg BD for 3 doses followed by 12 mg/kg OD **Paed dose: For neonates:** 16mg/kg on day 1 f/b 8mg/kg OD **After neonatal period:** 10mg/kg divided q12h for 3 doses f/b 6mg/kg/q24h | | the chosen dose (6 or 12 mg/kg) should be administered every 48 hours and 72 hours, respectively. Maximum dose in patients on HD: 10 mg/kg every 48 to 72 hours. | 200 mg / 400 mg | 200 mg 1.5 ml of WFI per 200 mg | 100 ml of NS | | 30 min | with CBC weekly |

| SL. No | Name | Daily Dose | Maximum daily dose | Dose modification with CrCl (ml/min) | Available | Recon-stitute | Further Dilution | Incompatibility | Infusion time (mins) | Additional comments |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | |
| 21 | **Daptomycin** Inj | 4-6 mg/kg/day for SSTI, 10-12 mg/kg/day for severe infections and endocarditis 8-12 mg /kg Q24H<br><br>**Paed dose:**<br>**Age 1-6 yrs**: 10-12 mg/kg OD<br>**Age 7-11 yrs:** 7-9 mg/kg OD<br>**Age 12-17 yrs:** 7-9 mg/kg OD<br>Note: Higher dose is recommended for S.aureus bacteremia | | < 30: every 48 hours | 350mg | | 350 mg in 100 ml of NS | Dextrose solution | 30 min | Check CPK on day 7, Avoid statins |
| 22 | **Tigecycline** Inj | 100 mg IV stat followed by 50 mg 12 hourly Child Pugh Class C- 100 mg IV loading dose followed | 200 mg ( maximum tolerated dose) | NC | 50 mg | 5 ml of NS | 50 mg in 100 ml of NS | Should not be administered through the same line -AmB-d, ABLC, diazepam, | 60 min | Give IV Tigecycline with food to decrease nausea and vomiting Carries a black-box warning for VAP/HAP, potential to cause pancreatitis, risk of |

| SL. No | Name | Daily Dose | Maximum daily dose | Dose modification with CrCl (ml/min) | Available | Recon-stitute | Further Dilution | Incompatibility | Infusion time (mins) | Additional comments |
|---|---|---|---|---|---|---|---|---|---|---|
| | | by 25 mg 12 hourly<br>**For hospital acquired infections or Acinetobacter**, 200 mg IV stat, followed by 100 mg IV q12h<br><br>**Paed dose:**<br>**Age 8 to <12 years**:<br>1.2mg/kg q12h<br>**Age 12-17 yrs**:<br>50mg q12h | | | | | | esmoprazole, omeprazole | | increased mortality. Potential to interact with warfarin. It can cause fetal harm if given to pregnant woman |
| 23 | **Clindamycin** Inj. | **Usual dose**:<br>600-900 mg every 8 hourly<br>**Oral dose**:<br>300 mg three-four times a day<br><br>**Paed dose:**<br>40mg/kg/24h divided q6-8h | 2700 mg ( 900 mg 8 hourly) | NC | 300 / 600 mg | 20 ml of WFI | 20 ml of NS | It is incompatible with **Ampicillin**, phenytoin, barbiturates, aminophylline, calcium gluconate and magnesium sulphate | 20 min | Diarrhoea (20%)<br>C. difficile colitis (0.01-10%), minor reversible transaminases alterations.<br>The neuromuscular blockade action may be potentiated. **Rifampicin** a strong inducer of CYP3A4 may reduce its level. It should not be |

| SL. No | Name | Daily Dose | Maximum daily dose | Dose modification with CrCl (ml/min) | Available | Recon-stitute | Further Dilution | Incompatibility | Infusion time (mins) | Additional comments |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | coadministered with **Erythromycin** as invitro antagonism has been demonstrated |
| 24 | **Amikacin** Sulphate Inj. | 15 mg/kg IV OD. Dosing beyond 48 hours should be accompanied by determination of peak levels done after 1 hr of dosing (56-64mcg/ml), and Trough concentration (<1mcg/ml) Ideal body weight (IBW) should be used for dose calculation **Paed dose:** 15-22.5mg/kg/ 24h divided q8-12h | 1 g | 40-59, :15 mg/kgq36h 30-39-15mg/kgq48h <30- Not recommended Patient on intermittent dialysis, the dose should be given after dialysis | 500 / 100 mg | 1 ml of WFI / 500 mg | 100 ml of N.S. | all antibiotics | 60 min | Administration with agents causing the following side effects should be avoided Nephrotoxicity (polymyxins, cisplatin, **Vancomycin**, amphotericin), ototoxicity (ethacrynic acid, furosemide), neuromuscular blockade (suxamethonium, halogenated hydrocarbon inhalation, opioids, citrated anticoagulated blood) |
| 25 | **Gentamicin** Inj. | 4-5 mg/kg/day - | 1 g | Cr CL 40-60, -5mg/kg q36hr | 60 / 80 mg | 2 ml of WFI | 50 ml | all antibiotics | 20 min | Administration with agents carusing the |

| SL. No | Name | Daily Dose | Maximum daily dose | Dose modification with CrCl (ml/min) | Available | Recon-stitute | Further Dilution | Incompatibility | Infusion time (mins) | Additional comments |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 7mg/kg may be necessary in critically ill patients)<br>Split dose may be preferable in infective endocarditis (1mg/kg Q8H or 3mg/kg/day OD,,<br>Peak (3-5mg/L) and trough:<br><1mg/l levels should be targeted<br>Ideal body weight (IBW) should be used for dose calculation<br>**Paed dose:**<br>3-6mg/kg/24h divided q8h | | <40_4 mg/kg, next dose should prefereably be on the basis of concentration and if definitely needed | | | | | | following side effects should be avoided Nephrotoxicity(polymyxins, cisplatin, **Vancomycin**, amphotericin), ototoxicity (ethacrynic acid, furosemide), neuromuscular blockade (suxamethonium, halogenated hydrocarbon inhalation, opioids, citrated anticoagulated blood) |
| 26 | **Tobramycin Inj.** | 4-5mg/kg q 24h<br>7mg/kg may be necessary in critically ill | 1 g | Cr CL 40-60, -5mg/kg q36hr<br><40_4 mg/kg, next | 60 / 80 mg | 2 ml of WFI | 50 ml | All antibiotics | 20 min | Administration with agents causing the following side effects should be avoided |

| SL. No | Name | Daily Dose | Maximum daily dose | Dose modification with CrCl (ml/min) | Available | Recon-stitute | Further Dilution | Incompatibility | Infusion time (mins) | Additional comments |
|---|---|---|---|---|---|---|---|---|---|---|
| | | patients)<br>Peak and (3-5mg/L), trough: <1mg/l<br>tobramycin levels should be targeted<br>Ideal body weight (IBW) should be used for dose calculation<br>**Paed dose:**<br>**<5 yrs:**<br>2.5mg/kg/dose divided q8h<br>**>/= 5yrs**:<br>2-2.5mg/kg/dose divided q8h | | dose should preferably be on the basis of concentration and if definitely needed | | | | | | Nephrotoxicity(polymyxins, cisplatin, **Vancomycin**, amphotericin), ototoxicity (ethacrynic acid, furosemide), neuromuscular blockade (suxamethonium, halogenated hydrocarbon inhalation, opioids, citrated anticoagulated blood) |
| 27 | **Azithromycin**<br>Inj. | **For most infections**:<br>500 mg OD<br>**Enteric fever**:<br>(20 mg/kg/day)<br><br>**Paed dose:**<br>**usual dose:** | 1g | NC | 500 mg | 4.8 ml of WFI | 250-500 ml of NS | - | 20 min | Empty stomach<br>ECG: QTc prolongation.<br>Potential for drug interactions with the following agents needs to be watched for – carbamazepine, digoxin, fluconazole, nelfinavir, |

| SL. No | Name | Daily Dose | Maximum daily dose | Dose modification with CrCl (ml/min) | Available | Recon-stitute | Further Dilution | Incompatibility | Infusion time (mins) | Additional comments |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 10mg/kg on day 1, f/b 5mg/kg OD for 4 days<br>**High Dose in typhoid fever:**<br>10-20mg/kg24h divided q12h for 10-14 days | | | | | | | | efavirenz, indinavir, zidovudine, warfarin |
| 28 | Ciprofloxacin<br>Inj | 200-400 mg 8-12 Hourly<br><br>**Paed dose:**<br>20-30mg/kg/24h divided q12h | 800 mg | < 50 : 50% of dose<br>OD | 200 mg | - | 100 ml of N.S. | Solutions containing multivalent cations such as magnesium | 60 min | Use of tizanidine is contraindicated with **Ciprofloxacin**. Clinically significant interactions may occur when it is given with phenytoin, theophylline, cyclosporine, drugs known to cause prolongation of QT interval, methotrexate, NSAIDs, duloxetine, Warfarin |
| 29 | Levofloxacin<br>Inj. | 500-750 mg OD<br><br>**Paed dose:**<br>20mg/kg/24h divided q12h for children <5yrs | 750 mg | 50-10 : 50% of dose<br>OD<br>< 10 : 25 % of dose<br>OD or 50% | 500 mg | - | 100 ml of N.S. | Solutions containing multivalent cations such as magnesium | 60-90 min | Caution should be exercised ehen administered with NSAIDs |

| SL. No | Name | Daily Dose | Maximum daily dose | Dose modification with CrCl (ml/min) | Available | Recon-stitute | Further Dilution | Incompatibility | Infusion time (mins) | Additional comments |
|---|---|---|---|---|---|---|---|---|---|---|
| | | age | | dose every 48 hrs | | | | | | |
| 30 | **Ofloxacin** Inj | 400 mg 12 Hourly **Paed dose:** 15-20mg/kg/24h divided q12h | 800 mg | < 10 :50 % of dose OD | 200 mg | - | 100 ml of N.S. | Heparin solutions | 60 min (Slow infusion) | Maximum dose is 400 mg in patients with cirrhosis Maintain adequate Hydration |
| 31 | **Metronidazole** Inj. | Loading dose of 15 mg/kg, then 7.5 mg/kg 8 hourly or 15 mg/kg q12h Adults: usual dose 500 mg 8 hourly or 1g q12h **Paed dose:** 15mg/kg/24h divided q8h | 4 g | < 10: 50% of usual dose 12 hourly | 500 mg | - | 100 ml of N.S. | - | 30 min | End stage liver disease: 50% of usual dose 12 Hourly |
| 32 | **Colistimethate sodium (Colistin)** **Inj** | Loading dose of 9-12 million unit ( MU) followed by 4.5mu q12h Nebulized **Colistin**: 4.5 million units, q12 hourly Intrathecal/ventr | 9 million units | Cr CL 50-79: 2.5-3.8 mg CBA/kg/day in 2 divided doses CrCL 30-49: 2.5 mg/kg/da o.d Cr Cl:10-29:1.5 | CBA 1 mg=30,000 U of CMS (It is advisable to read the manufacturer's instruction | 10 ml of 0.9 % NS | 40 ml of 0.9 % NS | Mixing drugs in infusion, injections, nebulizer solutions. **Erythromycin**, **Tetracycline**, cephalothin may | 30 min for each 1 million unit | Neurotoxicity, nephrotoxicity, transient sensory disturbances, facial paraesthesias, confusion, psychosis, nephrotoxicity |

| SL. No | Name | Daily Dose | Maximum daily dose | Dose modification with CrCl (ml/min) | Available | Recon-stitute | Further Dilution | Incompatibility | Infusion time (mins) | Additional comments |
|---|---|---|---|---|---|---|---|---|---|---|
| | | icular dose of **Colistin**: 125,000 IU/day<br><br>**Paed dose:** Loading dose: 75,000 IU/kg stat f/b 35,000 -50,000 IU/kg/24h divided q8h | | mg CBA /kg every 36 Hours | since it may vary | | | lead to precipitation | | |
| 33 | **Polymyxin B** | 15,000 to 25,000 U/kg/day iv divided every 12 horus Intrathercal/Intra ventricular- 50,000 U once daily for 3 to 4 days, then every alternate day **Paed dose:** 15,000-30,000 units/kg/24h divided q12h | 25,000 U/kg/day | NA | 5 LU | 5% dexrose | 300-500ml of 5% Dextrose for continuous drip, For intrathecal administration dissolve in NS | Unstable in alkaline solutions | 30-60 mins | May enhance the neuromuscular blocking effect of neuromuscular blockers. Concomitant administration with nephrotoxic and neurotoxic drugs should be avoided |

## 7.B. Antifungal Drugs[1]

| SL. No | Name | Daily Dose | Maximum daily dose | Dose modification with CrCl (ml/min) | Available | Recon-stitute | Further Dilution | Incompatibility | Infusion time (mins) | Additional comments |
|---|---|---|---|---|---|---|---|---|---|---|
| 1. | **Amphotericin B – Deoxycholate (AmB-d)** | 0.5-1.5 mg/kg/day in D-5% over 24 hours<br><br>**Paed dose:** 0.3-1.5mg/kg Once Daily (OD) | 1.5 mg /kg | Not required | 50 mg | 5 ml of WFI | 500 ml of 5% Dextrose | NS - precipitates with 0.9% NS | 4 hours | Test doses are unnecessary 24h infusion and saline loading, with 1 L of saline before AmB associated with less nephrotoxicity. Avoid nephrotoxic agents-NSAIDS, aminoglycosides. Good hydration with K rich diet |
| 2. | **Amphotericin B-liposomal** | 3-5mg/kg/day, once a day<br><br>**Paed dose:** 3-5mg/kg/ day, OD | 5mg/kg | Not required | 50mg | 12 ml of sterile WFI | 5%Dextrose to give a final concentration of 1-2 mg/ml | NS - precipitates with 0.9% NS. Any other drug | 120 minutes | Use of corticosteroids may potentiate hypokalemia. Concomitant administration with other nephrotoxic drugs should be avoided |

| SL. No | Name | Daily Dose | Maximum daily dose | Dose modification with CrCl (ml/min) | Available | Recon-stitute | Further Dilution | Incompatibility | Infusion time (mins) | Additional comments |
|---|---|---|---|---|---|---|---|---|---|---|
| 3. | **Fluconazole** | **For candidemia:** loading dose of 12 mg/kg IV stat followed by maintenance dose of 6 mg/kg/day **Usual dose:** loading dose of 800 mg followed by maintenance dose of 200 (400mg) mg o.d **Paed dose:** loading dose IV / PO 10mg/kg f/b 5-6mg/kg/24h | 1200 mg | < 50 : 50 % of dose HD: 100 % dose post HD | 100ml contains 200 mg | - | - | - | 20 min | Interactions: Prolonged QTc with hypokalemia, hypomagnesimia, cardiomyopathy, Ivabradine, cisapride, astemizole, terfenadine Fluconazole significantly increase levels of cyclosporine, tacrolimus, rifabutin ( uveitis), phenytoin, theophylline **Rifampicin** decreases levels of fluconazole. Hypoglycemia with oral hypoglycemic, PT prolongation with coumarin-type anticoagulation |
| 4. | **Voriconazole** | Loading dose of 6 mg/kg 12 hourly followed by 4 mg/kg 12 hourly*2 doses | | NC IV preparation containing cyclodextrin should not be | 200 mg | 19 ml of WFI for each 20 mg of voriconazole | 180 ml of 0.9% NS for each each 20 mg of | Must not be mixed or coadministered with medical products or electrolytes | 60 min | Dose reduction : 50 % of dose in Childpugh Class A/B Watch for Visual hallucinations, LFT alterations |

| SL. No | Name | Daily Dose | Maximum daily dose | Dose modification with CrCl (ml/min) | Available | Recon-stitute | Further Dilution | Incompatibility | Infusion time (mins) | Additional comments |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Target trough concentration of 1-5 mg/l<br><br>**Paed dose:**<br>IV:<br>Loading dose: 9 mg/kg q12h for 2 doses f/b 8 mg/kg q12h<br>**Oral:**<br>9 mg/kg q12h | | administered in Patients with CrCL < 50 | | | voricona zo le | Blood products must not be administered with voriconazole TPN infusion can be administered | | Contraindicated with **Rifampicin**, carbamazepine, long acting barbiturates, phenytoin, Ivabradine. Interactions with warfarin, Tacrolimus and cyclosporine |
| 5. | **Caspofungi n** | Loading dose of 70 mg* on day one followed by 50 mg OD Endocarditis 150mg OD; step down to azole therapy<br>**Paed dose:**<br>70mg/m2 BSA/ dose on day 1 f/b 50mg/m2 BSA/dose OD | 70 mg | NC | 70 mg/50 mg | 10.5 ml of 0.9 % NS or WFI | 0.9% NS ( 250 ml for 70 mg) & 100 ml for 50 mg | Not compatible with dextrose containing solutions Must not be mixed or coadministered with medical products or electrolytes | 60 min | Watch for:<br>Allergic reactions, nausea, vomiting, diarrhea, LFT alterations, anemia<br>Interactions: Cyclosporine increases Caspofungin AUC by 35%.<br>Cyclosporine levels are unchanged<br>Caspofungin decreases Tacrolimua 12 hour blood concentrations<br>Caspofungin levels are reduced by phenytoin, **Rifampicin**, dexamethasone, |

| SL. No | Name | Daily Dose | Maximum daily dose | Dose modification with CrCl (ml/min) | Available | Recon-stitute | Further Dilution | Incompatibility | Infusion time (mins) | Additional comments |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | Efavirenz, nevirapine, & carbamazepine |
| 6. | **Anidulafungin** | Loading dose of 200 mg followed by 100 mg OD<br><br>**Paed dose:**<br>Loading dose 1.5-3 mg/kg f/b 0.75-1.5mg/kg OD | 200 mg | NC | 100 mg | 10.5 ml of 0.9 % NS or WFI | 0.9% NS ( 250 ml for 70 mg) & 100 ml for 50 mg | Not compatible with dextrose containing solutions<br>Must not be mixed or coadministered with medical products or electrolytes | 60 min | Watch for:<br>Allergic reactions, nausea, vomiting, diarrhea, LFT alterations, anemia |
| 7. | **Micafungin** | 100 mg OD<br>(No loading dose)<br>**Paed dose:**<br></= 30kg:<br>3mg/kg OD<br>>/= 30kg:<br>2.5mg/kg OD | 100 mg | NC | 100 mg | Package insert | Package insert | Must not be mixed or coadministered with medical products or electrolytes | 60 min | Few cases of immunemediated hemolysis have been reported |

WFI, Water for Injection; NC, No Change, f/b-followed by, BSA-Body Surface Area

## 7.C. Drugs Dosages in Paediatrics

| Name of the Antibiotic | Dosage | | |
|---|---|---|---|
| | **Neonates** | **Children** | **Disease Specific setting beyond neonatal period** |
| **Amoxicillin** | Not indicated | 50mg/ Kg divided bid or tid | Pneumonia, sinusitis, acute otitis media |
| **Amoxicillin Clavulanate** | Not indicated | 50 mg / kg of amoxycillin divided bid or tid | SSTI, Second line in sinusitis and acute otitis media |
| **Ampicillin** | 200 mg/kg/day div q6h | 150–200 mg/kg/day div q6h | Pneumonia severe |
| **Azithromycin** | Azithromycin 10 mg/kg PO, IV q24h for 5 days | Erythromycin 40–50 mg/kg/day PO div tid or qid | Diphtheria pharyngitis, dental abscess, group A streptococcus pharyngitis with penicillin allergy |
| **Clarithromycin** | Not indicated | 15 mg/kg/day div bid PO | Pertussis<br>Non tuberculous mycobacteria |
| **Clindamycin** | 30 mg/kg/day IV div q8h | 30 mg/kg/day IV div q8h | CA- MRSA, aspiration pneumonia |
| **Ciprofloxacin** | >2Kg - 25 mg/Kg div q12h | 30 mg/kg/day PO div bid. | Acute exacerbation in cystic fibrosis, dysentery, typhoid if susceptible |
| **Metronidazole** | 15mg/Kg/ dose q24h | 30–40 mg/kg/day IV div q8h | Amoebiasis, tetanus, |
| **Ceftriaxone** | 100 mg/kg/day div q12h | 100 mg/kg/day div q24h | Pneumonia (pneumococcal) |
| **Cefotaxime** | 100 - 200mg/ Kg div q12h to q6h | 150- 200mg/kg day div q8h | meningitis |
| **Cefuroxime** | Not indicated | 20–30 mg/kg/day max 1 g/day (PO)<br>Up to 100 mg/kg/ day, max 3 g/day (IV) | Bone and joint infections |

| | | | |
|---|---|---|---|
| **Cefpodoxime** | Not indicated | 10 mg/kg/day, max 400 mg/day div q12h | |
| **Cefixime** | NA | 8 mg/kg/day, max 400 mg/day PO<br>20mg/kg /day | Urinary tract infection<br>Enteric fever |
| **Cefazolin** | 75 - 100 mg/Kg div q8h | 100 mg/kg/day IV div q8h | Acute bacterial lymphadenitis, osteomyelitis |
| **Cephalexin** | Not indicated | 50–75 mg/kg/day PO div tid<br><br>100 mg/kg/day PO div tid | Acute bacterial lymphadenitis, SSTI<br>Chronic osteomyelitis |
| **Cloxacillin** | 150 mg/kg/day IV div q6h | 150 mg/kg/day IV div q6h | Osteomyelitis – MSSA |
| **Gentamicin** | >35 weeks GA– 4 - 5mg/kg q24h | 5mg/kg q24h | Urinary tract infection |
| **Amikacin** | >35 weeks GA – 15mg/Kg/ dose q24h | 15mg/Kg/ dose q24h | Sepsis, urinary tract infection |
| **Vancomycin** | >28 wk of GA – 15mg/kg/ day div q12h<br>Dose and dosing frquency varies with serum creatinine levels | 40 -60 mg/kg/day IV div q8h | MRSA osteomyelitis |
| **Meropenem** | 60 mg/kg/day div q8h | 60 mg/kg/day div q8h | Lemierre syndrome, Brain abscess, Febrile neutropenia, Documented ESBL containing gram negative bacilli in pyelonephritis |
| **Linezolid** | | 30 mg/kg/day q8h | CA- MRSA in osteomyelitis, endocarditis, empyema |
| **Piperacillin tazobactam** | 300 mg/ Kg div q8h | 300 mg/ Kg div q8h | Sepsis |

## 7.D. Drugs in Pregnancy

### FDA Classification

| Rating | Conditions | Examples |
|---|---|---|
| **A** | **Controlled studies show no harm to Human & Animal feus in any trimester of pregnancy** | |
| **B** | **Insufficient human study, No harm in animal study** | Penicillin, Cephalosporin, Carbapenem, Vancomycin (oral), Daptomycin, Erythromycin, Roxithromycin, Azithromycin, Fosfomycin, Polymyxins, Clindamycin, Nitrofurantoin, INH, Ethambutol, Bedaquiniline, Amphotericin-B, Chloroquine, Mefloquine, Aciclovir, Zidovudine, Didanosine, Lamivudine, Emtricitabine, Tenofovir, Nevirapine, Ritonavir, Dolutegravir, Enfuvirtide, |
| **C** | **Insufficient human study, Harmful effect in animal study** | Vancomycin (IV), Teicoplanin, Oritavancin, Telavancin, Dalbavancin, Clarithromycin, Chloramphenicol, Dapsone, Metronidazole, Tinidazole, Fluoroquinolones, Pyrazinamide, Rifampicin, Echinocandins, Itraconazole, Miconazole, Posaconazole, Isavuconazole, Quinine, Pyrantel Pamoate, Indinavir, Entecavir, Adefovir, Oseltamivir, |
| **D** | **Positive evidence of risk (potential benefit overweigh the risk)** | Kanamycin, Gentamicin, Tobramycin, Amikacin, Minocycline, Linezolid, Tedizolid, Quinupristin-Dalfopristin, Sulfonamides, CoT, Streptomycin, Delamanid, Terbinafine, Fluconazole, Ketoconazole, |

| | | |
|---|---|---|
| | | Voriconazole, Griseofulvin, Albendazole, Mebendazole, Valaganciclovir, |
| **X** | **Contraindicated in pregnancy** | Tetracyclines, Tigecycline, Primaquine, Ribavirin, |

| | |
|---|---|
| **Antimicrobial Drugs contraindicated in first Trimester** | Metronidazole, Tinidazole<br>Trimethoprim-Sulfamethoxazole<br>Fluconazole, Efavirenz,<br>Pyrimethamine, Mefloquine<br>ACT Combinations (Amodiaquine–Artesunate, Mefloquine–Artesunate, and DHA–Piperaquine) |
| **Drugs contraindicated in second Trimester** | ACE inhibitors |
| **Drugs contraindicated in third Trimester** | Nitrofurantoin,<br>Trimethoprim-Sulfamethoxazole<br>Chloramphenicol |
| **Drugs contraindicated throughout pregnancy** | Griseofulvin, Ribavirin, Aminoglycosides, Tetracycline, Primaquine |
| **Drugs safe during Pregnancy** | Antiviral – Oseltamivir, Acyclovir Macrolides, Flucloxacillin, Phenoxymethylpenicillin (Penicillin V) and the broad-spectrum Penicillin such as Amoxicillin and Ampicillin, Cephalosporins, Antitubercular drugs |

## 7.E. Drugs in Lactation

| | |
|---|---|
| **Drugs contraindicated in Lactation** | Amiodarone<br>Antineoplastics<br>Cytotoxic drugs<br>Gold salts<br>Iodine<br>Lithium<br>Radiopharmaceuticals<br>Retinoids (oral)<br>drugs of abuse |
| **Drugs safe during Lactation** | Heparin, corticosteroids (upto 40mg prednisolone), acyclovir |

# Chapter – 8 : Antimicrobial Prophylaxis Guidance

## 8-1) Antibiotic Prophylaxis before Surgery[1]

1) A Single dose of pre-operative antibiotic is enough and repeat doses may be required if the duration of surgery extends beyond two half-lives of the antibiotic used (>4 hours in case of **Cefazolin** and **Cefuroxime**) or if the volume of blood loss is > 1.5 Lit
2) No role for surgical prophylaxis in clean surgeries without implant/prosthesis
3) No role for surgical prophylaxis in an infected or dirty wounds
4) All antibiotics needed to be administered within 1 hour of incision except for **Vancomycin** and **Fluoroquinolones** which are needed to be infused 2 hours prior to incision
5) In case of **Penicillin** or Cephalosporin allergy, **Clindamycin** or **Vancomycin** can be considered as alternatives

| Operations | Likely Pathogens | Prophylactic antibiotic 60-120 min before surgery |
|---|---|---|
| **1.Placement of all grafts, prostheses, or implants**<br>**2. Cardiac surgery**<br>**3. Neurosurgery**<br>**4. Breast**<br>**5. Vascular Surgery** | Staphylococcus aureus; CoNS | **Cefazolin** 2 Gm IV<br>OR<br>**Cefuroxime** 1.5 Gm IV |
| **Ophthalmic** | S. aureus; CoNS; Streptococci; Gram negative bacilli | Topical **Moxifloxacin** given as 1 drop every 5–15 min for 5 doses |
| **Orthopedic**<br>**Total joint replacement, closed fractures/use of nails, bone plates, other internal fixation devices, functional repair without implant/device, trauma** | Staphylococcus aureus; CoNS; Gram-negative bacilli | **Cefazolin 1.5g IV**<br>**or**<br>**Vancomycin 1g IV if MRSA cover is needed.** |
| **Non-cardiac thoracic**<br>**Thoracic (lobectomy, pneumonectomy wedge resection, other non-cardiac mediastinal procedures), closed tube thoracostomy** | Staphylococcus aureus; CoNS; Streptococcus pneumonia; gram-negative bacilli | **Cefazolin** 2 Gm IV<br>**OR**<br>**Cefuroxime** 1.5 Gm IV<br>**OR**<br>**Ampicillin-sulbactam** 3Gm IV |
| **1.Appendicectomy**<br>**2.Biliary tract surgery**<br>**3.Colorectal surgery** | Gram-negative bacilli; anaerobes | **Cefazolin** 2 Gm IV<br>**OR**<br>**Cefuroxime** 1.5 Gm IV **Plus** |

| | | |
|---|---|---|
| **4.Gastroduodenal surgery** | | **Metronidazole** 500 mg IV |
| **Head and neck (major procedures with an incision through oropharyngeal mucosa)** | Staphylococcus aureus; Streptococci; oropharyngeal anaerobes (e.g., peptostreptococci) | **Ampicillin-sulbactam** 3Gm IV<br>**OR**<br>**Cefazolin** 2 Gm IV **+**<br>**Metronidazole** 500 mg IV |
| **Obstetric and gynecologic** | Gram-negative bacilli; Enterococci; group B streptococci; anaerobes | **Cefazolin** 2 Gm IV<br>**OR**<br>**Ampicillin-sulbactam** 3Gm IV |
| **Urologic** | Gram-negative bacilli | Prophylaxis based on pre-operative urine culture susceptibility pattern OR<br>**Amikacin** 1 g IV for Endourological procedures |

## 8.2. Infective Endocarditis Prophylaxis[15]

**Table 1 : Cardiac Conditions Associated With the Highest Risk of Adverse Outcome From Endocarditis for Which Prophylaxis With Dental Procedures Is Reasonable**

**1**. Prosthetic cardiac valve or valve repair with prosthetic valve material.

-Prosthetic heart valve (surgical or transcatheter)

-Cardiac valve repair with prosthetic material (including annuloplasty rings or clips)

**2**. Durable mechanical circulatory support device (ventricular assist device or artificial heart).

**3**. Previous IE.

**4**. Certain types of congenital heart disease including: *

-Unrepaired cyanotic congenital heart disease (patients with palliative shunts and conduits are still considered unrepaired).

-Completely repaired congenital heart defect with prosthetic material or device (eg, septal closure device), during the first six months after surgical or transcatheter placement. #

-Repaired congenital heart disease with residual defect at the site or adjacent to the site of a prosthetic patch or prosthetic device.

-Prosthetic pulmonary artery valve or conduit (surgical or transcatheter; eg, Melody valve and Contegra conduit).

**5.** Cardiac transplant recipients with valve regurgitation attributable to a structurally abnormal valve.

**6**. Left atrial appendage occlusion device, during the first six months after percutaneous or surgical placement.

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

†Prophylaxis is reasonable because endothelialization of prosthetic material occurs within 6 months after the procedure.

**Table 2: Dental Procedures for Which Endocarditis Prophylaxis Is Reasonable for Patients in Table-1**

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

***The following procedures and events do not need prophylaxis:**

i) routine anesthetic injections through non infected tissue,

ii) taking dental radiographs,

iii) placement of removable prosthodontic or orthodontic appliances, adjustment of orthodontic appliances, placement of orthodontic brackets, shedding of deciduous teeth, and bleeding from trauma to the lips or oral mucosa.

**Table 3. Regimens for a Dental Procedure**

| Situation | | Agent | Regimen: Single dose 30-60 Min before procedure | |
|---|---|---|---|---|
| | | | **Adults** | **Children** |
| **Oral** | **Penicillin** Sensitive | **Amoxicillin** | 2 g | 50 mg/Kg |
| | Allergic to **Penicillin** or **Ampicillin** | **Cephalexin*** (or) | 2 g | 50 mg/Kg |
| | | **Clindamycin** (or) | 600 mg | 20 mg/Kg |
| | | **Azithromycin** or **Clarithromycin** | 500 mg | 15 mg/Kg |
| | | **Doxycycline** | 100 mg | <45kg, 2.2 mg/kg<br>>45kg, 100mg |
| **Unable to take oral** | **Penicillin** Sensitive | **Ampicillin** (or) | 2 g IM/IV | 50 mg/Kg IM/IV |
| | | **Cefazolin** (or) **Ceftriaxone** | 1 g IM/IV | 50 mg/Kg IM/IV |
| | Allergic to **Penicillin** or **Ampicillin** | **Cefazolin** (or) **Ceftriaxone**** (or) | 1 g IM/IV | 50 mg/Kg IM/IV |
| | | **Clindamycin** (or) | 600 mg IM/IV | 20 mg/Kg IM/IV |

* or other first or second gen cephalosporin in equivalent adult or paediatric dosage

** Cephalosporins should not be used in an individual with a history of anaphylaxis, angioedema or utricaria with **Penicillin** **or** **Ampicillin.** In such cases, vancomycin may be used (adults: 15 to 20 mg/kg IV, not to exceed 2 g per dose; children: 15 mg/kg IV to a maximum dose of 1 g).

Antibiotics should be administered 30 to 60 minutes prior to the procedure (an exception is intravenous vancomycin, which should be administered 120 minutes prior to the procedure. If antibiotic prophylaxis is inadvertently not administered prior to the dental procedure, it may be administered up to two hours after the procedure

**Recommendations for Respiratory Tract , GI or GU Tract Procedures**

- The administration of prophylactic antibiotics solely to prevent endocarditis is **not recommended** for patients who undergo who undergo GU or GI and respiratory tract procedures

## 8.3A) Recommended post exposure prophylaxis for exposure to hepatitis B virus[13]

<table>
<tr><th rowspan="2">Health Care Personnel (HCP) Status$</th><th colspan="2">Post Exposure Testing</th><th colspan="2">Post Exposure Prophylaxis</th><th rowspan="2">Post Vaccination Serologic Testing †</th></tr>
<tr><th>Source Patient (HBsAg)</th><th>Health Care Personnel (anti-HBs)</th><th>HBIG*</th><th>Vaccination</th></tr>
<tr><td>Documented responder§ after complete series (≥ 3 doses)</td><td colspan="5">No Action Needed</td></tr>
<tr><td rowspan="2">Documented Non responder¶ after 6 doses</td><td>Positive / Unknown</td><td>_____**</td><td>HBIG x 2 Separated by 1 Month</td><td>----</td><td>No</td></tr>
<tr><td>Negative</td><td colspan="4">No Action Needed</td></tr>
<tr><td rowspan="3">Response unknown after 3 doses</td><td>Positive / Unknown</td><td>< 10 mIU/mL**</td><td>HBIG x 1</td><td rowspan="2">Initiate revaccination</td><td rowspan="2">Yes</td></tr>
<tr><td>Negative</td><td>< 10 mIU/mL</td><td>None</td></tr>
<tr><td>Any result</td><td>≥ 10 mIU/mL</td><td colspan="3">No Action Needed</td></tr>
<tr><td rowspan="2">Unvaccinated / Incompletely Vaccinated or Vaccine Refusers</td><td>Positive / Unknown</td><td>_____**</td><td>HBIG x 1</td><td rowspan="2">Complete Vaccination</td><td rowspan="2">Yes</td></tr>
<tr><td>Negative</td><td>_____</td><td>None</td></tr>
</table>

**$** Persons who have previously been infected with HBV are immune to reinfection and do not require post exposure prophylaxis

***** HBIG should be administered intramuscularly as soon as possible (upto 48 hours) after exposure when indicated. The effectiveness of HBIG when administered >7 days after percutaneous, mucosal, or nonintact skin

exposures is unknown. HBIG dosage is 0.06 mL/kg.

† Should be performed 1–2 months after the last dose of the HepB vaccine Series (and 4–6 months after administration of HBIG to avoid detection of Passively administered anti-HBs) using a quantitative method that allows detection of the protective concentration of anti-HBs (≥10 mIU/mL).

§ A responder is defined as a person with anti-HBs ≥10 mIU/mL after ≥3 Doses of HepB vaccine.

¶ A nonresponder is defined as a person with anti-HBs <10 mIU/mL after ≥6 doses of HepB vaccine.

** HCP who have anti-HBs <10mIU/mL, or who are unvaccinated or incompletely vaccinated, and sustain an exposure to a source patient who is HBsAg-positive or has unknown HBsAg status, should undergo baseline testing for HBV infection as soon as possible after exposure, and follow-up testing approximately 6 months later. Initial baseline tests consist of total anti-HBc; testing at approximately 6 months consists of HBsAg and total anti- HBc.

## 8.3 B) Recommended post exposure prophylaxis for exposure to hepatitis C virus[13, 14, 40]

- HCV PEP with Direct Acting Antiviral (DAA) therapy is not routinely recommended.
- The risk for transmission of HCV from percutaneous exposures (0.2%) and mucocutaneous exposures (0%) is low (4) and in most situations does not justify giving DAAs to several hundred exposed HCP because of potential side effects; furthermore, efficient duration of PEP has not been established.

- DAA therapy is highly efficacious in eradicating acute and chronic infections therefore, new HCV infections should be identified early and treated, and the strategy of testing and treating if transmission occurs is recommended.
- **Follow up testing should be performed:**

  Anti-HCV seroconversion typically occurs 8 to 11 weeks after exposure. Nucleic acid testing for HCV RNA can be considered for persons who are immunocompromised or have liver disease since delayed seroconversion have been documented among persons with immunosuppression. Nucleic acid testing for HCV should also be used for those who were anti-HCV positive/HCV RNA negative at baseline.

  Three to six weeks after the exposure – nucleic acid testing for HCV RNA should be performed.

  Four to six months after the exposure – anti-HCV testing is suitable for evaluating the HCV status at this time point, with follow up nucleic acid testing for HCV RNA testing if positive.

  Early detection and treatment of acute HCV infection using sequential quantitative HCV RNA PCR is recommended.

  **To consider as acute HCV infection and initiate treatment in the following situations:**

1. If HCV RNA is positive (with rising RNA titres) and HCV Ab negative.
2. If initial HCV RNA is negative and HCV Ab is positive, recheck HCV RNA at 12 weeks is positive.
3. Initial HCV RNA and HCV Ab positive with fluctuating RNA titres (>1 log on recheck).

   If treatment is deferred continue to monitor HCV RNA to evaluate for clearance.

## 8.3 C) Recommended Occupational post exposure prophylaxis for exposure to HIV[13, 16,17]

**Establish eligibility for PEP:**

PEP must be initiated as soon as possible after occupational exposure like **Needle Stick injury**, preferably within 2 hours, but certainly within 72 hours. Two main factors determine the risk of infection: the nature of exposure and the status of the source patient.

**Counselling for PEP:**

Exposed persons (clients) should receive appropriate information about what PEP is about and the risk and benefits of PEP in order to provide informed consent.

**Prescribe PEP[16,17]:**

As PEP for HIV has its greatest effect if begun within 2 hours of exposure, it is essential to act immediately. There is little benefit if more than 72 hours have lapsed but PEP can still be used if the healthcare worker presents after 72 hours of exposure. The prophylaxis needs to be continued for 28 days.

**NACO's recommended PEP regimens (2021) are tabulated in Table[17]**

| Exposed Person | Preferred Regimen for PEP Drugs and Dosages | Alternate Regimen (If the referred Regimen is not available or Contraindicated) |
|---|---|---|
| **Adolescents and Adults (>10 years of age and >30 kg weight)** | Tenofovir (300 mg) + Lamivudine (300 mg) + Dolutegravir (50 mg) (FDC: One tablet OD) | Tenofovir (300 mg) +Lamivudine (300 mg), (FDC: One tablet OD) +Lopinavir (200 mg)/Ritonavir (50 mg) (two tablets BD), OR, Tenofovir (300 mg) +Lamivudine (300 mg) +Efavirenz (600 mg) (FDC: One tablet OD) |
| **Children (>6 years of age and >20 kg weight)** | Zidovudine + Lamivudine (Dosage as per weight band) +Dolutegravir (50 mg) (One tablet OD) | If Hb <9 g/dl: Abacavir + Lamivudine (dosage as per weight band) +, Dolutegravir (50 mg), (One tablet OD) |
| **Children (<6 years of age or <20 kg weight)** | Zidovudine + Lamivudine +Lopinavir/ritonavir (Dosage as per weight band) | If Hb <9 g/dl: Abacavir + Lamivudine + Lopinavir/ritonavir (Dosage as per weight band) |
| • The first dose of PEP should be administered immediately (within 2 hours) and preferably within 72 hours of exposure.<br>• Healthcare personnel should be counselled about the safety of the PEP drugs.<br>• Duration of PEP is 28 days, regardless of PEP regimen. | | |

In case of highly treatment-experienced source, initiate first dose as per above guidelines and expert opinion should be sought urgently by phone/e-mail from CoE/ART Plus centre.

In cases of sexual assault, the same principles need to be followed in adults and adolescents. For children who have suffered assault and must be administered PEP, the dosage should be as perage and weight bands and haemoglobin levels.

In all cases, appropriate and adequate counselling must be provided regarding possible side effects, adherence and follow-up protocol.

Adherence information is essential with psychological support. More than 95% adherence is important to maximize the efficacy of the medication in PEP.

**Dual drug regimen should not be used any longer in any situation for PEP**.

## 8.4. A. Antimicrobial prophylaxis and surveillance in HSCT patients[1, 33-39]

| **HSCT pre-engraftment** | | |
|---|---|---|
| Surveillance culture | Fecal surveillance and throat swab cultures not recommended. | These tests detect colonisation with MDR GNBs, VRE and MRSA. However, this microbial flora is dynamic and does not necessarily translate to invasive disease. |
| Antibiotic prophylaxis | No routine antibiotic prophylaxis recommended | |
| Antifungal prophylaxis | Routine (against yeast) : Fluconazole 400mg OD with renal dose adjustment in case of AKI/CKD | Indicated in all allogenic HSCT (unless mold active agents are used); may be considered in autologous HSCT<br><br>Initiated along with conditioning regimen<br><br>May be administered as IV or oral (including nasogastric tube)<br><br>Alternatives for intolerance, ADRs, DDIs : Echinocandins, other triazoles<br><br>Duration of primary prophylaxis:<br>-Autologous : Till engraftment<br>-Allogenic : Till engraftment; may be continued upto D+75 |

| | | |
|---|---|---|
| | Active against molds:<br>Posaconazole, Voriconazole<br><br>Emerging evidence for Isavuconazole<br><br><br><br><br>Dosing :<br>Posaconazole : 300mg P/O or IV Q12h on day 1 as loading dose followed by 300mg OD from day 2 onwards<br>(trough levels->0.5 µg/mL)(1)<br><br>Voriconazole : 400mg BD P/O or IV Q12h on day 1 as loading dose followed byb 200mg Q12h from day 2 onwards<br>(trough levels->1-2microgram/ml)(2)<br><br>Isavuconazole : 200mg Q8h for 6 doses (D1-2) followed by 200mg OD from day 3 onwards | Indicated for high risk allogeneic HSCT with following scenarios:<br>-Centres with >6% rate of IPA<br>-Acute Myeloid Leukemia undergoing induction therapy.<br>-Anticipated delayed engraftment (>28 days)<br>-Prolonged neutropenia prior to transplant<br>-With GVHD/pre-transplant h/o IFI:<br>Till substantial immunosupressants are no longer required<br>Initiated along with conditioning regimen<br><br>May be administered as IV or per oral (including nasogastric tube)<br><br>Ideal to assess trough levels if TDM* facilities are available.<br><br>Alternatives for breakthrough, intolerance, ADRs, DDIs: Previously unused triazole, Amphotericin B, Echinocandins or combinations of these agents |
| Antiviral prophylaxis | Acyclovir, Valacyclovir<br><br>Dosing :<br>Acyclovir :<br>P/O : 800mg BD (VZV)<br>P/O : 400mg BD (HSV)<br>IV : 5mg/kg Q12h<br><br>Valacylcovir :<br>P/O : 500mg BD<br><br>*Both require renal dose adjustment | Pre-engraftment for prevention of HSV<br>Post engraftment for prevention of VZV<br>Not active against CMV<br><br>Initiated along with conditioning regimen<br><br>May be administered as IV/Oral<br><br>Continued in the post transplant period upto 6 months in autologous and 1 year for allogeneic BMT; may be extended in case of GVHD |

| **HSCT post engraftment at discharge.** | | |
|---|---|---|
| Antibiotic prophylaxis | **Cotrimoxazole**<br><br>Dosing : 1 double strength (960 mg) tablet, daily/ twice weekly | Initiated post-engraftment at discharge<br>Prevents/reduces risk of Toxoplasma, Nocardia, Listeria monocytogenes, Pneumocystis carinii, Isospora belli, common bacterial pathogens of respiratory and urinary tract<br><br>Recommended for all autologous and allogenic HSCT recipients<br><br>Duration :<br>1. Autologous HSCT :<br>3-6 months<br>2. Allogenic HSCT:<br>—Without GVHD : 6-12 months<br>—With GVHD : Till substantial dose of immunosupressants are no longer required |
| | Oral penicillin<br><br>Dosing : 400 mg orally twice daily | Duration of prophylaxis :<br>Uncertain<br>Usually upto 1 year post transplant; may be extended till substantial immunosupressants are no longer required<br><br>Alternatives :<br>Amoxicillin 500mg BD<br>Cephalexin 250mg BD<br>Azithromycin 250mg OD<br><br>Also recommended in patients with<br>1. 1. H/O splenectomy<br>2. Functional asplenia<br>3. Failure to receive Pneumococcal vaccine/anticipated poor response |

| | | |
|---|---|---|
| Antifungal prophylaxis | Routine (against yeast) : Fluconazole<br><br>Active against molds: Posaconazole, Voriconazole<br><br>Emerging evidence for Isavuconazole | Indications, dosing, formulations and alternatives and as mentioned above<br><br>Duration of prophylaxis :<br>-Allogenic : Till engraftment; may be continued upto D+75<br><br>Indications, dosing, formulations and alternatives and as mentioned above<br><br>Duration of prophylaxis :<br><br>-Without GVHD : Till engraftment; may be continued upto D+75<br><br>-With GVHD/pre-transplant h/o IFI: Till substantial immunosupressants are no longer required |
| Antiviral Prophylaxis for CMV | Letermovir<br>P/O: 480mg OD upto day 100 | -Routine duration : D+100 |
| CMV surveillance | Autologous HSCT : Not recommended<br><br>Allogenic HSCT :<br><br>1. High risk patients : D-/R+, D+/R+, D+/R-<br><br>2. 2. Low risk patients : D-/R- | -Initiation : At engraftment<br>-Frequency: Weekly<br>-Routine duration : D+100<br>-Extended duration : Till D+365 in cases with<br>a. CMV viremia in first 100 days<br>b. Mismatched/matched unrelated transplant<br>c. GVHD with substantial immunosuppression<br><br>-Initiation : At engraftment<br>-Frequency: Weekly/fortnightly<br>-Routine and extended duration as |

| | | |
|---|---|---|
| CMV pre-emptive therapy | Preferred agents:<br><br>-Ganciclovir<br>Dosing: 5mg/kg IV Q12h<br><br>-Valganciclovir<br>Dosing: 900mg P/O BD<br><br>-Foscarnet<br>Dosing: 60mg/kg IV Q8h<br><br>Alternative:<br><br>Maribavir<br>-In case of neutropenia or renal insufficiency<br>-Dosing: 400mg P/O BD | mentioned above<br><br>Indications for pre-emptive therapy:<br>-No established cut off<br>-Commonly employed threshold for pre-emptive therapy: 500-1000 copies/mL<br><br>Monitoring on therapy:<br>-Weekly VL (PCR)<br><br>Duration:<br>-Minimum: 2 weeks<br>-Definitive: Till VL is no longer detectable |

## 8.4.B. Recommended Vaccines and Timing Post Allogeneic HCT in All Recipients

| Timing | Vaccine | Recommendation | Schedule | Comment |
|---|---|---|---|---|
| | | | | |
| **3 – 6 months** post-transplant | COVID-19 vaccine | All HCT recipients | 2 or 3 dose | |
| | Pneumococcal vaccine | All HCT recipients | 3 doses of PCV13 are given 1-2 months apart.<br><br>4th dose is given at least 6 months after the 3rd dose and at least 12 months after transplant (whichever is later). | Fourth dose:<br>▪ Patients without GVHD: PPSV23<br>▪ Patients with GVHD: PCV13 ( due to poor response to PPSV) |
| | | | | |
| **6 – 12** | Inactivated Influenza | All HCT recipients | 1 dose annually<br><br>* Can be given as early as 3 | ▪ If given early, a second dose should be administered at |

| | | | | |
|---|---|---|---|---|
| **months**<br><br>Post-transplant | vaccine | | months in the setting of a community outbreak or transplant happening before peak season. | least 4 weeks after initial dose.<br>▪ The high-dose vaccine elicits higher protective antibody titers compared with standard-dose IIV. |
| | Tetanus, diphtheria, and pertussis vaccine (DTaP) | All HCT recipients | 3 doses, 1-2 months apart<br><br>* Low dose pertussis and diphtheria vaccines are poorly immunogenic. | ▪ An alternative schedule includes 1 dose of Tdap followed by either 2 doses of DT or Td, with all doses spaced 1-2 months apart. |
| | Hib-conjugate vaccine | All HCT recipients | 3 doses, 1-2 months apart | |
| | Inactivated polio vaccine (IPV) | All HCT recipients | 3 doses, 1-2 months apart | ▪ Post-vaccination serology can be checked 4-5 years after vaccination for those at higher risk of exposure |
| | Hepatitis B vaccine | All HCT recipients | 3 doses (0, 1, and 6) – use high dose 40 mcg | ▪ Test serology ≥1 month after the 3rd dose to assess the response to vaccine. If anti-HBs titers < 10mIU/mL, an additional series of 3 vaccines to be given. |
| | Recombinant Zoster Vaccine | All HCT recipients | 2 doses, 2-6 months apart<br><br>(minimum interval = 4 weeks) | ▪ Administer the first dose of RZV at least a month prior to cessation of antiviral prophylaxis.<br>▪ Perform VZV serology at ≥ 24 months and if antibodies negative, give 2 doses of LAVV. |

- DTaP, IPV, Hep B, and Hib are available as a hexavalent vaccine (Hexaxim) which is administered intramuscularly as 3 dose series, 1-2 months apart. Booster dose of hexaxim 1 year later can be considered.

## 8.4. C. Recommended Vaccines and Timing Post Allogeneic HCT in Selected Recipients

| Timing | Vaccine | Indications | Schedule | Comment |
|---|---|---|---|---|
| **6 – 12 months**<br>Post-transplant | Hepatitis A vaccine | If risk factors are present (eg, CLD due to GVHD or viral hepatitis, travel to endemic areas) | 2 doses, 6 months apart | ▪ Poor seroconversion rate |
| | Human papillomavirus vaccine (4vHPV or 9vHPV) | All recipients aged 12-26 years, regardless of HPV history | 3 dose (0, 1-2, 6 months) | ▪ Better responses are obtained at >12 months after transplant |
| | Meningococcal conjugate vaccine (MCV-4) | All recipients aged 11 to 18 years or if other risk factors are present (eg, asplenia, student living in campus, residing in or traveling to areas of hyperendemicity or epidemicity) | 2 doses, 2 months apart | ▪ Immunogenicity of a single dose of MenACWY conjugate vaccine is poor. |
| | | | | |
| **≥ 24 months**<br>Post-transplant | MMR | HCT recipients who meet **all** the following criteria for administration of live vaccines:<br>▪ Measles seronegative \| VZV seronegative<br>▪ No active GVHD and disease in remission<br>▪ No systemic immunosuppressive therapy for 12 months including monoclonal antibodies<br>▪ No IVIG in last 3-8 months (the "2-1-8" mnemonic) | Single dose OR<br>2 doses, 6 months apart | ▪ Lack of serological testing should not preclude vaccination as long as other criteria are met. |
| | Varicella vaccine | | Single dose OR<br>2 doses, 2 months apart | ▪ VZV serology should be performed for all recipients (including those who received Shingrix) at 24 months. |
| | Yellow fever vaccine | HCT recipients who cannot avoid traveling to endemic areas and have no active GVHD, and is not on immunosuppression | One dose at least 10 days before travel | |

**Vaccinations Following CAR-T**

1. Patients should demonstrate immune reconstitution prior to vaccination, defined as CD4+ >0.2 × 109/L, CD19 or CD20+ B cells >0.2 × 109/L.
2. Patients should not be receiving concomitant immunosuppressive treatment including cytotoxic chemotherapy, systemic corticosteroids, T-cell-depleting or anti-lymphocyte agents, or IVIg within the previous 2 months.
3. IIV ideally should be given 2 weeks before lymphodepleting chemotherapy or after 3 months' post CAR-T therapy.
4. Other non-live vaccines should be administered no sooner than 6 months after completion of therapy
5. Live vaccines should be different until at least 1 year following CART and require demonstration of immune reconstitution.

## 8.5. Opportunistic Infection Prophylaxis [17]

### 8.5 i) Co-trimoxazole Prophylaxis (CPT)[17]

Routine prophylaxis with **Co-trimoxazole** is provided under the national programme. CPT is efficacious against several organisms, including Toxoplasma, PCP and several organisms causing diarrhoea in HIV infected persons. Recent evidence has shown that CPT helps prevent morbidity and mortality in adults with both early and advanced HIV disease.

Under the national programme,

**Primary CPT may be initiated in the following scenarios**:

If CD4 is not available (or result pending): WHO clinical stage 3 and 4

If CD4 is available: HIV infected adults with CD4 <200 cells/$mm^3$ or CD4 <350 cells/$mm^3$ with symptomatic or WHO clinical stage of 3 or 4 irrespective of CD4

**Secondary CPT may be initiated in the following scenarios**:

For all patients who have completed successful treatment for PCP until CD4 is >200

**Timing the initiation of Co-trimoxazole in relation to initiating ART**:

Start **Co-trimoxazole** prophylaxis first.

Start ART subsequently as early as possible if the patient can tolerate **Co-trimoxazole** and has no symptoms of allergy (rash, hepatotoxicity)

Meanwhile, make use of the time for adherence and treatment preparation Dosage of **Cotrimoxazole** in adults and adolescents

**Dosage:**

One double-strength tablet daily or two single-strength tablets once daily– total daily dose of 960 mg (800 mg SMZ + 160 mg TMP)

**Cotrimoxazole for pregnant women**

Women who fulfil the criteria for CPT should continue on it throughout pregnancy.

If a woman requires CPT during pregnancy, it should be started regardless of the stage of pregnancy Breastfeeding women should continue CPT where indicated

Dapsone 100 mg per day can be considered in patients with sulpha allergy or **Co-trimoxazole** desensitization may be attempted but not in patients with a previous severe reaction to CTX or other sulpha-containing drugs

**Monitoring**:

No specific laboratory monitoring is required in patients receiving **Co-trimoxazole**

**When to stop prophylaxis (Co-trimoxazole or dapsone) in patients on ART**:

If CD4 count >200 for at least 6 months *and* If patient is on ART for at least 6 months, is asymptomatic and well

If CPT is started at CD4 levels between 200–350 cells/mm3: CD4 counts should have increased, patient is on ART for at least 6months, is asymptomatic and well; before CPT is stopped.

NACO provides CD4 assessment free of cost to all patients as per medical eligibility.

**8.5 ii) Prophylaxis for CMV retinitis**:

-Primary prophylaxis-Not indicated

Secondary: oral Valganciclovir

Discontinue secondary prophylaxis If CD4 count >100

**8.5 iii) Prophylaxis for Cryptococcus meningitis**

-Primary prophylaxis -Not indicated

Secondary: fluconazole

Discontinue secondary prophylaxis If CD4 count >100

**8.5 iv)_Prophylaxis for Oral and oesophageal candidiasis**

Primary Prophylaxis-Not indicated

Secondary Prophylaxis-Not applicable

**8.5 v) Prophylaxis for NTM**

Primary Prophylaxis-Not indicated

Secondary Prophylaxis-Not applicable

**8.5 v) Prophylaxis for Tuberculosis**

Primary Prophylaxis-Isoniazid and Rifapentine daily for 28 Days

Secondary Prophylaxis-Not applicable for recent therapy.

**Co-trimoxazole desensitization:**

If the patient reports a history of hypersensitivity to sulpha-containing drugs, start him/her on a desensitization regimen as an in-patient.

Desensitization can be attempted two weeks after a non-severe (grade 3 or less) **Co-trimoxazole** reaction which has resulted in a temporary interruption in the use of the drug.

**Co-trimoxazole** desensitization has been shown to be successful and safe in approximately 70% of patients with previous mild to moderate hypersensitivity.

Desensitization should not be attempted in individuals with a history of severe **Co-trimoxazole** or other sulphonamide reaction. If a reaction occurs, the desensitization regimen should be stopped. Once the patient recovers fully, dapsone at a dosage of 100 mg per day may be tried.

Some patients may be allergic to both **Co-trimoxazole** and dapsone. There are no other prophylaxis drug options in resource-limited settings.

**Protocol for Co-trimoxazole desensitization**

| **Step** | **Dosage** |
|---|---|
| Day 1 | 80 mg SMX + 16 mg TMP (2 ml oral suspension) |
| Day 2 | 160 mg SMX + 32 mg TMP (4 ml oral suspension) |
| Day 3 | 240 mg SMX + 48 mg TMP (6 ml oral suspension) |
| Day 4 | 320 mg SMX + 64 mg TMP (8 ml oral suspension) |
| Day 5 | One single-strength SMX-TMP tablet (400 mg SMX + 80 mg TMP) |
| Day 6 | Two single-strength SMX-TMP tablets or one double-strength tablet (800 mg SMZ + 160 mg TMP) |
| **Reference:** Guidelines on **Co-trimoxazole** prophylaxis for HIV-related infections among children, adolescents and adults in resource-limited settings: Recommendations for a public health approach. World Health Organization, 2006.<br>**Note:** **Co-trimoxazole** oral suspension contains 40 mg TMP + 200 mg SMX per 5 ml | |

# Chapter – 9: National Immunization Schedule

| Age | Vaccines Given |
|---|---|
| Birth | BCG, OPV-0 dose, Hepatitis B-Birth Dose |
| 6 Weeks | OPV-1, Pentavalent-1 (DPT, HiB, HBV), RVV-1, fIPV-1, PCV-1 |
| 10 Weeks | OPV-2, Pentavalent-2 (DPT, HiB, HBV), RVV-2 |
| 14 Weeks | OPV-3, Pentavalent-3 (DPT, HiB, HBV), RVV-3, PCV-2, fIPV-2 |
| 9-12 Months | MR-1, JE-1*, PCV-Booster |
| 16-24 Months | MR-2, JE-2*, DPT-Booster, OPV-Booster |
| 5-6 Years | DPT-Booster 2 |
| 10 Years | Td |
| 16 Years | Td |
| Pregnant Mother | Td-1, Td-2 or Td Booster** |

***JE in endemic districts only**

**** one dose if previously vaccinated within 3 years**

## Dose, Route of Administration of Vaccines in National Immunization Schedule

| Vaccine | When to give | Dose | Route | Site |
|---|---|---|---|---|
| **For Infants** | | | | |
| Bacilli Calmetti Guerin (BCG) | At Birth or as early as possible till one year of age | Upto 1 month-0.05 ml<br>After I month-0.1 ml | Intra Dermal | Left Upper Arm |
| Hepatitis B-<br>Birth Dose | At Birth or as early as possible within 24 hours | 0.5 ml | Intra muscular | Antero lateral side of mid thigh |
| Oral Polio Vaccine (OPV)-<br>O dose | At Birth or as early as possible within first 15 days | 2 drops | Oral | Oral |
| OPV-<br>1, 2 & 3- dose | At 6, 10, 14 Weeks (can be given till 5 Years of age) | 2 drops | Oral | Oral |
| Pentavalent<br>( DPT, HiB, HBV)<br>1, 2 & 3 | At 6, 10, 14 Weeks (can be given till one Year of age) | 0.5 ml | Intra muscular | Antero lateral side of mid thigh |
| Pneumococcal Conjugate Vaccine (PCV) | Two Primary doses at 6 & 14 weeks followed by Booster dose at 9-12 Months | 0.5 ml | Intra muscular | Antero lateral side of mid thigh |
| Rota Virus (RVV) | At 6, 10, 14 Weeks (can be given till one Year of age) | 5 drops (liquid vaccine) 2.5 ml (Lyophilized vaccine) | Oral | Oral |
| Inactivated Polio Vaccine (fIPV) | Two fractional dose at 6 & 14 weeks of age | 0.1 ml | Intra Dermal two fractional dose | Right Upper Arm |
| Measles Rubella (MR )<br>(1st dose) | 9 completed months-12 months (Measles can be given till 5 Years of age) | 0.5 ml | Sub Cutaneous | Right Upper Arm |
| Japanese Encephalitis (JE) - 1 | 9 completed months-12 months | 0.5 ml | Sub Cutaneous (Live attenuated Vaccine)<br><br>Intra muscular (Killed Vaccine) | Left Upper arm (Live attenuated Vaccine)<br><br>Anterolateral aspect of Mid thigh (killed vaccine) |

| | | | | |
|---|---|---|---|---|
| Vitamn-A (1st dose) | At 9 completed months with MR vaccine | 1 ml ( 1 Lakh IU) | Oral | Oral |
| **For Children** | | | | |
| Diphtheria, Pertusis & Tetanus (DPT) Booster-1 | 16-24 Months | 0.5 ml | Intra muscular | Antero lateral side of mid thigh |
| OPV Booster | 16-24 Months | 2 drops | Oral | Oral |
| MR-2 dose | 16-24 Months | 0.5 ml | Sub Cutaneous | Right Upper Arm |
| JE-2 dose | 16-24 Months | 0.5 ml | Sub Cutaneous (Live attenuated Vaccine) Intra muscular (Killed Vaccine) | Left Upper arm (Live attenuated Vaccine) Anterolateral aspect of Mid thigh (killed vaccine) |
| Vitamin-A (2nd to 9th dose) | 16-18 months, then one dose every 6 months upto the age of 5 years | 2 ml (2 Lakh IU) | Oral | Oral |
| Diphtheria, Pertusis & Tetanus (DPT) Booster-2 | 5-6 Years | 0.5 ml | Intra muscular | Upper Arm |
| Td | 10 Years & 16 Years | 0.5 ml | Intra muscular | Upper arm |
| **For Pregnant Women** | | | | |
| Td-1 | Early in Pregnancy | 0.5 ml | Intra muscular | Upper arm |
| Td-2 | 4 weeks after Td-1 | 0.5 ml | Intra muscular | Upper arm |
| Td-Booster | If received 2 TT/Td doses in a pregnancy within last 3 years | 0.5 ml | Intra muscular | Upper arm |

# Chapter – 10 Treatment guidelines for Malaria

**Doses of ACT based regimen[1, 20,21]:**

| **Artemether + Lumefantrine Based ACT** | | |
|---|---|---|
| **Body weight (kg)** | **Dose (mg) of artemether + lumefantrine given twice daily for 3 days** | |
| 5 to < 15 | 20 + 120 | |
| 15 to < 25 | 40 + 240 | |
| 25 to < 35 | 60 + 360 | |
| ≥ 35 | 80 + 480 | |
| **Artesunate + Amodiaquine Based ACT** | | |
| **Body weight (kg)** | **Artesunate + amodiaquine dose (mg) given daily for 3 days** | |
| 4.5 to < 9 | 25 + 67.5 | |
| 9 to < 18 | 50 + 135 | |
| 18 to < 36 | 100 + 270 | |
| ≥ 36 | 200 + 540 | |
| **Artesunate + Mefloquine Based ACT** | | |
| **Body weight (kg)** | **Artesunate + mefloquine dose (mg) given daily for 3 days** | |
| 5 to < 9 | 25 + 55 | |
| 9 to < 18 | 50 + 110 | |
| 18 to < 30 | 100 + 220 | |
| ≥ 30 | 200 + 440 | |
| **Dihydroartemisinin + Piperaquine Based ACT** | | |
| **Body weight (kg)** | **Dihydroartemisinin + piperaquine dose (mg) given daily for 3 days** | |
| 5 to < 8 | 20 + 160 | |
| 8 to < 11 | 30 + 240 | |
| 11 to < 17 | 40 + 320 | |
| 17 to < 25 | 60 + 480 | |
| **Artesunate + Sulfadoxine / pyrimethamine Based ACT** | | |
| **Body weight (kg) /Colour of Blister pack** | **Artesunate dose given daily for 3 days (mg)** | **Sulfadoxine / pyrimethamine dose (mg) given as a single dose on day 1** |
| 5 to < 10-(Pink) | 25 mg | 250 / 12.5 |
| 10 to < 25 –(Yellow) | 50 mg | 500 / 25 |
| 25 to < 50 –(Green) | 100 mg | 1000 / 50 |
| ≥ 50 –(White) | 200 mg | 1500 / 75 |
| | | |

## Chloroquine Sensitive Plasmodium vivax Treatment[21]:

**Adult Dose**: The Total dose of **chloroquine** is 25 mg/kg body weight divided over three days-i.e.10 mg/kg on day 1, 10 mg/kg on day 2 and 5 mg/kg on day 3. **Primaquine** is given in a dose of 0.25 mg/kg daily for 14 days

| **Age Group in Years** | **Day 1** | | **Day 2** | | **Day 3** | | **Day 4-14** |
|---|---|---|---|---|---|---|---|
| | CQ (150 mg base) | PQ (2.5 mg) | CQ (150 mg base) | PQ (2.5 mg) | CQ (150 mg base) | PQ (2.5 mg) | PQ (2.5 mg) |
| **< 1** | ½ | 0 | ½ | 0 | ¼ | 0 | 0 |
| **1-4 Yrs** | 1 | 1 | 1 | 1 | ½ | 1 | 1 |
| **5-8 Yrs** | 2 | 2 | 2 | 2 | 1 | 2 | 2 |
| **9-14 Yrs** | 3 | 4 | 3 | 4 | 1 ½ | 4 | 4 |
| **>14 Yrs** | 4 | 6 | 4 | 6 | 2 | 6 | 6 |

## Treatment of Malaria [1, 20,21]:

| Types | P.falciparum | P.vivax, P. ovale, P. malariae or P. knowlesi |
|---|---|---|
| **Uncomplicated Malaria** (except pregnant women in their first trimester) | ACT (AL) regimens should provide 3 days' treatment with an artemisinin derivative. | **a)** In areas with chloroquine-susceptible infections, treat adults and children with either chloroquine or ACT.<br>**b)** In areas with chloroquine-resistant infections, treat adults and children with malaria with ACT |
| **Uncomplicated Malaria for** pregnant women in their first trimester | **Artemether lumefantrine** (initial dose, followed by the second dose 8 hours later, then 1 dose orally twice daily for the following two days) (or)<br>**Quinine** (10 mg/kg tid)+ **Clindamycin** (20 mg base/kg/day (up to 1.8 grams) orally divided tid for seven days | **a)** In areas with chloroquine-susceptible infections, treat with chloroquine.<br>**b)** In areas with chloroquine-resistant infections, treat with Artemether-lumefantrine |
| **To prevent relapse** (except pregnant women, infants aged < 6 months, women breast feeding infants aged < 6 months, and people with G6PD deficiency) | Primaquine 45mg P.O×1dose after completion of Artesunate treatment | 14-day course of primaquine |
| **To prevent relapse in people with G6PD deficiency** | | giving primaquine base at 0.75 mg/kg body weight once a week for 8 weeks, with close medical supervision for potential primaquine-induced haemolysis |
| **To prevent relapse in Pregnant and breastfeeding women** | | consider weekly chemoprophylaxis with chloroquine until delivery and breastfeeding are completed, then, on the basis of G6PD status, treat with primaquine to prevent future relapse |

| | |
|---|---|
| **Severe Malaria** (including infants, pregnant women in all trimesters and lactating women) | Artesunate 2.4 mg/kg body weight IV/IM at admission, then at 12 and 24 h, then once a day for at least 24 hours or clinically stable followed by full course of oral ACT for 3 days |
| **Patients co-infected with HIV** | To avoid artesunate + SP if they are being treated with **Co-trimoxazole**, |

# Chapter – 11 Treatment of Tuberculosis as per NTEP guidelines

| Type of TB | Type of Regimen[18] | Drugs | Extension Criteria |
|---|---|---|---|
| **Drug susceptible TB** | DS-TB Regimen | 2 months H,R,E,Z<br>4 months H,R,E | In certain EP TB cases (like TB Spine, Bone TB, etc) in consultation with the specialist |
| **H Mono / Poly DR-TB** | H mono/poly DR-TB regimen | 6 months Lfx, R,E,Z | Extension for 3 months in patients having: Extensive disease, uncontrolled comorbidity, Extra Pulmonary TB, Smear positive at the end of 4th month |
| **MDR/RR and XDR TB** | Shorter oral Bedaquiniline-containing MDR/RR-TB regimen BPaLM | Bdq, Pa, Lzd, Mfx | Duration can be extended from 26-39 weeks |
| | 9-11month shorter oral MDR/RR-TB regimen | (2) Lzd (4-6) Lfx Cfz Z E Hh (6-9) Bdq (5) Lfx Cfz Z E (linezolid based)<br>(4-6) Lfx Cfz Eto Z E Hh (6-9) Bdq (5) Lfx Cfz Z E )(ethionamide based) | |
| | **18-20 months longer oral M/XDR-TB regimen** | (6 or longer) Bdq (18-20) Lfx Lzd Cfz Cs | If the 5m/4m culture report is negative Linezolid tapered to 300 mgs |
| All drug resistant (MDR) TB to be referred to nodal DR-TB centre.<br>The decisions for enrolment on the BPaLM or 9-11 month shorter MDR/ RR-TB regimen or 18month longer M/ XDR-TB regimen will be made by the nodal DR-TB centre (NDR-TBC) or district DR-TB centre (DDRTBC) in consultation with respective N/DDR-TBC committee, as deemed necessary, based on the results of the molecular and/ or LC-DST (a single breakpoint concentration based for FQ) for second-line anti-TB drugs (SLD) for individual patient and the eligibility criteria. | | | |
| **TB infection** | TB preventive treatment | 6 H ( 6months daily H monotherapy) | |
| | | 3 HP ( 3 months weekly P & H-12 dosages) | |
| | | 3 HR ( 3 months of isoniazid and rifampicin daily) | |

Bdq-Bedaquiline,

Cfz-Clofazimine,

CP-Continuation Phase,

Cs-Cycloserine,

Dr-TB-drug Resistant TB

DS-TB-drug Sensitive TB

E-Ethambutol,

Eto-Ethionamide,

FQ-Fluoroquinolones,

H-Isoniazid,

$H^h$-High dose Isoniazid

IP-Intensive Phase

Km/Am-Kanamycin/**Amikacin**

Lfx-**Levofloxacin**

Lzd-**Linezolid**,

MDR-Multi Drug Resistance

$Mfx^h$-High dose **Moxifloxacin**,

P-Rifapentin,

R-**Rifampicin**,

RR-**Rifampicin** Resistance

XDR-Extensively Drug resistant, Z-Pyrazinamide

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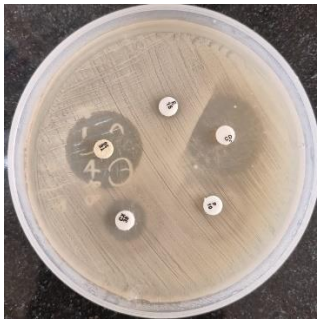
**PHOTO DESCRIPTION**



**Staph aureus (MRSA)** showing

Erythromycin-**Resistant**, Clindamycin **–"D"** shape near Erythromycin---**Induced Clindamycin Resistance**

**Photo Courtesy-Madras Medical College**

**Elizabethkingia meningoseptica** -A GNB showing

E test strip Vancomycin **Sensitive**

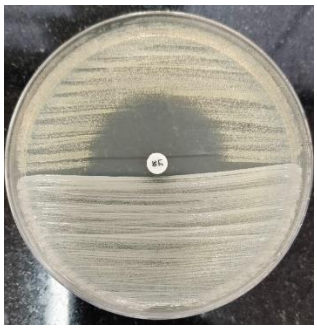
**Source: Dr.B.Appalaraju, MD, Coimbatore**

**Bergeyella zoohelcum** -A GNB showing

Penicillin-**Sensitive**

**Source: Dr.B.Appalaraju, MD, Coimbatore**

**(with permission)**

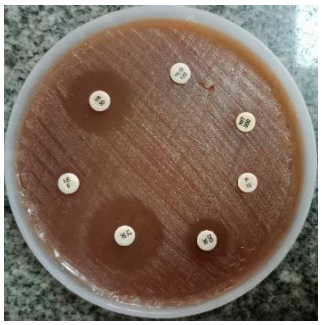


**Staph hemolyticus** showing Linezolid-Resistant

(**Control**-ATCC Staph aureus in the upper half of plate)

**Source: Dr.B.Appalaraju, MD, Coimbatore**

**(with permission)**

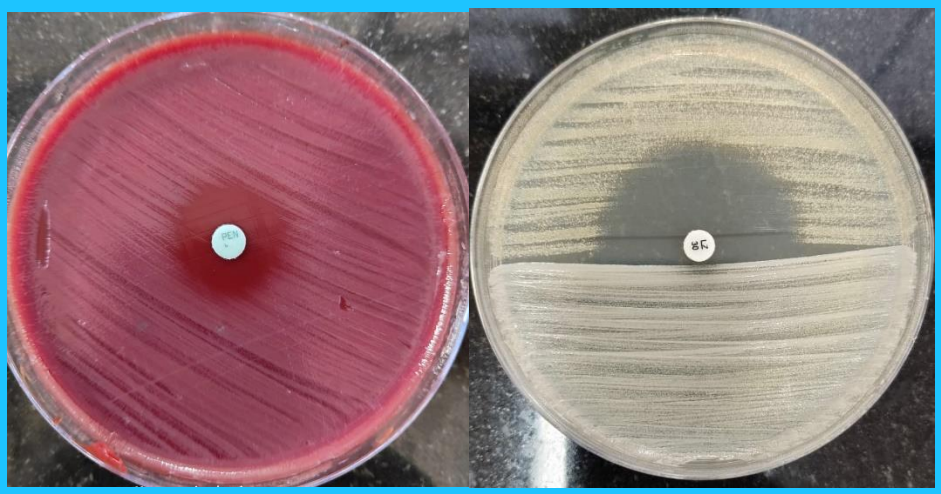


**Enterococcus faecium** showing

Vancomycin, Linezolid-**Sensitive**,

Penicillin, High level Gentamicin-**Resistant**

**Photo Courtesy-Stanley Medical College**



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