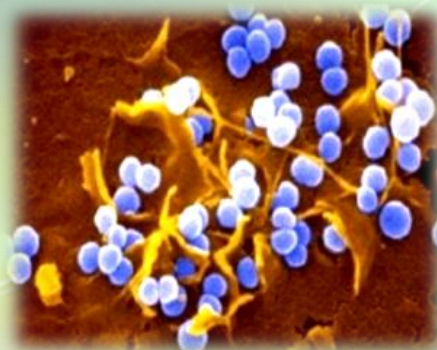




National Treatment Guidelines for Antimicrobial Use in Infectious Diseases



Version 1.0 (2016)

NATIONAL CENTRE FOR DISEASE CONTROL
Directorate General of Health Services
Ministry of Health & Family Welfare
Government of India

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Foreword

Antimicrobial resistance in disease pathogens has become a matter of great public health concern globally including in our Country. The factors responsible for this are widespread use and availability of practically all the antimicrobials across the counter meant for human as well as animal consumption. Though, there are definite policies/guidelines for appropriate use of antimicrobials at national level in specific national health programmes being run in the Country e.g. Revised National Tuberculosis Control Programme (RNTCP), National AIDS Control Programme, National Vector Borne Disease Control Programme, etc, the same are not available for other diseases /pathogens of public health importance, like Enteric fever, Diarrhoeal disease, Respiratory infections, etc., to name a few.

I am happy to note that the National Centre for Disease Control (NCDC) is bringing out a publication on **National Antimicrobial Use Guidelines for Infectious Diseases**, which will pave the way for rationalising the use of antimicrobials in the health care facilities in the Country, thereby reducing the development of antimicrobial resistance.

NCDC is also coordinating the national programme on containment of antimicrobial resistance in the Country and these guidelines are a timely and appropriate step in this direction. I hope that the clinicians in our Country, both in the public as well as private sector, would use these guidelines to the maximum for the benefit of the patients.

I congratulate NCDC and all the contributors who have worked tirelessly for preparing this document.



(Jagat Prakash Nadda)

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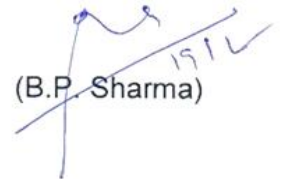


Message

Global containment of antimicrobial resistance has so far been based on two broad strategies i.e. antimicrobial stewardship and hospital infection control. The race against time to develop newer antimicrobials can never be won unless we develop antimicrobial resistance containment policies. The need of the hour is a guarded approach to the use of antimicrobials to prevent resistance. Combating and preventing the growing antimicrobial resistance in the World and in India require all stakeholders to come together and work towards developing appropriate methodology.

Recent studies indicate a very high use of antibiotics in the community in our country, most of which is unwarranted. It is indeed a pleasure to see the experts from various disciplines of medical science coming together to prepare the "National Antimicrobial Use Guidelines for Infectious Diseases" for our country. Such guidelines will definitely help to restrict inappropriate use of antimicrobial agents, optimize selection, dose, route and duration of treatment for best outcomes, minimising detrimental adverse events, excessive costs and most importantly emergence of resistance.

I congratulate NCDC and the entire team for their effort to bring out these guidelines on antimicrobial use, which is the need of the hour. I hope, this document will be beneficial to all the stake-holders including physicians, surgeons and other specialists, both in public and private sector.


(B.P. Sharma)

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दिनांक/Dated.....

MESSAGE

Emergence of antimicrobial resistance in pathogens has become a matter of great public health concern. Antimicrobial resistance is well recognised as a global threat to human health. Infections caused by antimicrobial-resistant microorganisms in hospitals are associated with increased morbidity, mortality and healthcare costs. Resistance has emerged even to newer and more potent antimicrobial agents like carbapenems and colistin. Selection and spread of resistant microorganisms in the presence of antimicrobials is facilitated by irrational use of drugs, self-medication & misuse of drugs.

It is estimated that 50% or more of hospital antimicrobial use is inappropriate. There is a need for increased education and awareness about antimicrobial resistance among the public and health-care professionals. In this regard, NCDC under the national programme on containment of antimicrobial resistance has prepared a very useful document i.e National antimicrobial use guidelines for common infectious diseases in the country. I really appreciate the mammoth efforts put in by the group of experts comprising clinicians, microbiologists and infectious disease specialists both from the public as well as the private sector of the country who have given their valuable input for the document. I hope that this effort would bring the desirable effects in bringing down the AMR burden in the country.

I wish the NCDC team a great success in disseminating this document widely across the country.


(Dr. Jagdish Prasad)



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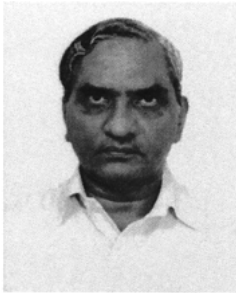
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ACKNOWLEDGEMENT


Antimicrobial resistance (AMR) has emerged as increasingly worrisome situation globally leading to increased morbidity, mortality and health care cost. Similarly in India, it is an important public health issue which needs prioritization as it has socio-economic impact.

Although many disease specific treatment guidelines have already been developed by different national health programmes for TB, Malaria, HIV/AIDS etc; there was a felt need to develop national treatment guidelines for use of antimicrobials in infectious diseases. Judicious use of antimicrobials by health professionals will contribute substantially in preventing emergence of AMR.

The Ministry of Health & Family Welfare has launched 'National Programme for Containment of AMR under 12th Five Year Plan (2012-17), one of the key activities under the programme is to promote the rational use of antimicrobials. The evidence-based National Treatment Guidelines are aimed at enhancing appropriate usage of antimicrobials and recommends the antimicrobial treatment for common infectious diseases. It is also underscored that these guidelines do not replace the need for consultation for expert advice and should always be tailored to individual patient needs. These guidelines will be reviewed and revised periodically based on changing pattern of AMR.

I gratefully acknowledge the valuable inputs from the expert group members, reviewers and other contributors in the collaborative effort of shaping the National Treatment Guidelines for Antimicrobial use in infectious diseases.

I sincerely hope that this document will be of immense help for prevention and containment of AMR to medical practitioners, academia, regulatory authorities, health and hospital administrators.


(Dr. S. Venkatesh)

Chapter 1 INTRODUCTION

Infections caused by microorganisms have threatened human life since time immemorial. During the pre-antibiotic era, these have been a major concern for the high morbidity and mortality in humans. Some of the virulent organisms with the potential to spread infection from one infected person to another at a very rapid rate may cause worldwide pandemics, epidemics or outbreaks. With the discovery of the first antibiotic, "the magic bullet" Penicillin in the year 1943, patients could be effectively cured of many life-threatening infections. This gave a huge relief to the medical practitioners. Next three decades saw the development and discovery of a wide variety of antimicrobial agents. Subsequently, the pace of discovery of newer molecules declined from 1970 to 1987. It has reached a "discovery void" level from 1987 onwards up till now. This is the post-antibiotic era in which the medical practitioners have to treat and manage all types of infections with equal or greater efficiency.

Spontaneous natural development of antimicrobial resistance in the microorganisms in nature is a slow process. However, the frequent and inappropriate use of a newly discovered antimicrobial drug leads to the development of altered mechanisms in the pathophysiology of the concerned microbes as a survival strategy. Such antibiotic selection pressure kills the susceptible microbes and helps in selective replication of drug resistant bacteria. These resistant bacteria already existed in the population along with the susceptible ones or susceptible bacteria acquired resistance during antimicrobial treatment. Ultimately, such resistant bacteria multiply abundantly and entirely replace the susceptible bacterial population. This results in treatment failure or ineffective management of such infected patients. Antimicrobial resistance has been observed and reported with practically all the newly discovered antimicrobial molecules till date. Antimicrobial resistance makes the treatment of patients difficult, costly and sometimes impossible.

Emergence of antimicrobial resistance in pathogens has become a matter of great public health concern. Antimicrobial resistance is well recognised as a global threat to human health. Infections caused by antimicrobial-resistant micro-organisms in hospitals are associated with increased morbidity, mortality and healthcare costs. Resistance has emerged even to newer and more potent antimicrobial agents like carbapenems. Selection and spread of resistant microorganisms in the presence of antimicrobials is facilitated by:

- Irrational use of drugs
- Self-medication
- Misuse of drugs

Antimicrobial resistance is closely linked to inappropriate antimicrobial use. It is estimated that 50% or more of hospital antimicrobial use is inappropriate. There is a need for increased education and awareness about antimicrobial resistance among the public and health-care professionals. One needs to develop and improve the surveillance system for antimicrobial resistance and infectious diseases in general, particularly through improved linkage of data. Nothing will work unless we improve diagnostic testing to ensure more tailored interventions and respond to the opportunities afforded by advances in genomic technologies and point of care testing.

Since 'post antibiotic era' is reported to be "discovery void"; antimicrobial resistance is considered to be the most serious health threats especially for the common infections like sepsis, diarrhea, pneumonia, urinary tract infection, gonorrhoea, malaria, tuberculosis, HIV, influenza. Presently, carbapenem resistance is reported worldwide in more than 50% of strains of *Klebsiella pneumoniae* causing health care associated infections like pneumonia, blood stream infections, infections in the newborn and intensive care units. More than 50% of *Escherichia coli* strains causing urinary tract infections are reported worldwide to be resistant to fluoroquinolones. Similarly, patients suffering from gonorrhoea are reported to be resistant to the last resort of antibiotics - third generation cephalosporins. High mortality (64%) was seen among patients infected with Methicillin resistant *Staphylococcus aureus* (MRSA). Over all, the antimicrobial resistance is associated with higher mortality rate, longer hospital stay, delayed recuperation and long term disability.

Similar observations on the emergence of antimicrobial resistance in gram-negative and gram-positive bacteria are reported also from India. The resistance range varies widely depending on the type of health care setting and the geographical location, availability of antimicrobials in hospitals and over the counter, prescribing habits of treating clinicians coming from different streams of medicine like allopathy, homeopathy, ayurvedic or quacks. The drug resistance has been reported to develop in a microbial population to an antibiotic molecule following its improper and irrational use. To combat the problem of ineffective management of infections and their complications caused by drug resistant microorganisms, it is imperative to report such problems and generate national data at all levels of healthcare settings thus leading to a better tracking and monitoring system in the country.

The published reports in the country reveal an increasing trend of drug resistance in common diseases of public health importance i.e. Cholera: showing high level of resistance to commonly used antimicrobials e.g. Furazolidone (60-80%), Cotrimoxazole (60-80%) and Nalidixic Acid (80-90%), Enteric fever: Chloramphenicol, Ampicillin, Cotrimoxazole (30-50%), Fluoroquinolones (up to 30%), Meningococcal infections: Cotrimoxazole, Ciprofloxacin and Tetracycline (50-100%), Gonococcal infections: Penicillin (50-80%), Ciprofloxacin (20-80%). Resistance is also seen in Meningococcal infections, malaria, leprosy, kala-azar, TB, & HIV. Recently, NDM-1 positive bacteria have also been reported. Factors responsible for emergence of antimicrobial resistance could be widespread use and availability of practically all the antimicrobials over the counter for human, animal and industrial consumption. There are definite policies/guidelines for appropriate use of antimicrobials at national level in specific national health programmes (e.g. RNTCP, National AIDS Control Programme, National Malaria Control Programme etc.) etc

For other pathogens of public health importance like enteric fever, diarrhoeal disease, respiratory infections etc., the individual hospitals are following their own antimicrobial policies and hospital infection control guidelines.

Reliable Indian data on antimicrobial resistance (AMR) for important pathogens of public health importance is an essential pre-

requisite for developing/modifying appropriate guidelines for use of antimicrobials. Currently, there is no accepted national database of antimicrobial resistance in different pathogens except for those where there is a specific national health programme. Despite many microbiology laboratories (in both public as well as private sector) performing routine antibiotic susceptibility testing (AST) of at least bacterial pathogens, the data is neither analysed regularly nor disseminated for use by clinicians / public health experts / programme managers. Quality control and data sharing by these laboratories are other important issues that need attention.

Recently, Ministry of health has launched 'National programme for AMR Containment' in 2012-2017, and one of the key activities initiated under the programme is AMR surveillance with a network of ten laboratories across the country. Currently, the National programme for Containment of AMR is generating AMR data for common bacterial pathogens from various surveillance network sites across the country. The data generated from these surveillance sites shall be useful to understand the magnitude and trend of drug resistance and identify the emergence of resistance, and will enable to accordingly update the treatment guidelines.

Furthermore, need for antibiotics can be reduced by spreading the knowledge of infection control measures and adopting and implementing the hospital infection control practices, formation of active hospital infection control teams in each hospital working round the clock and monitoring and containing the spread of infections. The importance of hand hygiene cannot be more emphasized in helping to control the spread of infections from one patient to another. Access to clean water also helps in the containment of waterborne diseases and outbreaks and infections. Lastly, preventing the acquisition of an infection by vaccination for different microbial infections will also help in reducing the need for prescription of antibiotics.

Implementation of an antibiotic stewardship program - a multidisciplinary program in the country will help to find out the lacunae and improve upon the rational use of antibiotic with appropriate interventions and strategies.

To contain the further development of antimicrobial resistance with no new drug on the horizon and bring the existing levels of reported resistance in the country, it is imperative to have standardized national treatment guidelines for the practitioners so that they rationally use the currently available antimicrobial agents effectively for a long duration and manage their patients more effectively.

How to use these guidelines?

These guidelines list the recommended treatments for common infectious diseases that are based on scientific evidence, literature review and are consistent with the already existing international guidelines and formulated with the collective opinion of a wide group of recognised national experts. The topics covered in this document include empiric treatment choices for different syndromes, infections of specific body sites, and in certain special settings; antimicrobial choices for multi-drug resistant bacterial pathogens; optimizing and monitoring use of antimicrobials; preventive strategies for healthcare associated infections, case definitions and diagnosis of common infections.

It is emphasized that antimicrobials should be prescribed only when they are necessary in treatment following a clear diagnosis. Not all patients need antibiotics; non-drug treatment may be suitable and this has been emphasized in these guidelines.

In all cases, the benefit of administering the medicine should be considered in relation to the risk involved. This is particularly important during pregnancy where the risk to both mother and foetus must be considered.

The content of these treatment guidelines will undergo a process of continuous review. Comments or suggestions for improvement are welcome.

These suggestions may be sent to: amrsurveillance@gmail.com

DISCLAIMER:

This publication provides only suggestive guidelines and the opinions expressed herein reflect those of the contributors. The protocols described herein are general and may not apply to a specific patient. They should NOT supplant clinical judgment, factors like hemodynamics of specific patients, availability of antimicrobials and local antibiogram of healthcare setting.

SYNDROMIC APPROACH FOR EMPIRICAL THERAPY OF COMMON INFECTIONS

Empirical or presumptive anti-infective therapy is based on a clinical diagnosis combined with evidence from the literature and from the educated experience of the probable pathogens causing the infection. To optimize an accurate microbiological diagnosis, clinicians should ensure that diagnostic specimens are properly obtained and promptly submitted to the microbiology laboratory, preferably before the institution of antimicrobial therapy. All attempts should be made to establish diagnosis of the patients based on the facilities available to the treating doctor and affordability of the patients.

Definitive therapy depends on the microbiologic diagnosis by isolation or other direct evidence of pathogen.

According to WHO, presumptive treatment is a one-time treatment given for a presumed infection in a person, or group of people, at high risk of infection.

Presumptive treatment is prescribed typically while waiting for the culture report or in situations where the facilities for doing these tests is not available, is difficult or not cost effective or is impractical. However in certain situations the empirical therapy prescribed as prophylaxis also (e.g surgical prophylaxis, high prevalence, repeated risk of exposure).

The syndromic approach is based on the presence of consistent groups of symptoms and easily recognized signs caused by a single pathogen or a mixture of pathogens.

Before starting presumptive therapy ensure the following

1. Send and follow up on standard investigations for all suspected infections for correct and accurate diagnosis and prognosis.
2. Antibiotics SHOULD be started only after sending appropriate cultures if facilities are available. Similarly any change in antibiotic MUST be guided by sensitivity profile.
3. Assess the factors affecting activity of antimicrobials such as renal excretion, interactions and allergy before prescribing antibiotics.
4. Review of antibiotic therapy MUST be done daily and the therapy escalated or deescalated accordingly especially after the culture reports are available.

Empirical Therapy is justified in patients with life threatening infections, in ICU settings and while awaiting results of culture.

The **timing of initial therapy** should be guided by the patient's condition and urgency of the situation. In critically ill patients e.g. patients in septic shock or bacterial meningitis therapy should be initiated immediately after or concurrently with collection of diagnostic specimens. In other conditions where patient is stable, antimicrobial therapy should be deliberately withheld until appropriate specimens have been collected and submitted to the microbiology laboratory e.g when treating a patient of osteomyelitis or sub-acute endocarditis. Premature usage of antimicrobial in such cases can preclude opportunity to establish a microbiological diagnosis, which is critical in the management of these patients.

Merits and limitations of **empiric vs definitive antimicrobial therapy** should be very clear to the treating doctor prescribing antimicrobials. As the laboratory results pertaining to microbiological tests do not become available for 24 to 72 hours, initial therapy for infection is often empiric and guided by the clinical presentation. Therefore, a common approach is to use broad-spectrum antimicrobial agents as initial empiric therapy with the intent to cover multiple possible pathogens commonly associated with the *specific clinical syndrome*. However, once laboratory results of microbiology tests are available with identification of pathogen along with antimicrobial susceptibility data, every attempt should be made to narrow the antibiotic spectrum. This is a critically helpful and integral component of antimicrobial therapy because it can reduce cost and toxicity and significantly delay the emergence of antimicrobial resistance in the community. Antimicrobial agents with a narrower spectrum should be directed at the most likely pathogens for the duration of therapy for infections such as community-acquired pneumonia, urinary tract infections, soft tissue infections etc. in an OPD setting because specific microbiological tests are not routinely performed or available or affordable.

Due considerations should be given to the **bactericidal vs bacteriostatic** nature of the antimicrobial agents. Bactericidal drugs, which cause death and disruption of the bacterial cell, include drugs that primarily act on the cell wall (e.g., β -lactams), cell membrane (e.g., daptomycin), or bacterial DNA (e.g., fluoroquinolones). Bacteriostatic agents (e.g. sulfonamides and macrolides) inhibit bacterial replication without killing the organism by inhibiting metabolic pathways or protein synthesis in bacteria. However, some antimicrobials are bactericidal against certain organisms may act as bacteriostatic against others and vice versa. Unfortunately such distinction is not significant *in vivo*. Bactericidal agents are preferred in the case of serious infections to achieve rapid cure (e.g in cases of meningitis and endocarditis).

There are few conditions where **combination antimicrobial therapy** is contemplated. These include conditions where synergism of antimicrobials established or cases of infection with specific microbes, where monotherapy is not generally recommended (e.g., treatment of endocarditis caused by *Enterococcus* species with a combination of penicillin and gentamicin). It also includes critically ill patients who may require empiric therapy before microbiological etiology and/or antimicrobial susceptibility can be determined (e.g. suspected healthcare-associated infections with *Acinetobacter baumannii* or *Pseudomonas aeruginosa*). Other conditions where combination therapy may be required include cases where

there is a need to extend the antimicrobial spectrum beyond a use of a single agent is the treatment of polymicrobial infections. Also, it may be used where treatment is initiated for pan-resistant organisms and to prevent emergence of resistance.

Host factors like age, physiological state of the patient (e.g. pregnancy and lactation), organ function (e.g. renal or hepatic function), genetic variation (e.g. G6PD deficiency), allergy or intolerance must be kept in mind while prescribing antimicrobial therapy. Due consideration should be given to the efficacy of an antimicrobial agent at the site of infection (e.g. first- and second-generation cephalosporins and macrolides do not cross the blood-brain barrier and are not recommended for central nervous system infections. Fluoroquinolones achieve high concentrations in the prostate and are preferred oral agents for the treatment of prostatitis).

The contents of this chapter include the commonest infections encountered in healthcare practice. The first section gives treatment guidelines for the adult patients while the second part gives same for the pediatric and neonatal infections. The table below describes the infective syndromes, likely causative agents and the empirical antibiotic therapy advocated against them.

How to use this table:

The table is divided into sections as indicated below. Each section has 5 rows. Row 1 lists the clinical condition. Row 2 lists the most likely agents responsible for this condition, row 3 lists the first line antibiotics while row 4 lists the alternative antibiotic. The alternate antibiotic may be prescribed in cases when the first line antibiotics cannot be used due to hypersensitivity or patient's clinical parameters or non-availability of first line drugs. The table is divided into following subsections:

Presumptive therapy for adult patients suspected of infection

- A. Gastrointestinal & Intra-Abdominal Infections
- B. Central Nervous System Infections
- C. Cardiovascular Infections
- D. Skin & Soft Tissue Infections
- E. Respiratory Tract Infections
- F. Urinary Tract Infections
- G. Obstetrics And Gynaecological Infections
- H. Bones And Joint Infections
- I. Eye Infections
- J. Ear Infections
- K. Infections in Burn and Plastic Surgery
- L. Fungal Infections
- M. Febrile Neutropenia
- N. Post-Cardiovascular Surgery Infections
- O. Pediatric Infections
- P. Neonatal Infections
- R. Post Solid Organ Transplant
- S. Surgical Antimicrobial Prophylaxis

A. GASTROINTESTINAL & INTRA-ABDOMINAL INFECTIONS

Condition	Likely Causative Organisms	Empiric (presumptive) antibiotics/First Line	Alternative antibiotics/Second Line	Comments
<i>Acute Gastroenteritis</i> <i>Food poisoning</i>	Viral, Enterotoxigenic & Enteropathogenic <i>E. coli</i> <i>S. aureus</i> , <i>B. cereus</i> , <i>C. botulinum</i>	None	None	Rehydration (oral/IV) essential
<i>Cholera</i>	<i>V. cholerae</i>	Doxycycline 300mg Oral stat Azithromycin Oral in children (20mg/kg) and pregnant women (1g)	Azithromycin 1gm Oral stat or Ciprofloxacin 500mg BD for 3 days	Rehydration (oral/IV) is essential Antibiotics are adjunctive therapy.
<i>Bacterial dysentery</i>	<i>Shigella sp.</i> , Campylobacter, Non-typhoidal salmonellosis	Ceftriaxone 2gm IV OD for 5 days or oral cefixime 10-15 mg/kg/day x 5 days	Azithromycin 1g OD x 3days	For Campylobacter the drug of choice is azithromycin.
	Shiga toxin	Antibiotic Treatment		Antibiotic

	producing <i>E. coli</i>	not recommended.		use associated with development of hemolytic uremic syndrome.
Amoebic dysentery	<i>E. histolytica</i>	Metronidazole 400mg Oral TDS for 7-10 days	Tinidazole 2gm Oral OD for 3 days	Add diloxanide furoate 500 mg TDS for 10d
Giardiasis	<i>Giardia lamblia</i>	Metronidazole 250-500mg oral TID x 7-10 d	Tinidazole 2 gm oral x 1 dose	
Enteric fever	<i>S. Typhi</i> , <i>S. Paratyphi A</i>	<u>Outpatients:</u> Cefixime 20mg/kg/day for 14 days or Azithromycin 500 mg BD for 7 days. <u>Inpatients:</u> Ceftriaxone 2 g IV BD for 2 weeks +/-Azithromycin 500 mg BD for 7 days	Cotrimoxazole 960 mg BD for 2 weeks	Majority of strains are nalidixic acid resistant. Ceftriaxone to be changed to oral cefixime when patient is afebrile to finish total duration of 14days.
Biliary tract infections (cholangitis, cholecystitis)	Enterobacteriaceae (<i>E. coli</i> , <i>Klebsiella sp.</i>)	Ceftriaxone 2gm IV OD or Piperacillin-Tazobactam 4.5gm IV 8 hourly or Cefoperazone-Sulbactam 3gm IV 12hourly For 7-10 days	Imipenem 500mg IV 6hourly or Meropenem 1gm IV 8hourly For 7-10 days	Surgical or endoscopic intervention to be considered if there is biliary obstruction. High prevalence of ESBL producing <i>E. coli</i> , <i>Klebsiella sp.</i> strains. De-escalate therapy once antibiotic susceptibility is known.
Hospital acquired diarrhea	<i>C. difficile</i>	Metronidazole 400 mg oral TDS for 10 days	Severe disease: start Vancomycin 250 mg oral 6h empirically.	
Spontaneous bacterial Peritonitis	Enterobacteriaceae (<i>E. coli</i> , <i>Klebsiella sp.</i>)	Cefotaxime 1-2 gm IV TDS or Piperacillin-Tazobactam 4.5gm IV 8 hourly or Cefoperazone-Sulbactam 3gm IV 12h	Imipenem 500 mg IV 6hourly or Meropenem 1gm IV 8hourly	Descalate to Ertapenem 1 gm IV OD for 5-7 days once the patient improves
Secondary peritonitis, Intra-abdominal abscess/ GI perforation	Enterobacteriaceae (<i>E. coli</i> , <i>Klebsiella sp.</i>), <i>Bacteroides</i> (colonic perforation), Anaerobes	Piperacillin-Tazobactam 4.5gm IV 8 hourly or Cefoperazone-Sulbactam 3gm IV 12hourly in severe infections In very sick patients, if required, addition of cover for yeast (fluconazole iv 800 mg loading dose day 1, followed by 400 mg	Imipenem 1g IV 8hourly or Meropenem 1gm IV 8hourly or Doripenem 500 mg TDS or Ertapenem 1 gm IV OD	Source control is important to reduce bacterial load. If excellent source control – for 5-7 days; other wise 2-3 weeks suggested.

		2 nd day onwards) & and for Enterococcus (vancomycin /teicoplanin) may be contemplated		
Pancreatitis Mild- moderate		No antibiotics		
Post necrotizing pancreatitis: infected pseudocyst; pancreatic abscess	<i>Entrobacteriaceae, Enterococci, S. aureus, S. epidermidis, anaerobes, Candida sp.</i>	Piperacillin-Tazobactam 4.5 gm IV 8 hourly empirically or Cefoperazone-Sulbactam 3gm IV 8 hourly in severe infections In very sick patients, if required, addition of cover for yeast (fluconazole iv 800 mg loading dose day 1, followed by 400 mg 2 nd day onwards) & and for Enterococcus (vancomycin /teicoplanin) may be contemplated For 7-10 days	Imipenem-Cilastatin 500mg IV 6hourly or Meropenem 1gm IV 8hourly or Doripenem 500mg IV 8h	Duration of treatment is based on source control and clinical improvement
Diverticulitis Mild- OPD treatment	<i>Gram-Negative Bacteria Anaerobes</i>	Amoxicillin-Clavulanate 625mg TDS for 7 days	Ciprofloxacin + Metronidazole for 7 days	
Diverticulitis moderate	<i>Gram- Negative Bacteria Anaerobes</i>	Ceftriaxone 2gm IV OD +metronidazole 500 mg IV TDS or Piperacillin-Tazobactam 4.5 gm IV 8 hourly empirically or Cefoperazoe-Sulbactam 3gm IV 8 hourly		BL-BLI agents have very good anaerobic cover, so no need to add metronidazole.
Diverticulitis Severe	<i>Gram- Negative Bacteria Anaerobes</i>	Meropenem 1gm IV 8hrly or Imipenem Cilastatin 500mg IV 6 hourly		Duration based on improvement
Liver Abscess	<i>Polymicrobial</i>	Amoxicillin-clavulanate/ 3rd generation cephalosporin + Metronidazole 500mg I.V.TID / 800mg oral TID for 2 weeks	Piperacillin-Tazobactam IV	Ultrasound guided drainage indicated inlarge abscesses, signsof imminent rupture andno response to medicaltreatment.

B. CENTRAL NERVOUS SYSTEM INFECTIONS

Condition	Likely Causative Organisms	Empiric antibiotics (presumptive antibiotics)	Alternative antibiotics	Comments
Acute bacterial Meningitis	<i>S. pneumoniae</i> , <i>H. influenzae</i> , <i>Neisseria meningitidis</i>	Ceftriaxone 2 g IV 12hourly/ Cefotaxime 2 g IV 4-6hourly 10-14 days treatment	Chloramphenicol if patient is allergic to penicillin	Antibiotics should be started as soon as the possibility of bacterial meningitis becomes evident, ideally within 30 minutes. Do not wait for CT scan or LP results. No need to add vancomycin as primary agent, as ceftriaxone resistant <i>Pneumococcus</i> is not common in India. <i>Listeria</i> is also rare in India and so ampicillin is also not indicated Adjust therapy once pathogen and susceptibilities are known.
Meningitis-Post-neurosurgery or Penetrating head trauma	<i>Staphylococcus epidermidis</i> , <i>Staphylococcus aureus</i> , <i>Propionibacterium acnes</i> , <i>Pseudomonas aeruginosa</i> , <i>Acinetobacter baumannii</i>	Meropenem 2gm IV 8 hourly AND Vancomycin 15mg/kg IV 8 hourly For 14 days.		May need intra ventricular therapy in severe cases
Meningitis with basilar skull fractures	<i>S. pneumoniae</i> , <i>H. influenzae</i>	Ceftriaxone 2gm IV 12 hourly For 14 days		Dexamethasone 0.15mg/kg IV 6 hourly for 2-4 days (1st dose with or before first antibiotic dose)
Brain abscess, Subdural empyema	Streptococci, Bacteroides, Enterobacteria-ceae, <i>S. aureus</i>	Ceftriaxone 2 gm IV 12hourly or Cefotaxime 2 gm IV 4-6hourly AND Metronidazole 1 gm IV 12hourly Duration of treatment to be decided by clinical & radiological response, minimum two months required.	Meropenem 2gm IV 8hourly	Exclude TB, Nocardia, Aspergillus, Mucor If abscess <2.5cm & patient neurologically stable, await response to antibiotics. Otherwise, consider aspiration/surgical drainage and modify antibiotics as per sensitivity of aspirated/drained secretions.

C. CARDIOVASCULAR INFECTIONS

Condition	Likely causative Organism	Empiric antibiotics (presumptive antibiotics)	Alternative antibiotics	Comments
<p><i>Infective Endocarditis:</i> <i>Native valve (awaiting cultures) Indolent</i></p>	<p>Viridans Streptococci, other Streptococci, Enterococci</p>	<p>Penicillin G 20MU IV divided doses, 4 hourly or Ampicillin 2gm iv 4h AND Gentamicin 1mg/kg im or iv 8h Duration: 4-6 weeks</p>	<p>Vancomycin 15mg/kg IV 12 hourly (maximum 1g 12 hourly)/teicoplanin 12mg/kg IV 12 hourly x 3 doses followed by 6 - 12 mg once daily IV depending upon severity + Gentamicin 1mg/kg IM or IV 8 hourly Duration: 4-6 weeks or Daptomycin 6mg/kg IV once a day Duration: 4-6 weeks</p>	<p><i>If patient is stable, ideally wait blood cultures.</i></p> <p>Antibiotic choice as per sensitivity results. Guidance from Infectious disease specialist or clinical microbiologist is recommended</p>
<p><i>Infective Endocarditis:</i> <i>Native valve (awaiting cultures)</i> <i>In Severe Sepsis</i></p>	<p><i>S.aureus</i> (MSSA or MRSA) Risk for gram-negative bacilli</p>	<p>Vancomycin 25-30 mg/kg loading followed by 15-20 mg/kg IV 12 hourly (maximum 1gm 12 hourly)/teicoplanin 12mg/kg IV 12 hourly x 3 doses followed by 6 -12 mg once daily IV depending upon severity AND Meropenem 1gm IV 8h Duration: 4-6 weeks</p>	<p>Daptomycin 6mg/kg IV once a day AND Meropenem 1gm IV q8h Duration: 4-6 weeks</p>	<p>Modify antibiotics based on culture results and complete 4-6 weeks of antibiotics</p>

<i>Infective Endocarditis: Prosthetic Valve awaiting Cultures</i>		Vancomycin 15mg/kg IV 12 hourly (maximum 1gm 12 hourly)/teicoplan in 12mg/kg IV 12 hourly x 3 doses followed by 6 -12 mg once daily IV depending upon severity + Gentamicin 1mg/kg q12h IV	Daptomycin can be used in place of Vancomycin/ Teicoplanin for patients unresponsive to or intolerant of Vancomycin/Tei coplanin or with Vancomycin/Gly copeptide- resistant isolates	Antibiotic choice as per sensitivity. Guidance from Infectious disease specialist or microbiologist is recommended.
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D. SKIN & SOFT TISSUE INFECTIONS

Condition	Likely Causative Organisms	Empiric antibiotics (presumptive antibiotics)	Alternative antibiotics	Comments
<i>Cellulitis</i>	<i>Streptococcus pyogenes</i> (common), <i>S.aureus</i>	Amoxicillin- Clavulanate 1.2gm IV TDS/625 mg oral TDS or Ceftriaxone 2gm IV OD	Clindamycin 600-900mg IV TDS	Treat for 5-7 days.
<i>Furunculosis</i>	<i>S.aureus</i>	Amoxicillin- Clavulanate 1.2gm IV/Oral 625 TDS or Ceftriaxone 2gm IV OD Duration – 5-7 days	Clindamycin 600-900mg IV TDS	Get pus cultures before starting antibiotics
<i>Necrotizing fasciitis</i>	<i>Streptococcus pyogenes, S. aureus,</i> anaerobes, Enterobacteriaceae (polymicrobial)	Piperacillin- Tazobactam 4.5gm IV 6hourly or Cefoperazone- Sulbactam 3gm IV 12hourly AND Clindamycin 600-900mg IV 8 hourly Duration depends on the progress	Imipenem 1g IV8hourly or Meropenem 1gm IV 8hourly AND Clindamycin 600-900mg IV TDS/linezolid 600 mg IV BD/daptomycin 6mg/kg/day	Early surgical intervention crucial

E. RESPIRATORY TRACT INFECTIONS

Condition	Likely Causative Organisms	Empiric antibiotics (presumptive antibiotics)	Alternative antibiotics	Comments
Community acquired Pneumonia	<i>S. pneumoniae</i> , <i>H.influenzae</i> , Legionella, <i>E.coli</i> , <i>Klebsiella sp.</i> , <i>S.aureus</i>	<u>Mild to moderate cases</u> Amoxicillin-500mg-1 g TDS oral. If IV indicated, amoxicillin-clavulanate 1.2 g IV TDS or Ceftriaxone 2g IV OD For <u>Severe cases</u> Amoxicillin-clavulanate 1.2 g IV TDS Or Ceftriaxone 2g IV OD Duration 5-8 days	Piperacillin-Tazobactam 4.5gm IV 6 hourly or Imipenem 1g IV 6hourly or Cefoperazone-Sulbactam 3gm IV 12 hourly	If MRSA is a concern, add Linezolid 600mg IV/Oral BD If atypical pneumonia suspected, Doxycycline 100mg bd or Azithromycin 500 mg oral/IV OD
Lung abscess, Empyema	<i>S. pneumoniae</i> , <i>E.coli</i> , <i>Klebsiella sp.</i> , <i>Pseudomonas aeruginosa</i> , <i>S.aureus</i> , anaerobes	Piperacillin-Tazobactam 4.5gm IV 6hourly or Cefoperazone-Sulbactam 3gm IV 12 hourly	ADD Clindamycin 600-900mg IV 8hourly	3-4 weeks treatment required
Acute pharyngitis	Viral	None required		As most cases are viral no antimicrobial therapy required
	<i>Group A β-hemolytic Streptococci (GABHS)</i> , <i>Group C, G Streptococcus</i> ,	<i>Oral Penicillin v 500mg BD</i> or <i>Amoxicillin 500 mg Oral TDS for 10 days</i>	<i>In case of penicillin allergy:</i> <i>Azithromycin 500mg OD for 5 days</i> or <i>Benzathine penicillin 12 lac units IM stat</i>	<i>Antibiotics are recommended to reduce transmission rates and prevention of long term sequelae such as rheumatic fever</i>
Ludwig's angina Vincent's angina	Polymicrobial (Cover oral anaerobes)	Clindamycin 600 mg IV 8 hourly or Amoxicillin-Clavulanate 1.2gm IV	Piperacillin-Tazobactam 4.5gm IV 6 hourly	Duration based on improvement
Acute bacterial rhinosinusitis	Viral, <i>S. pneumoniae</i> , <i>H.influenzae</i> , <i>M. catarrhalis</i>	Amoxicillin-clavulanate 1gm oral BD for 7 days	Moxifloxacin 400mg OD for 5-7days	
Acute bronchitis	Viral	Antibiotics not required	-	-
Acute bacterial exacerbation of COPD	<i>S. pneumoniae</i> <i>H. influenzae</i> <i>M. catarrhalis</i>	Amoxicillin-clavulanate 1gm oral BD for 7 days	Azithromycin 500 mg oral OD × 3 days	

F. URINARY TRACT INFECTIONS

Asymptomatic bacteriuria NOT to be treated except pregnant women and immunocompromised patients. All cases of dysuria may not be UTI. Refer to Obstetrics and gynaecology infections for treatment of asymptomatic bacteriuria in pregnant women.

Condition	Likely Causative Organisms	Empiric antibiotics (presumptive antibiotics)	Alternative antibiotics	Comments
Acute uncomplicated Cystitis	<i>E.coli</i> , <i>Staphylococcus saprophyticus</i> (in sexually active young women), <i>Klebsiella pneumoniae</i>	Nitrofurantoin 100 mg BD for 7 days or Cotrimoxazole 960mg BD for 3-5 days or Ciprofloxacin 500 mg BD for 3-5 days	Cefuroxime 250 mg BD for 3-5 days	Get urine cultures before antibiotics & modify therapy based on sensitivities.
Acute uncomplicated Pyelonephritis	<i>E.coli</i> , <i>Staphylococcus saprophyticus</i> (in sexually active young women), <i>Klebsiella pneumoniae</i> , <i>Proteus mirabilis</i>	Amikacin 1 g OD IM/IV or Gentamicin 7 mg/kg/day OD (Monitor renal function closely and rationalise according to culture report) Complete total duration of 14 days	Piperacillin-Tazobactam 4.5g IV 6 hourly or Cefoperazone-Sulbactam 3g IV 12 hourly or Ertapenem 1 g IV OD	Urine culture and susceptibilities need to be collected before starting antimicrobial treatment to guide treatment.
Complicated Pyelonephritis	<i>Escherichia coli</i> , <i>Klebsiella pneumoniae</i> , <i>Proteus mirabilis</i> , <i>Pseudomonas aeruginosa</i> , <i>Enterococcus sp.</i> Frequently multi-drug resistant organisms are present	Piperacillin-Tazobactam 4.5gm IV 6 hourly or Amikacin 1 g OD IV or Cefoperazone-Sulbactam 3gm IV 12 hourly	Imipenem 1g IV 8 hourly or Meropenem 1gm IV 8 hourly	Get urine cultures before antibiotics & switch to a narrow spectrum agent based on sensitivities. Treat for 10-14 days. De-escalate to Ertapenem 1 gm IV OD, if Imipenem/meropenem initiated. Monitor renal function if aminoglycoside is used.
Acute prostatitis	Enterobacteriaceae (<i>E.coli</i> , <i>Klebsiella sp.</i>)	Doxycycline 100 mg BD or Co-trimoxazole 960 mg BD.	In severe cases, Piperacillin-Tazobactam 4.5gm IV 6 hourly or Cefoperazone-sulbactam 3gm IV 12 hourly or Ertapenem 1 gm IV OD or Imipenem 1g IV 8 hourly or Meropenem 1gm IV 8 hourly	Get urine and prostatic massage cultures before antibiotics & switch to narrow spectrum agent based on sensitivities and then treat total for 3-4 weeks. Use Ciprofloxacin (if sensitive)

G. OBSTETRICS AND GYNAECOLOGICAL INFECTIONS

- Fluoroquinolones are contraindicated in 1st trimester.
- Cotrimoxazole is contraindicated in 1st trimester.
- Doxycycline is not recommended in nursing mothers. If need to administer doxycycline discontinuation of nursing may be contemplated.

Infections	Likely organism	Primary treatment (presumptive antibiotics)	Alternate treatment	Remarks
Asymptomatic Bacteriuria > 1,00,000 cfu/ ml of bacteria of same species in 2 urine cultures obtained 2-7 days apart. Treat as per sensitivity result for 7 days.		Nitrofurantoin 100 mg Oral, BD for 7 days or Amoxicillin 500 mg Oral BD x 7-10 days .	Oral cephalosporins, TMP-SMX or TMP alone	Screen in 1st trimester. Can cause pyelonephritis in upto 25% of all pregnant women. 30 % Chance of recurrence after empirical therapy 1. Few direct effects, uterine hypo perfusion due to maternal anemia dehydration, may cause fetal cerebral hypo perfusion. 2. LBW, prematurity, premature labour, hypertension, preeclampsia, maternal anemia, and amnionitis. Need to document pyuria (Pus cells > 10/HPF)
Group B streptococcal Disease, Prophylaxis and Treatment	Group B Streptococci	IV Penicillin G 5 million units. (Loading dose) then 2.5 -3 million units IV QID until delivery. or Ampicillin 2 gm IV (Loading dose) then 1 gm QID until delivery	Cefazolin 2 gm IV (Loading Dose) and then 1 gm TID Clindamycin 900 mg IV TID or vancomycin IV or teicoplanin for penicillin allergy	Prevalance very low so the prophylaxis may be required only on culture documented report Associated with high risk of pre-term labour, still birth, neonatal sepsis
Chorioamnionitis	Group B streptococcus, Gram negative bacilli, chlamydiae, ureaplasma and anaerobes, usually Polymicrobial		Clindamycin/ vancomycin/ teicoplanin and cefoperazone-sulbactam If patient is not in sepsis then IV Ampicillin	Preterm Birth, 9-11% death rate in preterm infant's unfavourable neurologic outcome, lesser risk to term infants.
Septic abortion	Bacteroides, <i>Prevotella bivia</i> , Group B, Group A Streptococcus, Enterobacteraeaceae, <i>C. trachomatis</i> , <i>Clostridium perfringens</i> .	Ampicillin 500 mg QID + Metronidazole 500mg IV TDS if patient has not taken any prior antibiotic (start antibiotic after sending cultures) If patient has been	Ceftriaxone 2g IV OD	

		partially treated with antibiotics, send blood cultures and start Piperacillin-Tazobactam or Cefoperazone-sulbactam till the sensitivity report is available.		
Endomyometritis and Septic Pelvic Vein Phlebitis	Bacteroides, Prevotella biviaus, Group B, Group A Streptococcus, Enterobactereaceae, <i>C. trachomatis</i> , <i>Clostridium perfringens</i>		Same as above.	
Obstetric Sepsis during pregnancy	Group A beta-haemolytic Streptococcus, <i>E.coli</i> , anaerobes.	If patient is in shock and blood culture reports are pending, then start Piperacillin-Tazobactam or Cefoperazone-sulbactam till the sensitivity report is available and modify as per the report. If patient has only fever, with no features of severe sepsis start amoxicillin clavulanate oral 625TDS/IV 1.2 gm TDS Or Ceftriaxone 2gm IV OD+ Metronidazole 500mg IV TDS +/-gentamicin 7mg/kg/day OD if admission needed. MRSA cover may be required if suspected or colonized (Vancomycin/ Teicoplanin)		
Obstetric Sepsis following pregnancy	<i>S. pyogenes</i> , <i>E. coli</i> , <i>S. aureus</i> <i>S. pneumoniae</i> , Meticillin-resistant <i>S. aureus</i> (MRSA), <i>C. septicum</i> & <i>Morganella morganii</i> .	Same as above	Sources of sepsis outside Genital tract Mastitis UTI Pneumonia Skin and soft tissue (IV site, surgical site, drain site etc.)	
Syphilis				Refer to STD program guidelines
Tuberculosis in pregnancy	Similar to NON PREGNANT population with	Please refer RNTCP guideline WHO has advocated that, all the first line drugs are		Very small chance of transmission of infection to fetus.

	<p>some exceptions (see comment and chapter 8)</p>	<p>safe in pregnancy and can be used except streptomycin. SM causes significant ototoxicity to the fetus (Pyrazinamide not recommended by US FDA)</p> <p>1. Mother and baby should stay together and the baby should continue to breastfeed. 2. Pyridoxine supplementation is recommended for all pregnant or breastfeeding women taking isoniazid as well as to neonate who are being breast fed by mothers taking INH.</p>	<p>Late diagnosis can predispose to LBW, prematurity.</p>
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VIRAL INFECTIONS (NO ANTIBIOTICS TO BE GIVEN)

<p>Influenza In pregnancy (seasonal And H1N1)</p> <p>The best preventive strategy is administration of single dose of killed vaccine.</p>	<p>Oseltamivir 75 mg Oral BD for 5 days</p>	<p>Nebulization with Zanamvir respules (2) 5 mg each, BD for 5 days</p>	<p>1. Tendency for severe including premature labor & delivery.</p> <p>2. Treatment should begin within 48 hrs of onset of symptoms.</p> <p>3. Higher doses commonly used in non pregnant population (150 mg) are not recommended in pregnancy due to safety concerns.</p> <p>4. Chemoprophylaxis can be used in significant exposures.</p> <p>5. Live (nasal Vaccine) is contraindicated in pregnancy.</p>	<p>Direct fetal infection rare</p> <p>Preterm delivery and pregnancy loss.</p>
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<p>Varicella</p>	<p>>20 wks of gestation, presenting within 24 hours of the onset of the rash,</p> <p>Aciclovir 800mg Oral 5 times a day IV acyclovir recommended for the treatment of severe complications,</p> <p>> 24 hrs from the onset of rash, antivirals are not found to be useful.</p>	<p>VZIG should be offered to susceptible women < 10 days of the exposure. VZIG has no role in treatment once the rash appears.</p> <p>The dose of VZIG is 125 units / 10kg not exceeding 625 units, IM.</p>	<p>Chickenpox during pregnancy does not justify termination without prior prenatal diagnosis as only.</p> <p>A minority of fetuses infected develop fetal varicella syndrome.</p>
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PARASITIC INFECTIONS

<p>Acute Toxoplasmosis in pregnancy</p>		<p><18 weeks gestation at diagnosis</p> <p>Spiramycin 1 gm Oral qid until 16-18 weeks/Pyrimathamine + sulphadizine. Alternate every two weeks–</p>	
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		<p>If PCR Positive -</p> <p>>18 weeks gestation and documented fetal infection by positive amniotic fluid PCR.</p> <p>Pyremethamine 50 mg Oral BD x 2 days then 50 mg OD</p> <p>+ Sulphadiazine 75 mg/kg Oral x 1 dose then 50mg/kg bd</p> <p>+ Folinic Acid (10-20 mg Oral daily) for minimum of 4 weeks or for duration of pregnancy.</p>	
Malaria In pregnancy	As per national program		
GENITAL TRACT INFECTIONS			
Candidiasis	Candida species	<p>Fluconazole oral 150 mg single dose</p> <p>For milder cases- Intravaginal agents as creams or suppositories clotrimazole, miconazole, nystatin. Intravaginal azoles, single dose to 7-14 days.</p>	Non-pregnant- If recurrent candidiasis, (4 or more episodes/year) 6 months suppressive treatment with fluconazole 150 mg oral once a week or clotrimazole vaginal suppositories 500 mg once a week.
Bacterial vaginosis	Polymicrobial	<p>Metronidazole 500mg Oral BD x 7 days</p> <p>Or metronidazole vaginal gel 1 HS x 5 days</p> <p>Or Tinidazole 2 g orally ODx 3 days Or 2% Clindamycin Vaginal cream 5 gm HS x 5 days</p>	Treat the partner.
Trichomoniasis	Trichomonas vaginalis	<p>Metronidazole 2 gm single dose or 500 mg Oral BD X 7 days or</p> <p>Tinidazole 2 gm Oral single dose For treatment failure – retreat with Metronidazole 500 mg Oral BD X 7 Days, if 2nd failure Metronidazole 2 gm Oral OD X 3-5 days</p>	Treat sexual partner with metronidazole 2 gm single dose
Cervicitis /Urethritis Mucopurulent gonococcal	Polymicrobial	Ceftriaxone 250 mg IM Single dose + Azithromycin 1 gm single dose OR Doxycycline 100mg BD x 7 day	
Pelvic Inflammatory Disease (Salpingitis & tubo-ovarian abscess)	<i>S. aureus</i> , Enterobacteriaceae, gonococci, gardenella	<p>Outpatient treatment Ceftriaxone 250 mg IM/IV single dose plus +/- Metronidazole 500 mg BD x 14 days Plus Doxycycline 100 mg BD x 14 Days</p> <p>Inpatient Treatment Clindamycin +ceftriaxone till patient admitted then change to OPD treatment</p>	Drainage of tubo-ovarian abscess wherever indicated Evaluate and treat sex partner
Mastitis without abscess	<i>S. aureus</i>	<p>Amoxycillin clavulunate/Cephalexin 500 mg QID/ OR Ceftriaxone 2 gm OD OR</p> <p>MRSA- based on sensitivities Add Clindamycin 300 QID or Vancomycin 1 gm IV 12 hourly /teicoplanin 12mg/kg IV 12 hourly x 3 doses followed by 6 once daily IV</p>	
Mastitis with abscess		<p>Drainage with antibiotic cover for MRSA</p> <p>Clindamycin 300 QID or Vancomycin 15mg/kg IV 12 hourly (maximum 1gm 12 hourly)/teicoplanin 12mg/kg IV 12 hourly x 3 doses followed by 6 mg once daily IV</p>	

H. BONES AND JOINT INFECTIONS

Condition	Likely causative Organisms	Empiric antibiotics	Alternative antibiotics	Comments
Acute osteomyelitis OR Septic arthritis	<i>S.aureus</i> , <i>Streptococcus pyogenes</i> Enterobacteriaceae	Ceftriaxone 2g IV OD Followed by Oral therapy by Cloxacillin 500mg q 8h Or Cephalexin 500mg q 6h	Piperacillin-tazobactam 4.5gm IV q 6h or Cefoperazone-sulbactam 3gm IV q 12h AND Clindamycin 600-900mg IV TDS	Treat based on culture of blood/synovial fluid/bone biopsy Orthopedic Consultation is essential for surgical debridement Duration: 4-6 weeks (From initiation or last major debridement)
Chronic Osteomyelitis OR Chronic synovitis		No empiric therapy		Definitive treatment guided by bone/synovial biopsy culture. Treat for 6 weeks minimum Investigate for TB, Nocardia, fungi. Extensive surgical debridement. Total duration of treatment depends on the joint and the organism. Choose antibiotic based on sensitivity.
Prosthetic joint infection	Coagulase negative staphylococci, <i>Staphylococcus aureus</i> , Streptococci Gram-negative bacilli, <i>Enterococcus</i> , Anaerobes	Ceftriaxone 2g IV OD. Add Vancomycin 1gm IV BD or Teicoplanin 800mg x 3 doses followed by 400mg Once daily		4 weeks

I. EYE INFECTIONS

Eyelid infections	Likely organisms	First line/ Suggested Regimen	Alternate regimen	Remarks
Blephritis	Unclear <i>S.aureus</i> , <i>S.epidermidis</i>	Lid margin care with baby shampoo & warm compresses 24 hourly. Artificial tears if associated with dry eye.		
External Hordeolum	<i>S. aureus</i>	Hot pack		
Internal Horedeolum				
Blephritis	MSSA/ <i>S. epidermidis</i>	Oral Cloxacillin 250-500 mg qid or Oral Cephalexin 500mg QID	Lid margin care with baby shampoo & warm compresses 24 hourly. Artificial tears if associated with dry eye.	
	MRSA	Oral Trimethoprim sulphamethoxazole 960 mg BD or Linezolid 600mg BD		
Cunjuctival infections				
Viral conjunctivitis (pink eye)		No antibiotics required treat for symptoms		Highly contagious. If pain & photophobia the suggestive of keratitis.
Bacterial conjunctivitis	<i>S.aureus</i> , <i>S.pneumoniae</i> , <i>H.influenzae</i>	Ophthalmologic solution: Gatifloxacin 0.3%, levofloxacin 0.5%, Moxifloxacin 0.5% 1-2 drops q2h while awake during 1st 2 days, then q4-8h upto 7 days		Uncommon causes- Chlamydia trachomatis N.gonorrhoeae
Corneal infections				
Herpes Simplex keratitis	H.simplex type 1&2	Trifluridine ophthalmic soln 1drop 2 hourly, up to 9times/day until re-epithilised. then 1 drop 4 hourly upto 5 times/day for total duration of 21days	Ganciclovir 0.15% ophthalmic gel for acute herpetic keratitis.	Flurescine staining shows topical dendritic figures.30-50% recur within 2yr.
Varicella Zoster ophthalmicus	Varicella–zoster virus	Famciclovir 500mg BD Or TID OR Valacyclovir 1gm oral TID X 10days	Acyclovir 800mg 5 times/d x 10days	.
Acute bacterial keratitis (No comorbidities)	<i>S.aureus</i> , <i>S.pneumoniae</i> , <i>S.pyogenes</i> , <i>Haemophilus spp</i>	Moxifloxacin topical(0.5%):1 drop 1 hourly for first 48hr,then reduce as per response	Gatifloxacin 0.3% ophthalmic Solution 1drop 1 hourly for 1st 48hrs then reduce as per response	Moxifloxacin. Preferable. Treatment may fail against MRSA.
Acute Bacterial (Contact lens users)	<i>P.aeruginosa</i>	Tobramycin or Gentamicin 14mg/ml + Piperacilin or Ticarcillin eye drops (6-	Ciprofloxacin ophthalmic 0.3% or Levofloxacin	

		12mg/mL) q15-60 min around the clock 24-72hr, then slowly reduce frequency	ophthalmic 0.5%	
Fungal keratitis	Aspergillus, Fusarium, Candida and others	Natamycin (5%) 1drop 1-2 hourly for several days, then 3-4 hourly for several days depending on response	Amphotericin B (0.15%) 1 drop q1-2 hourly for several days depending on the response	Empirical therapy is not recommended.
Protozoan (soft contact lens users)	Acanthamoeba spp.	Optimal regimen uncertain Suggested –(Chlorhexidine 0.02% or Polyhexamethylenebiguanide 0.02%) + (Propamidineisethionate 0.1% or Hexamidine 0.1%) eye drops 1drop every 1 hourly during day time, taper according to clinical response	-	Uncommon. Trauma & soft contact lenses are risk factors
Orbital infections				
Orbital cellulitis	<i>S.pneumoniae</i> , <i>H.influenzae</i> , <i>M.catarrhalis</i> , <i>S.aureus</i> , Anaerobes, Group A Streptococcus, Occasionally Gram Negative bacilli post trauma.	Cloxacillin 2 gm IV q4h+ Ceftriaxone 2 gm IV q24 hourly+ Metronidazole 1gm IV 12h	If Pencilin/Cephalosporin allergy: Vancomycin 1gm iv q12h + levofloxacin 750 mg IV once daily + Metronidazole iv 1gm 24h	If MRSA is suspected substitute cloxacillin with Vancomycin
Endophthalmitis Bacterial	Post-ocular surgery	<i>S.epidermidis</i> <i>S. aureus</i> , Streptococci, enterococci, Gram- negative bacilli	Immediate ophthalmological consultation. Immediate vitrectomy+ intravitreal antibiotics (Inj Vancomycin + Inj ceftazidime)	Adjuvant systemic antibiotics (doubtful value in post cataract surgery endophthalmitis) Inj Vancomycin+ Inj Meropenem
	Hematogenous	<i>S.pneumoniae</i> , <i>N.meningitidis</i> , <i>S. aureus</i> , Group B streptococcus, <i>K. pneumoniae</i>	Intravitreal antibiotics Inj Vancomycin + Inj ceftazidime + Systemic antibiotics Inj Meropenem 1gm iv q8h /Inj Ceftriaxone 2gm iv q24h + Inj Vancomycin 1g iv q12h	
Endophthalmitis Mycotic (Fungal)	Candida sp, Aspergillus sp.	Intravitreal amphotericin B 0.005-0.01 mg in 0.1 ml Systemic therapy: Amphotericin B 0.7-1mg/kg + Flucytosine 25mg/kg qid	Liposomal Amphotericin B 3-5mg/kg Or Voriconazole	Duration of treatment 4-6 weeks or longer depending upon clinical response. Patients with

			chorioretinitis and ocular involvement other than endophthalmitis often respond to systemically administered antifungals
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J. EAR INFECTIONS

Ear infection	Likely Etiology/	Suggested Regimen	Alternate	Remarks
Malignant otitis externa	<i>P. aeruginosa</i> (in >90% cases)	Piperacilin+Tazobactam 4.5gm IV 6h Or Imipenem/Meropenem Ciprofloxacin	Ceftazidime	Debridement usually required. Rule out osteomyelitis; Do CT or MRI, If bone involved , treat for 4-6 wks.
Acute otitis media	<i>S. pneumoniae</i> <i>H. influenzae</i> <i>Morexella catarrhalis</i>	Amoxicillin+clavulanate 90/6.4mg /kg/day bid or cefpodoxim /cefuroxime axetil 250mg BD	Ceftriaxone 50mg/kg I/M for 3 days	Treat children <2 years If >2 years, afebrile and no ear pain- consider analgesics and defer antibiotics Duration of treatment If age <2 years: 10 days If age >2 years : 5-7 days
Mastoiditis				
Acute	<i>S.pneumoniae</i> <i>S.aureus</i> <i>H.influenzae</i> <i>P.aeruginosa</i>	Cefotaxime 1-2 gm iv 4-8 hourly Ceftriaxone 2 gm iv OD		Modify as per culture Unusual causes- Nocardia, TB, Actinomyces.
Chronic	Polymicrobial	Piperacillin- tazobactam 4.5g IV 8h Meropenem 1 gm iv 8h		
Acute Pharyngitis/tonsillitis				
Exudative/Diffuse Erythema	Mostly viral Group A, C, G Streptococcus, Infectious mononucleosis,	Penicillin V oral x10 days or Benzathine Penicillin 1.2 MU IM x 1 dose or Cefdinir or cefpodoxime x 5 days		Penicillin allergic, Clindamycin 300-450 mg orally 6-8 hourly x 5 days. Azithromycin clarithromycin are alternatives.
Membranous pharyngitis	<i>C.diphtheriae</i> ,	Erythromycin 500 mg IV QID or Penicillin G 50,000 units/kg IV 12 hourly. Diphtheria antitoxin: Horse serum. <48 hrs:20,000-40,000 units, Nasopharyngeal membranes:40,000-60,000 units >3 days & bull neck : 80,000-1,20,000 units		
Epiglottitis(Supraglotis)	Children: <i>H.influenzae</i> , <i>S.pyogenes</i> , <i>S.pneumoniae</i> , <i>S.aureus</i> .	Cefotaxime 50 mg/kg IV 8 hourly or ceftriaxone 50 mg/kg IV 24 hourly	Levofloxacin 10 mg/kg IV 24 hourly + clindamycin 7.5 mg/kg IV 6 hourly.	

	Adult: Group A Streptococcus , <i>H.influenzae</i>			
Laryngitis(hoarseness)	Viral (90%)	No antibiotic indicated		

K. INFECTIONS IN BURNS PATIENTS

Condition	Likely Causative Organism	Empiric antibiotics	Alternative antibiotics	Comments
<i>For burns wound that is clinically or microbiologically not infected</i>				<i>Prophylactic parenteral antibiotics in burns are NOT indicated</i> Topical antibiotics to be given after debridement
<i>For burns wound that are clinically or microbiologically infected</i>	<i>Strep pyogenes, Enterobacter sp., S. aureus, S. epidermidis, Pseudomonas, fungi (rare)</i>	i. Burn wound sepsis Pipercillin-tazobactam or Cefoperazone-sulbactam or With or without: <ul style="list-style-type: none"> • Vancomycin //Teicoplanin (if there is suspicion for MRSA) • Antifungal Therapy – When extensive burns and patient not responding to antibiotics <ul style="list-style-type: none"> ○ If hemodynamically stable: fluconazole ○ If hemodynamically unstable: Echinocandin Burn wound cellulitis Cefazolin or Clindamycin or Vancomycin if there is suspicion for MRSA With and without (for burns involving the lower extremity or feet or burns in patients with diabetes) Pipercillin-tazobactam or cefoperazone-sulbactam	Carbapenem +/- Vancomycin/ Teicoplanin	Antibiotic choices are dependent on the antibiogram of the individual institution. Surgical debridement as necessary. Amphotericin B is toxic to all burn patient as renal system compromised, hence Caspofungin may be used.

Prophylaxis in Plastic Surgery

Surgical prophylaxis: Inj Cefuroxime 1.5 g/ Cefazolin IV just before incision single dose.

L .FUNGAL INFECTIONS

Routine antifungal prophylactic therapy in critically ill patients is NOT recommended. Fungal therapy is usually started based on positive cultures or systemic evidence of fungal infection. It is advised to take paired cultures if fungal infection is suspected. Evidence includes persistent sepsis / SIRS despite broad spectrum antibiotic (exclude sepsis, abscess, drug fever, DVT etc). Treat according to identification and antifungal sensitivity of Candida isolate.

Fluconazole IV/oral 800 mg OD first day (12mg/kg) and then 400 mg OD (6mg/kg from second day) if fluconazole naïve or sensitive

Or

2nd line Liposomal Amphotericin B (for *Candida krusei* and *C.glabrata* as inherently resistant to Fluconazole.) **or Caspofungin** (As Caspofungin is inherently inactive against Zygomycetes, Cryptococcus, Fusarium and Trichosporon Spp) Liposomal Amphotericin B IV 3mg/kg OD or Caspofungin dose: IV 70mg on Day 1 (loading), 50mg OD (<80kg) or 70mg OD (if >80kg) thereafter. Moderate to severe hepatic dysfunction: reduce the subsequent daily dose to 35mg OD. Check for drug interactions.

To be decided by Microbiologist/ID physician based on patient's hepatic / renal functions/Severity of infection /drug interactions e.g. rifampicin, carbamazepine, phenytoin, efavirenz, nevirapine, cyclosporin, dexamethasone, tacrolimus etc.

M. FEBRILE NEUTROPENIA

Febrile Neutropenia- definition

- Neutropenia-ANC<500/mm³ and expected to fall below 500/mm³ in 48hrs
- Fever -single oral temperature of 38.3°C (101⁰ F) on one occasion or 38°C (100.4⁰ F) on at least 2 occasions (1 hour apart)
- Neutropenic patients may not have usual signs of infection. Redness, tenderness and fever may be the only signs.

Protocol:

- Critical examination of areas usually harboring infections, including but not limited to, oral cavity, axillary region, scalp, groin, perineal region.
- Send blood Cultures 2 sets (each bottle 10ml x 4 bottles)
- Other relevant investigations: urea, creatinine, ALT, urine culture, Chest Xray, separate culture from central line, etc.

Patient-Haemodynamically stable

- Blood culture 2 sets
- Start IV Ceftriaxone
- No need to add glycopeptide in the initial regimen (except in specific situations, given below)

Patient-Haemodynamically unstable

- Start BL-BLI agent (Cefoperazone-Sulbactam/piperacillin-tazobactam)
OR
Carbapenem (meropenem/imipenem/doripenem)
- No need to add glycopeptide in the initial regimen (except in specific situations, given below)

Reassess after 48 hours:

If blood cultures are negative, haemodynamically stable but still febrile

- Reculture blood
- Add amikacin for 3 days
- Add colistin (instead of amikacin) if indicated (see below)

If blood cultures are negative, haemodynamically unstable but still febrile

- Inj Colistin (+/-Carbapenem) + glycopeptide + Echinocandin/L-Ampho B

Blood culture growing Gram negative bacilli

- Patient afebrile - continue the empirical antibiotic till antibiotic sensitivity is available.
- Rationalise as per susceptibility profiles

When to add glycopeptides?

1. Haemodynamic instability, or other evidence of severe sepsis, septic shock or pneumonia
2. Colonisation with MRSA or penicillin-resistant *S. pneumonia*

3. Suspicion of serious catheter-related infection e.g. *chills or rigours with infusion through catheter and cellulitis around the catheter exit site*
4. Skin or soft-tissue infection at any site
5. Positive blood culture for gram-positive bacteria, before final identification and susceptibility testing is available
6. Severe mucositis

When to add empirical colistin in febrile neutropenic patients?

1. Hemodynamic instability.
2. Colonisation with carbapenem resistant gram-negative bacteria.
3. Previous infection with carbapenem resistant gram-negative bacteria.
4. GNB in blood, sensitivity pending, persistent fever with haemodynamic instability.

Empirical Antifungal Therapy

- No response to broad spectrum antibiotics (3-5 days)-add L-Ampho B / echinocandin
- When a patient is located at a remote area and may not have access to emergency healthcare services, febrile neutropenia can be life-threatening. Under such circumstances, availability of broad-spectrum oral antibiotics with the patient can help them gain time to reach emergency healthcare service.

Useful tips

- Febrile after 72 hrs-CT chest and consider empirical antifungal.
- If fever persists on empirical antibiotics, send two sets blood cultures/day for 2 days
- Send further cultures if clinical deterioration
- Unexplained persistent fever in otherwise stable patient doesn't require change in empirical antibiotic regimen. Continue the regimen till ANC is >500 cells/mm³
- If glycopeptide started as a part of empirical regimen, STOP after 48 hrs, if no evidence of Gram positive infection
- Antibiotic treatment should be given for at least seven days with an apparently effective antibiotic, with at least four days without fever.
- Once Neutrophil count has recovered, with no culture positivity and hemodynamically stable; antibiotics can be stopped and patient observed, even if remains febrile. Evaluate for fungal infection, if at risk.

Antibiotic Prophylaxis

Though quinolone prophylaxis is recommended by International guidelines, it is not useful in Indian scenario due to high resistance.

Antiviral prophylaxis

- For HSV IgG positive patients undergoing allo-HSCT or leukemia induction needs acyclovir prophylaxis
- All patients being treated for cancer need to receive annual influenza vaccination with an inactivated vaccine.
- Neutropenic patients presenting with influenza like illness should receive empirical treatment with neuraminidase inhibitor.

Antifungal prophylaxis

a) Induction chemotherapy of Acute Leukemia: Posaconazole

b) Post allo BMT

Pre engraftment: Voriconazole/echinocandin

Post engraftment: Posaconazole

N. POST-CARDIOVASCULAR SURGERY INFECTIONS

Surveillance regarding the Infections following CTVS should be done in each institute

1. Antibiotic Prophylaxis to be guided by the institutional prevalence of MRSA infection and in patients at increased risk for MRSA colonization
2. Nasal screening before CTV surgery is recommended to rule out MRSA colonization

S. no.	Surgery	Antibiotic Prophylaxis			Comments
		1 st line	2 nd line	Special Antibiotic/Combination	
1.	CABG	Cefazolin	Cefuroxime	-	<p><i>Vancomycin /Teicoplanin to be used in case of high prevalence of MRSA infections only</i></p> <p>Using only Vancomycin/Teicoplanin is NOT recommended due to lack of coverage of GNB</p> <p>Vancomycin infusion to be given over 1 hour & to be started 2 hrs before the surgical incision</p> <p>Teicoplanin dosing to start with 800 mg x 3 doses and then 6 mg/kg to complete prophylaxis Duration of Prophylaxis: Continued till 48 hours after the surgery</p>

Empirical Treatment after appropriate specimen for stain & cultures have been collected

S. no.	Infection/ Syndrome	Likely Causative agents	Antibiotics			Comments
			1 st line	2 nd line	Special Antibiotic/Combination	
1	Sternotomy site infection	Not known	BL-BLI (Piperacillin-tazobactam, Cefoperazone-sulbactam, cefipime-tazobactam) with or without amikacin. With Vancomycin/teicoplanin	Daptomycin/Linezolid with carbapenem	Consider de-escalation to TMP/SMX , doxy/minocycline, cloxacillin, cefazolin, If these are sensitive	1) Removal of the foreign body (steel wires) should be considered
2	Infection of vascular catheters	Not known	BL-BLI (Piperacillin-tazobactam, Cefoperazone-sulbactam, cefipime-tazobactam) with or without amikacin with Vancomycin/teicoplanin	Carbapenem (Empirical anti-MRSA drug if the incidence of MRSA CRBSI is high)		Consider de-escalation as per the isolate, susceptibility, MICs, adverse effects, drug allergy
3	Pneumonia	Not known	BL-BLI (Piperacillin-tazobactam, Cefoperazone-sulbactam) with or without amikacin	Carbapenem		Consider de-escalation as per the isolate, susceptibility, MICs, adverse effects, drug allergy
4	Mediastinitis	Not known	BL-BLI (Piperacillin-tazobactam,	Carbapenem with or without		Consider de-escalation as per the isolate,

			Cefoperazone-sulbactam) with or without amikacin With Vancomycin/teicoplanin	Amikacin		susceptibility, MICs, adverse effects, drug allergy
5	<i>Urinary tract infection</i>	Not known	BL-BLI (Piperacillin-tazobactam, Cefoperazone-sulbactam with or without amikacin	Carbapenem with or without Amikacin		Consider de-escalation as per the isolate, susceptibility, MICs, adverse effects, drug allergy

Definitive Treatment after appropriate specimen for stain & cultures have been collected

S. No.	Infection/ Syndrome	Likely Causative agents	Antibiotics			Comments
			1 st line	2 nd line	Special Antibiotic/ Combination	
1	<i>Sternotomy site infection</i>	<p><i>Coagulase Negative Staphylococci</i></p> <p>MRSA</p> <p>Enterococcus</p> <p>GNB (Enterobacteriaceae, Pseudomonas, Acinetobacter)</p> <p>Candida</p>	<p>Vancomycin, Teicoplanin</p> <p>Vancomycin, Teicoplanin,</p> <p>Vancomycin, Teicoplanin,</p> <p>BL-BLI (Piperacillin-tazobactam, Cefoperazone-sulbactam, with or without amikacin</p> <p>L-AmB/AmB-d for 3 weeks followed by Fluconazole (If susceptible)</p>	<p>Daptomycin Linezolid</p> <p>Daptomycin Linezolid</p> <p>Carbapenem (Meropenem, Imipenem)</p>	<p>Consider de-escalation to Cotrimoxazole or Cloxacillin or Cefazolin</p> <p>Consider de-escalation to TMP/SMX or doxy/minocycline If these are sensitive</p> <p>Consider de-escalation to Ampicillin/ Ampisulbactam</p> <p>Consider de-escalation to oral agent if possible after 2-6 weeks of antibiotic therapy</p> <p>De-escalation to Fluconazole 800 mg loading followed by 200 mg BD</p>	<p>1) Consider MICs, risk of nephrotoxicity, bone penetration for choosing the antibiotic</p> <p>2) Removal of the foreign body (steel wires) should be considered</p> <p>3) Longer duration of duration – 6-12 months may be required</p> <p>For Candida osteomyelitis, longer duration of treatment (12 months) is recommended</p>

O. PEDIATRIC INFECTIONS

Specific Conditions

For Infant below 2 months age (more than 2kg):

Antibiotic	Each dose	Frequency		Route	Duration
		<7 days	>7days		
Inj. Cefotaxime + Inj. Gentamicin	50 mg/kg/dose	12 hrly	8 hrly	IV	2-3 weeks
	5 mg/kg/dose	24 hrly	24 hrly		
<i>2nd line therapy:</i> Meropenem+ Vancomycin	20 mg/kg/dose 15 mg/kg/dose	12 hly 12 hly	8hly 8hly	IV	2-3 weeks

- Treat bacterial meningitis due to Gram-negative bacilli or *Staphylococcus* sp for at least 21 days.

For 2 months and above –

Inj Ceftriaxone (100mg/kg/day-2 divided dosage) for 10 -14 days

2nd line therapy: Meropenem (120 mg/kg/day in 3 div doses) + Vancomycin (60mg /kg/day in 4 div doses) for 10-14 days

- In case Ceftriaxone is not available, Inj Cefotaxime (200mg/kg/d, 3-4 divided doses) is given for the same duration.
- However if strong clinical suspicion for *Staphylococcus* infection in the form of skin boils, arthritis or flowing external wounds – Inj. Vancomycin can be added. In such situations the regimen is given for minimum period of 3 weeks.
- With confirmed meningococcal disease, treat with intravenous Ceftriaxone for 7 days
- H influenzae type b meningitis is treated with intravenous Ceftriaxone for 10 days
- S pneumoniae meningitis is treated with intravenous Ceftriaxone for 14 days
- Bacterial meningitis due to *Staphylococcus* sp is treated for at least 21 days.

Chemoprophylaxis for Meningococcal Disease Contacts (including non-vaccinated Hospital Staff): To be effective in preventing secondary cases, chemoprophylaxis must be initiated as soon as possible (i.e. not later than 48 hours after diagnosis of the case). Mass chemoprophylaxis not needed.

Drug	Dose (Adults)	Dose (Children)	Route	Duration
Rifampicin	600mg/12hr	10mg/kg/12hr	Oral	Two Days
Ciprofloxacin	500mg	-	Oral	Single Dose
Ceftriaxone	250mg	<15yr – 125mg	IM	Single Dose
Azithromycin	500mg	10mg/kg	Oral	Single Dose

1) **LOWER RESPIRATORY TRACT INFECTION –**

Community acquired Pneumonia is categorized in to 2 types –Severe pneumonia (those with respiratory distress) and pneumonia (those with fast breathing only, treated on OPD basis).

(a) For **Severe Pneumonia** (Children with respiratory distress requiring indoor care)-

- Under 2 months of age:
 - Inj Cefotaxime / Ceftriaxone and Gentamicin for 10 days
- Over 2 months of age:
 - Inj. Ampicillin (50mg/kg/dose 6h) + Gentamicin (7.5mg/kg/day OD i.m or i.v) is used. Inj Ampicillin can be switched to Oral Amoxycillin (45mg/kg/day TDS) once child is stable and able to take oral feeds. Total treatment duration is 7-10 days.
 - In case of no response in 2 days the patient is assessed for complications like empyema, or infection at any other site. In the absence of any complication, a 3rd generation Cephalosporin (Cefotaxime 50mg/kg/dose 6h or Ceftriaxone 75- 100mg/kg/day in two divided doses, IV) is used and can be

switched to oral Cefopodoxime (10mg/kg/day BD) once the child is able to take orally. Total treatment duration is 7-10 days.

- In case the patient has severe sepsis/ septic shock, Inj. Piperacillin + Tazobactam (90mg/kg/dose 6h) + MRSA cover with IV Vancomycin (15mg/kg/dose 6h) is recommended.

Whenever *Staphylococcus aureus* is suspected in children (see Text Box), the various drug options are:

It is important to have high index of suspicion for staphylococcal infection as the initial choice of antibiotic does not cover this less common but a more severe infection adequately. Staphylococcal pneumonia is suspected if any child with pneumonia has:

- Rapid progression of the disease, or
- Pneumatocele, or Pneumothorax, or Effusion on chest X-ray, or
- Large skin boils or abscess or infected scabies or
- Post-measles pneumonia, which is not responding within 48 hours to the initial therapy.

To cover for staphylococcal infection, Cloxacillin or other antistaphylococcal drug should be added to the initial regimen as discussed in the text.

- In severe pneumonia, use Inj. Cloxacillin or Inj Clindamycin may be added to the initial regime. OR
- Oral or IV Co- Amoxycylavulanic acid can be used.
- In very severe necrotizing pneumonia or for a patient in septic shock, MRSA cover should be added with IV Vancomycin 25-30 mg IV loading followed by 15-20 mg/kg 8-12 Hourly /)/ Teicoplanin 12 mg/kg x3 doses followed by 6 mg/kg once a day or Linezolid (10mg/kg/dose 8h).
- The total duration for treatment for uncomplicated Staphylococcal pneumonia is 3-4 weeks.

(b) For **pneumonia** (OPD)

- Oral Amoxicillin (45mg/kg/day TDS) for a period of 5 days is recommended as the first choice. In case of non availability, one may use oral Co-trimoxazole (8mg/kg/day of TMP component BD).

Routine use of macrolide antibiotics for all cases of pneumonia is not advocated. Recent data suggests that (i) the routine addition of macrolides to children with CAP does not improve outcome (ii) selective use of macrolides would reduce their indiscriminate use and reduce antibiotic resistance.

Classically the mycoplasma pneumonia presents in an atypical fashion but literature suggests that it can sometimes be difficult to distinguish mycoplasma pneumonia from a pyogenic pneumonia.

Macrolide antibiotics should be considered in following clinical scenarios where the likelihood of mycoplasma pneumonia is high:

- a. Children with a subacute presentation with prolonged low grade fever, persistent cough, chest signs out of proportion to the radiographic abnormality (usually showing perihilar streaky infiltrates).
- b. Children with CAP (acute pneumonia like presentation with radiological evidence of patchy or lobar consolidation) who also have or develop extrapulmonary manifestations like myocarditis, hemolytic anemias, glomeronephritis, aseptic arthritis, CNS problems (aseptic meningitis, encephalitis, ataxia), etc.
- c. Non response to first line antibiotics in children who are immunized with Hib/PCV and have no suppurative complications of CAP.

In the first two conditions macrolide antibiotics can be used along with the first line therapy for CAP.

EMPHYEMA

- **Proper drainage** : Forms the main core of treatment.
- **Antimicrobial Therapy**:
 - Anti- Staphylococcal penicillin (Cloxacillin 100-200 mg/kg/day) along with 3rd generation cephalosporin like Ceftriaxone may be used as first line drug.
 - Co-Amoxyclav is alternative first line therapy.

- In seriously ill patients with disseminated staphylococcal disease and septic shock to cover for MRSA, Vancomycin is recommended. Vancomycin is less effective than the first line drugs for the commoner Methicillin sensitive strains of Staphylococcus aureus.
- Children may continue to be febrile for 5-7 days after starting antibiotic therapy in the case of S. pneumoniae and H. influenzae and for 10-14 days in the case of Staphylococcus aureus. The clinical response to therapy should be assessed with parameters such decrease in fever, normalization of lab parameters such as CBC count, CRP, decrease in drain volume, clearing in chest x-ray, improvement in the overall condition of the patient.
- The decline in toxicity and fever are good signs of likely response. In case of complete non response after 96 hours of treatment, high spiking fever and persistent drainage, second line treatment may be instituted. Vancomycin should be substituted instead of the first line cloxacillin or co-amoxiclav.
- All children with non response should be evaluated for presence of pus pockets in the pleural cavity by an ultrasound chest. Here the key lies in better drainage rather than in a change of antibiotics. Extraneous causes of fever should also be evaluated.

VENTILATOR ASSOCIATED PNEUMONIA:

Treat as per the sensitivity pattern of your ICU.

General Suggestion:

Potential Pathogens	Combination antibiotic therapy
<i>Pseudomonas aeruginosa</i> Or <i>Klebsiella pneumoniae</i> (ESBL) Or <i>Acinetobacter species</i>	Beta Lactam + beta lactamase inhibitor (Piperacillin – Tazobactam) Plus Either Aminoglycoside (Amikacin, Gentamicin, or Tobramycin) OR Antipseudomonal fluoroquinolone (Cipro/ Levofloxacin)
Methicillin – resistant <i>Staphylococcus aureus</i> (MRSA)	Vancomycin or Linezolid

Second line Therapy

- Meropenem – 60 mg/kg/day I/V every 8 hrly AND Vancomycin - 40 mg/kg/day I/V every 6 - 8 hrly

Third line Therapy

- Colistin base IV., 2.5 – 5 mg/kg/day I/V every 6 – 12 hrly (1mg= 30000 IU) AND Vancomycin - 40 mg/kg/day I/V every 6 - 8 hrly

UPPER RESPIRATORY TRACT INFECTIONS

As these are mostly viral in origin, **antibiotics are not needed** barring following situations.

(a) **Bacterial Pharyngotonsillitis** (Group A Streptococcus) –

Any of the following Antibiotic (route)	Children (<30kg) (days)	Children (>30kg) (days)
Penicillin V (Oral)	250 mg BID x 10 days	500 mg BID x 10 days
Amoxycillin (Oral)	40 mg/kg/day x 10 days	250 mg TID, can be given BID
Benzathine Penicillin G (IM)	6 Lakh units (Single Dose)	12 Lakh units (Single Dose)

While Penicillin is the drug of choice Amoxycillin is good alternative and used widely.

If the patient is **Penicillin allergic, the alternative drugs are**

Antibiotic (route)	Dose and duration
Erythromycin (oral)	40-50 mg/kg/day BID or TID x 10 days
Azithromycin (oral)	12 mg/kg OD x 5 days
First Generation Cephalosporin (oral) (10 days) (if only, it is non Type 1 allergy to penicillin)	Cefaclor (20-40 mg/kg/d in 3 divided doses) / Cephalexin (50 mg/kg/d in 3 divided doses)

(b) **Faucial diphtheria**

- Inj.Crystalline Penicillin (100,000-150,000 Units/kg/day I.V 6h) for 10 days in recommended. Alternativey, Inj.Procaine Penicillin 25,000-50,000 U/kg/day BD maximum of 12 lakh units i.m. can be used.
- In case of penicillin allergy, Erythromycin (40-50mg/kg/day TDS/QID for 14 days or Azithromycin 10mg/kg/day OD for 5 days can be given.

(c) Acute otitis media (AOM) –

- Oral Amoxicillin (45mg/kg/day TDS/50-60mg/kg/day in two divided doses) for 7 to 10 days is recommended.
- For severe cases (Severe Otagia and/ or Temp >39°C), Co-Amoxycillin Clavulanate (45 mg/kg/day po BD) or Inj.Ceftriaxone 75 mg/kg/day OD can be used.
- In case of penicillin allergy, Cefdinir (14 mg/kg/d in 2 divided doses) can be used
- Total duration of treatment is recommended for 7 to 10 days.

(d) Mastoiditis And Other Acute Ear Infection

- Inj. Amoxicillin-clavulanate OR 3rd Gen Cephalosporin (Ceftriaxone/ cefotaxime).

(e) CSOM

- Routinely systemic antibiotic is not recommended until there is exacerbation and these are referred to ENT

(f) Acute Sinusitis with URI-

- Oral Amoxycillin (45 mg/kg/day TDS) for 7-10 days is recommended. For severe cases, Amoxycillin Clavulanate (45 mg/kg/day oral BD) or Inj.Ceftriaxone 75 mg/kg/day OD can be used.

(g) Ludwig's Angina

- 1st line : Clindamycin IV 8 hourly or Amoxicillin-Clavulanate IV
- 2nd line : Piperacillin-Tazobactam IV 6 hourly

(h) Pertussis

- Erythromycin for 14 days, Azithromycin for 5 days, Clarithromycin for 7 days and have similar efficacy but differ in terms of cost, duration of therapy, side effects, tolerability, likelihood of drug interaction. Considering all factors, Azithromycin in a dose of 10 mg/kg once a day for 5 days in infants less than 6 months and 10 mg/kg on day 1 and then 5 mg/kg day on 2 to 5 days is the cheapest, shortest best tolerated and most convenient option and can be safely given to infants less than 1 month (unlike all other macrolides).

GASTRO-INTESTINAL DISEASES

(1) Dysentery

- (a) For inpatients- Inj Ceftriaxone (100mg/kg) for 5-7 days.
 - (b) For OPD cases
 - Cefixime (8mg/kg/day BD)
 - Or
 - Azithromycin 10-20 mg/ kg (ceiling dose of 1 gm) for 5 days.
 - In case of non response after 2 antibiotics, investigate for appropriate therapy.
- Fluoroquinolones are not preferred due to high level of resistance in many parts of the country.

(2) Cholera

- Single dose oral azithromycin 10 mg/ kg (ceiling dose of 1 gm) or Doxycycline (50mg for less than 3 years and 100 mg for those above).

(3) Enteric Fever

- (a) For OPD cases-
 - Oral Cefixime 20 mg/kg/day (max dose of 1200) for 14 days or azithromycin 10-20 mg/kg (ceiling dose of 1 gm) for 7-10 days. Antibiotic therapy should be continued till one week post-fever defervescence.
- (b) For inpatients
 - Inj Ceftriaxone 100 mg/ kg/day and shift to oral cefixime once fever resolves. Antibiotic therapy should be continued till one week post-fever defervescence.
 - Second line:
 - a) Ofloxacin 15mg/kg/d in two divided doses for 10-14 days. Antibiotic therapy should be continued till one week post-fever defervescence.
 - b) Chloramphenicol (50- 75mg/kg/day PO) x 14 days
 - c) TMP-SMX (8 mg/kg/day of TMP PO) x 14 days

(4) Peritonitis

For primary peritonitis in nephrotic syndrome: Inj. Ampicillin + Aminoglycoside **OR** inj. cefotaxime for primary peritonitis in a cirrhotic, inj. cefotaxime.

(5) Liver Abscess

1 st Line	2 nd Line	
Amoxycillin-clavulanate/ generation cephalosporin ± Aminoglycoside Metronidazole (30-50 mg/kg/d in 3 divided doses for 10-14 days) is added if Amoebic abscess suspected	3 rd Piperacillin-Tazobactam IV	Ultrasound guided drainage indicated in large abscesses, signs of imminent rupture and no response to medical treatment.

Total duration of therapy is 4-6 weeks

URINARY TRACT INFECTION (UTI)

a) Uncomplicated UTI (age > 2 months with lower UTI, without any urinary tract obstruction) –

Oral Cotrimoxazole (8-10mg of TMP component) /kg/day oral BD

OR

Cefixime (8-10 mg/kg/day BD) to be given for 7-10 days

OR

Co Amoxycillin+Clavulanic Acid (30-50 mg of Amoxicillin) for 7-10 days.

b) Complicated / Severe UTI (Febrile UTI, Systemic toxicity, renal angle tenderness or with any urinary structural abnormality) and all UTI in children less than 2 months should be treated with parenteral antibiotics.

Inj. Cefotaxime (150-200mg/kg/day 8h OR

Inj. Ceftriaxone (100mg/kg/day OD OR

Inj. Amikacin 15mg/kg OD

To be given for 10-14 days

c) In Immunocompromised host/ severe systemic sepsis or as second line for complicated UTI-

Inj. Piperacillin Tazobactam 90mg/kg/dose IV 6h) or Inj. Meropenem (20-40mg/kg/dose 8h) To be given for 10-14 days

FEBRILE NEUTROPENIA

1st Line	2nd Line	3rd Line
Ceftazidime (150 mg/kg/day in 3div doses)+ Amikacin (15-20mg/kg/day in 2 or 3 div doses)	Piperacillin + Tazobactam (200-300 mg/kg/day IV in 3-4 div doses)+ Vancomycin (40 mg/kg/day IV in 4 divided doses)	Meropenem (60 mg/kg/day in 3 div doses) + Amphotericin B (1 mg/kg/day IV for 2 weeks) or liposomal Amphotericin B 1-5 mg kg/day, usually 3 mg/kg/day

- Patients without an identified etiology who become afebrile within first 3-5 days of therapy and are clinically well with ANC of > 200 cells/cmm can be shifted to oral antibiotics (Cefixime or Co- Amoxy- Clavulanic acid) and therapy should be continued for minimum 7 days.
- However, if fever persists or ANC remains <200 parenteral therapy should be continued with 2nd line antibiotics
- In clinically stable patients without an identified etiology but with persistent neutropenia, therapy can be stopped after 2 weeks.

Presumptive therapy for initial antimicrobial coverage in critically ill children with severe sepsis and septic shock

Antibiotics should be administered within 1 hour of the identification of severe sepsis and septic shock, if possible, after obtaining appropriate cultures. The initial empiric antibiotic therapy should include one or more drugs that have activity against the likely pathogens and that penetrate the presumed source of sepsis. Initially, broad antibiotic coverage is recommended. Following are the general rules which can help for decision making:

- I. All children with septic shock should receive coverage for methicillin-resistant *Staphylococcus aureus* (MRSA) initially at recognition of the event.
- II. Coverage for enteric organisms should be added whenever clinical features suggest genitourinary and/or gastrointestinal sources (eg, perforated appendicitis or bacterial overgrowth in a child with short gut syndrome).
- III. Treatment for *Pseudomonas* species should be included for children who are immunosuppressed or at risk for infection like those with cystic fibrosis).
- IV. When treating empirically, antibiotics which can be given by rapid intravenous bolus (eg, beta-lactam agents or cephalosporins) should be administered first followed by infusions of antibiotics, such as vancomycin, that must be delivered more slowly.
- V. Ongoing antimicrobial therapy should be modified based upon culture results, including antimicrobial susceptibility and the patient's clinical course.

Suggested initial empiric antimicrobial regimens based upon patient age, immunocompetence, and previous antibiotic administration include:

1. Children >28 days of age who are normal immunocompetent patient:

- a) Ceftriaxone/Cefotaxime plus Vancomycin //Teicoplanin
- c) Consider adding an aminoglycoside (eg, gentamicin/amikacin) if possibility of genito- urinary source is likely
- d) Consider adding piperacillin-tazobactam / clindamycin / metronidazole if possibility of gastro-intestinal source

2. Children >28 days who are immunosuppressed or at risk for infection with *Pseudomonas* species:

- a) Ceftazidime or Cefepime plus Vancomycin/Teicoplanin
- b) add an aminoglycoside or carbapenem in settings where bacterial organisms with extended-spectrum beta-lactamase (ESBL) resistance are prevalent.
- c) addition of a carbapenem is favored over an aminoglycoside if the patient has received any broad-spectrum antibiotics like 3rd generation cephalosporin, aminoglycoside or fluoroquinolone within two weeks.

3. Children who cannot receive penicillin or who have recently received broad-spectrum antibiotics:

- a) Vancomycin/Teicoplanin plus Meropenem*

* Alternatives to Meropenam

- i) Aztreonam OR
- ii) Ciprofloxacin plus Clindamycin

4. Patients at increased risk of fungal infection (immunocompromised with persistent fever on broad spectrum antibiotics) or with an identified fungal source.

Add the following antifungals to the antimicrobial regimen

- a) Liposomal Amphotericin B or
- b) an echinocandin (eg, caspofungin, micafungin)

5. Patients with risk factors for rickettsial infection (eg, travel to or reside in an endemic region):

Add a tetracyclin antibiotic (eg, doxycycline) to the antimicrobial regimen

The empiric drug choice should be in accordance with the ongoing epidemic and endemic infections eg, H1N1, methicillin-resistant *S. aureus*, chloroquine-resistant malaria, penicillin-resistant pneumococci.

Control of the Infection Source

The source of the infection should be located and treated early and aggressively. Conditions requiring debridement or drainage include necrotizing pneumonia, necrotizing fasciitis, gangrenous myonecrosis, empyema, and abscesses. Perforated viscus requires repair and peritoneal washout. If intravascular access devices are a possible source of severe sepsis or septic shock, they should be removed promptly after other vascular access has been established.

Duration of antibiotic therapy for sepsis

It will depend on the foci of infection, immune status of the patient and response to the antibiotics. If there are no complications the duration of therapy is 7-10 days. Longer courses may be appropriate in patients who have a slow clinical response, undrainable foci of infection, bacteremia with *S. aureus*; some fungal and viral infections or immunologic

deficiencies, including neutropenia Use of procalcitonin levels or similar biomarkers may assist the clinician in the discontinuation of empiric antibiotics in patients.

Management of Central line/long line catheter-Related Infections -

1. Empirical coverage if suspecting gram-negative bacilli

Choice should be based on local antimicrobial susceptibility and the severity of disease a fourth-generation cephalosporin, carbapenem, or b-lactam/b-lactamase combination, with or without an aminoglycoside).

2. Empirical antimicrobial therapy if suspecting MRSA

- for health care settings with an elevated prevalence of MRSA- Vancomycin is recommended
- for institutions in which the most of MRSA isolates have vancomycin minimum inhibitory concentration (MIC) values 12 mg/mL- Daptomycin, should be used.
- Linezolid should not be used for empirical therapy.

3. Empirical combination antibiotic coverage for MDR gram-negative bacilli, such as *Pseudomonas aeruginosa*, should be used when CRBSI is suspected in

- Neutropenic patients
- severely ill patients with sepsis
- patients known to be colonized with such pathogens, until the culture and susceptibility data are available and de-escalation of the antibiotic regimen can be done.

4. Empirical therapy for suspected CRBSI involving femoral catheters in critically ill patients should include coverage for gram-positive pathogens, gram-negative bacilli and *Candida* species.

5. Empirical therapy if catheter-related candidemia is suspected *-

- Echinocandin or
- Fluconazole can be used in patients without azole exposure in the previous 3 months in health care settings where the risk of *Candida krusei* or *Candida glabrata* infection is very low.

*It should be suspected in septic patients with any of the following risk factors: total parenteral nutrition, prolonged use of broad-spectrum antibiotics, hematologic malignancy, receipt of bone marrow or solid-organ transplant, femoral catheterization, or colonization due to *Candida* species at multiple sites.

6. Antibiotic lock therapy should be used for catheter salvage; however, if antibiotic lock therapy cannot be used, systemic antibiotics should be administered through the colonized catheter.

Duration of antimicrobial therapy:

A. Uncomplicated Short term central venous or arterial catheter related blood stream infection

- Coagulase negative staph:
 - treat for 5-7 days, if the catheter is removed
 - treat for 10-14 days, if the catheter is retained
- Staph aureus :- treat for more than 14 days
- Enterococcus :- treat for 7-14 days
- Gram negative bacilli :- treat for 7-14 days
- Candida* sp. :- treat for 14 days after the first negative blood culture,

1. Remove the catheter
2. Treat with systemic antibiotics

B. Complicated Short term central venous or arterial catheter related blood stream infection

Four to 6 weeks of antibiotic therapy should be administered to patients with persistent fungemia or bacteremia after catheter removal (i.e., occurring more than 72 hours after catheter removal), and to patients who are found to have infective endocarditis or suppurative thrombophlebitis, and to pediatric patients with osteomyelitis.

BRAIN ABSCESS

Inj Ceftriaxone + Vancomycin OR

Inj Teicoplanin + Metronidazole,

Drain pus, rationalize antibiotics according to culture and sensitivity and continue for 3 to 4 week.

OSTEOMYELITIS –

Co-Amoxy clavulunic + Gentamicin

SEPTIC ARTHRITIS1st line Inj Co-Amoxy clavulunic + Gentamicin2nd line Inj Ceftriaxone//cefotaxime +/- Vancomycin**TETANUS** – Inj Crystalline Penicillin (2 lac IU /kg/ d /12 hourly) or Inj Metronidazole (mg/kg/d).**ACUTE ENDOCARDITIS** – Inj Crystalline Penicillin/ampicillin + Gentamicin for 3-4 weeks is given which is tailored depending upon culture & sensitivity report.**MALARIA** - As per National Malaria Control Program guidelines. See chapter 8.**TUBERCULOSIS IN CHILDREN**

Refer to RNTCP guidelines

ACUTE RHEUMATIC FEVER (ARF)

Antibiotic	Dose	Route	Frequency	Duration
Primary prophylaxis for rheumatic fever (Treatment of group A streptococcal tonsillo-pharyngitis) The primary goal of treating an ARF attack is to eradicate streptococcal organisms and bacterial antigens from the pharyngeal region. The antibiotic therapy is very effective if started within 9 days after onset of symptoms to prevent rheumatic fever specially carditis.				
Benzathine Penicillin G* [After sensitivity testing] According to weight of the child	weight ≥ 27 kg :- 1.2 million units weight < 27 kg :- 0.6 million units	Deep intramuscular injection	Only once Single dose	Single dose
Alternative antibiotics				
Azithromycin	12.5 mg/kg/day divided	Oral	OD	5 days
Amoxicillin	25–50mg/kg/day divided Adult dose 750-1500 mg/day	Oral	TDS	10 days
Cephalexin	15-20 mg/kg/dose	Oral	BD	10 days
Erythromycin	250 mg #OR 40 mg/kg/day divided	Oral	QID	10 days
Penicillin-V	250 mg Adult dose 500mg	Oral	QID	10 days
Secondary prophylaxis for rheumatic fever It involves continuous administration of antibiotics in patients with a previous attack of RF and/or rheumatic heart disease. It is mandatory for all patients who have had an attack of RF, whether or not they have residual rheumatic valvular heart disease.				
Benzathine Penicillin G	Same as above	same	same	Every 3-4 weeks
Penicillin V	Same	same	BD	See below
Sulfadiazine (patients allergic to penicillin)	weight >27 kg:- 0.5 g weight ≥27 kg:- 1 g	oral	OD	See below
Erythromycin (patients allergic to penicillin & sulfadiazine)	Same	same	BD	See below

*Contraindicated in penicillin allergy

maximum dose-500mg; contraindicated in liver disorders; can be given in patients with penicillin allergy; do not use if high rates of group A streptococcal macrolide resistance prevalent.

Duration for secondary prophylaxis:

It depends on the presence of carditis during the acute episode.

1. NO carditis: continue for 5 years after last attack or 18 years of age [whichever is longer]
2. Carditis present (healed carditis or mild mitral regurgitation): continue for 10 years after last attack or 25 years of age [whichever is longer]
3. Carditis present (established heart disease or following valve surgery or ballon mitral valvotomy): continue lifelong
4. Expert consultation should be sought if want to discontinue after 40 years of age instead of life-long prophylaxis as recurrence beyond this age is minimal.

PAEDIATRIC SURGICAL CASES

Clean Surgery	Clean Surgery likely to be contaminated	Contaminated/dirty Surgery or Peritonitis
<p>Surgeries like Uncomplicated Hernia, cyst excision, hydrocoele - No Pre-operative prophylaxis needed</p> <p>For all other surgeries under this group: Inj Ceftriaxone 50 – 75 mg/kg/day I.V or I/M single dose half an hour before surgery</p>	<p>For GI surgeries Inj Ceftriaxone 50 – 75 mg/kg/day, I.V or I/M 12 hly doses AND Metronidazole 20 – 30 mg/kg/day I/V every 8 hrly Given for 48hrs only.</p> <p>Urinary tract surgeries Inj Ceftriaxone 50 – 75 mg/kg/day I.V or I/M 12hrly doses Do not continue beyond 48hrs of surgery</p>	<p>All surgeries under this group Inj Ceftriaxone 50 – 75 mg/kg/day, I.V or I/M 12hrly doses AND Metronidazole 20 – 30 mg/kg/day I/V every 8 hrly AND Gentamicin 7.5mg/kg/d 24hrly IV or IM</p> <p>2nd Line Piperacillin + Tazobactam (200-300 mg/kg/day IV in 3-4 div doses) + Vancomycin (40 mg/kg/day IV in 4 divided doses)</p>

Cellulitis/ Abscesses	<p>Cloxacillin (50-100 mg/kg/d) in 3-4 divided doses OR Co- Amoxy-Clav OR Cefazolin (50 mg/Kg/d in 6-8 h doses)</p>	<p>Clindamycin (20-40mg/Kg/d in 6-8 hly doses)</p>	Treat for 5-7 days.
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P. NEONATAL INFECTIONS

a. SEPTICEMIA OR PNEUMONIA

1. In asymptomatic babies at high risk of sepsis eg. presence of foul smelling liquor or two or more risk factors listed below warrants the initiation of antibiotic therapy.

Risk factors for Early onset sepsis are :

- (a) Maternal fever (Temperature $\geq 38^{\circ}\text{C}$) before delivery or during labor
- (b) Membranes ruptured for more than 24 hours before delivery.
- (c) More than three vaginal examinations during labor.
- (d) Low birth weight (<2500 gms) or preterm babies.
- (e) Prolonged and difficult delivery with instrumentation.

(f) Perinatal asphyxia. (Apgar < 4 at 1 min of age)

(g) Meconium stained liquor.

2. A sepsis screen should be done in such infants. If two sepsis screens (NNF protocols) done at 12 hours interval or a single sepsis screen is negative and infant remains asymptomatic at 48 -72 hours, the antibiotics may be discontinued.

Antibiotic	Each dose	Frequency		Route	Duration(Days)
		< 7 days	> 7 days		
Inj. Ampicillin And Inj. Gentamicin	50 mg/kg/dose 5-7.5 mg/kg/dose	12 hrly 24 hrly	8hrly 24hrly	IV IV	7-10 7-10

- In cases with severe sepsis (Sclerema/ Shock / suspicion of meningitis) Inj Cefotaxime 200 mg/kg/day IV in 4 div doses) + Amikacin (15mg/kg/d) is recommended
- If sepsis is suspected to be health care associated or if there is no response in 48-72 hours of initial therapy or if there is documented resistance then change to injection Piperacillin- Tazobactam (200-300 mg/kg/day IV in 3-4 div doses) and Amikacin.
- Vancomycin can be added to the regime if staphylococcus is suspected.

b. NEONATAL MENINGITIS

	Antibiotic	Dose	Frequency		Route	Duration (Weeks)
			< 7 days	> 7 days		
First Line	Inj. Ampicillin and Inj. Gentamicin	100 mg/kg/dose	12 hrly	8 hrly	IV	3
		5-7.5 mg/kg/d	5 mg/kg/d 24 hrly	7.5 mg/kg/d 24hrly	IV	3
Second Line	Inj. Cefotaxime and Inj. Gentamicin	50 mg/kg/dose	12 hrly	8 hrly	IV	3
		5-7.5 mg/kg/d	5 mg/kg/d 24 hrly	7.5 mg/kg/d 24hrly	IV	3

Q. POST SOLID ORGAN TRANSPLANT

Post-operative infections following solid organ transplant (kidney, liver, heart, lung)

Condition	Likely causative Organisms	Empiric antibiotics	Alternative antibiotics	Comments
Post-op fever with hemodynamic stability	Usually not due to infection	None		Look for hematoma, DVT, transfusion related fever
Surgical site infection	<i>S. aureus</i> , Entero-bacteriaceae, <i>Pseudomonas</i> spp.			Treat based on culture and sensitivities
VAP/HAP	Entero-bacteriaceae, <i>Pseudomonas</i> spp., <i>Acinetobacter</i> spp.	Piperacillin-tazobactam 4.5g IV q6h or Cefoperazone-sulbactam 3g IVq8h	Imipenem 1g IV q8h or meropenem1g IV q8h	Modify based on culture of lower respiratory tract secretions.

CLABSI	<i>S. aureus</i> , Entero-bacteriaceae, Pseudomonas spp., Acinetobacter spp. Candida spp.	Vancomycin loading of 25-30 mg /kg in patients of septic shock followed by 15mg/kg IV 12 hourly (maximum 1gm 12 hourly)/teicoplanin 12mg/kg IV 12 hourly x 3 doses followed by 6 -12 mg once daily IV depending upon severity + Piperacillin-tazobactam 4.5g IV q6h or Cefoperazone-sulbactam 3g IVq8h For 2 weeks duration	Daptomycin 6 mg/kg IV od +Meropenem 1g IVq8h	Draw 2-3 blood culture sets with at least one from peripheral sites before starting antibiotics and modify based on culture. Removal of catheter must be contemplated.
CAUTI	Entero-bacteriaceae, Enterococci Candida spp.	Piperacillin-tazobactam 4.5g IV q6h or Cefoperazone-sulbactam 3g IVq8h	Imipenem 1g IV q8h or Meropenem 1g IV q8h	Do blood and urine cultures before starting antibiotics and modify based on culture. Removal of catheter must be contemplated.

R. SURGICAL ANTIMICROBIAL PROPHYLAXIS

- To be administered within 1 hr before the surgical incision.
- Single dose is recommended. Consider for second intra-operative dose in prolong surgery based on the choice of antibiotic used for prophylaxis.
- Prophylaxis should **not** be given beyond surgery duration (except for cardiothoracic surgery, up to 48 hours permissible)
- Choice of the prophylaxis should be based on the local antibiogram.

SURGERY	MEDICATION
Breast	Inj.Cefazolin 2gm or Inj.Cefuroxime 1.5gm IV stat
Gastroduodenal & biliary	Inj.Cefaperazone- Sulbactam 2gm IV stat & BD for 24hrs(maximum)
ERCP	Inj.Piperacillin-Tazobactam 4.5gm or Inj.Cefaperazone- Sulbactam 2gm IV stat
Cardiothoracic	Inj.Cefuroxime 1.5gm IV stat & BD for 48hrs
Colonic surgery	Inj.Cefaperazone- Sulbactam 2gm IV stat & BD for 24hrs(maximum)
Abdominal surgery (hernia)	Inj.Cefazolin 2gm or Inj.Cefuroxime 1.5gm IV stat
Head & Neck/ ENT	Inj.Cefazolin 2gm IV stat
Neurosurgery	Inj.Cefazolin 2gm or Inj.Cefuroxime 1.5gm IV stat
Obstetrics& Gynecology	Inj.Cefuroxime 1.5gm IV stat
Orthopaedic	Inj.Cefuroxime 1.5gm IV stat & BD for 24 hrs(maximum) or Inj.Cefazolin 2gm IV stat Open reduction of closed fracture with internal fixation- Inj.Cefuroxime 1.5gm IV stat and q 12h or Inj.Cefazolin 2gm IV stat and q 12h for 24 hrs
Trauma	Inj.Cefuroxime 1.5gm IV stat and q 12h (for 24 hrs) or Inj.Ceftriaxone 2gm IV OD
Urologic procedures	Antibiotics only to patients with documented bacteriuria
Trans- rectal prostatic surgery	Inj.Cefaperazone- Sulbactam 2gm IV stat

Chapter 3

Treatment of Multi-Drug Resistant Bacterial Pathogens

1. Methicillin- Resistant *S. aureus* (MRSA)

- a. These organisms are considered resistant to all penicillins, cephalosporins and macrolides.
- b. Though MRSA strains may be reported as susceptible to Fluoroquinolones, aminoglycosides, chloramphenicol and doxycycline in-vitro, these drugs are NOT to be used alone or as initial treatment for serious MRSA infections.
- c. Rifampicin use should be avoided in diseases other than Mycobacterial diseases.
- d. The drug of choice for treatment of infections due to MRSA is the glycopeptides i.e Vancomycin and Teicoplanin.
- e. Linezolid can be used to treat skin and soft tissue infections caused by MRSA.
- f. Mupirocin local application (intranasally bid x 5 days) for eradicating nasal carriage.
- g. Daptomycin: Daptomycin is an intravenous antibiotic approved to be used for the treatment of complicated skin infections and *Staphylococcus aureus* bacteraemia. Daptomycin should NOT be used for treatment of pneumonia due to its inactivation by surfactant.

2. Vancomycin Resistant Enterococcus (VRE)

Enterococci are a therapeutic challenge because of their intrinsic resistance to many antibiotics. The acquisition of resistance to vancomycin by enterococci has seriously affected the treatment and infection control of these organisms.

The treatment for VRE should be based on infection severity and in-vitro susceptibility of the strain to other antibiotics.

- **Linezolid:** Linezolid is the only drug specifically approved for the treatment of VRE-blood stream infections. Linezolid may be particularly useful in patients who require oral or outpatient therapy (when intravenous therapy is undesirable), who are intolerant to glycopeptides, or who have impaired renal function. Linezolid is a bacteriostatic agent; furthermore, linezolid toxicity when administered for prolonged courses may limit its use in VRE endocarditis.
- **Ampicillin:** Isolates that remain relatively susceptible to penicillin or ampicillin may be treated with high doses of these agents.
- **Daptomycin:** Not approved for treatment of VRE infection. Not approved for treatment of endocarditis. Limited clinical information for VRE, but bactericidal activity makes consideration of this agent as sole therapy in serious infections. However, emergence of resistance during therapy has been reported.
- **Doxycycline:** Not a first line therapy. For susceptible isolates, not for bacteremia or endocarditis. It should not be used as monotherapy.
- **Nitrofurantoin:** Uncomplicated UTIs have been treated successfully with nitrofurantoin.
- **Fosfomycin:** For urinary tract infections (cystitis) with isolates susceptible to fosfomycin.
- **Chloramphenicol:** For chloramphenicol-susceptible isolates of *E. faecium* and *E. faecalis*. Not a first-line therapy and it should not be used as monotherapy.
- **Gentamicin or streptomycin:** To be used in combination with ampicillin for the treatment of enterococcal endocarditis caused by organisms susceptible in vitro to either agent; streptomycin is used when gentamicin cannot be used because of resistance.
- **Tigecycline:** Tigecycline has *in vitro* activity against a broad spectrum of Gram-positive and -negative bacteria, anaerobes as well as multidrug-resistant pathogens such as MRSA and VRE. However, there is not much clinical data regarding its use for treatment of VRE infections.

3. Extended Spectrum Beta-Lactamases (ESBL) Producing Enterobacteriaceae.

- a. ESBLs are plasmid mediated β -lactamases that confer resistance to broad spectrum β -lactam antibiotics including third and fourth generation cephalosporins, aztreonam, and extended spectrum penicillins. These plasmids often encode mutations which confer resistance to other broad spectrum agents including aminoglycosides, co-trimoxazole and fluoroquinolones, resulting in organism resistant to most broad spectrum antibiotics.
- b. A major problem with ESBLs is their capacity to cause therapeutic failure with cephalosporins and aztreonam when host organism appears to be susceptible to these agents in laboratory tests. Hence, CLSI recommends that **laboratories should report ESBL producing isolates as resistant to all penicillins, cephalosporins (including cefepime and ceftazidime), and aztreonam irrespective of in-vitro test results.**
- c. The emergence of ESBL producing enterobacteriaceae is related to indiscriminate use of third generation cephalosporins.
- d. The carbapenems (Ertapenem, Meropenem and Imipenem) are currently considered the drug of choice for serious infections caused by these pathogens. Piperacillin-Tazobactam and Cefoperazone-Sulbactam may be considered options in mild infections and when ESBL producers are demonstrably susceptible *in vitro*.

4. Carbapenem- Resistant Enterobacteriaceae (CRE)

a) Mechanism of resistance :

- i. **Combinations of ESBL or AmpC and porin loss:** Porin loss is often unstable and may impose a fitness cost, meaning that these strains rarely spread. Ertapenem is particularly affected.
- ii. **Acquired carbapenemases**

b) Treatment :

- i. Most carbapenemase producers are extremely drug resistant: being resistant to β -lactam antibiotics, aminoglycosides, and β -lactam- β -lactam inhibitor combinations.
- ii. **Polymyxins, tigecycline & fosfomycin** are the agents with most frequent *in vitro* activity, but all have limitations. Dosage will vary with the patient and infection site, but should be on the principle of 'highest safe' rather than 'minimum potentially effective'; durations should be as standard for the infection type.
- iii. **Colistin** - Case reports of successful use in a range of infections due to carbapenemase producers.
- iv. **Tigecycline:** Active *in-vitro* vs. most carbapenem-resistant *E. coli*. Licensed for complicated skin and soft-tissue infections and complicated intraabdominal infections. Case reports of success in various infections with carbapenemase producers. Low blood concentrations; off-label use should be cautious for blood stream infections, unsuitable in urinary infections as only 22% excreted in urine. Excess deaths in some trials, especially ventilator associated pneumonia (not a licensed indication).
- v. **Others:** a few isolates are susceptible to other antibiotics including e.g. chloramphenicol, ciprofloxacin and cotrimoxazole. Most producers, however, are resistant to these drugs.

Recommended measures to control spread of Multi-drug resistant organisms (MDRO) :

- i. Improved laboratory detection and reporting of MDRO
- ii. Enhanced infection surveillance and control in ICUs
- iii. Prevent spread by barrier precautions : Gowns and gloves
- iv. Hand Washing
- v. Restricted use of 3rd generation cephalosporins

Chapter 4

Guidelines For Optimizing Use Of Key Antimicrobials

A. Antimicrobial Prescribing: Good Practice

1. Send for the appropriate investigations in all suspected infections as recommended. These are the minimum required for diagnosis, prognosis and follow up of these infections.
2. All attempts shall be made to send microbiological samples prior to initiating antimicrobial therapy. Rapid tests, such as Gram stain, can help determine therapeutic choices when decision on empiric therapy is required.
3. Differentiation between contamination, colonization and infection is important to prevent overuse of antimicrobials. Use hospital guidelines based on local antibiograms when choosing antimicrobial therapy whenever possible. If alternatives to those recommended as used, reasons in the case records should be documented.
4. Prescribing antibiotics just in case an infection is present is rarely justified. Where patients are in hospital close observation is usually a better option till the diagnosis is made.
5. **Choice of antibiotics:** This depends on antibiotic susceptibility of the causative organism. There are some infections, which can be treated by one of several drugs. The choice can be based on Toxicity, Efficacy, Rapidity of action, Pharmacokinetics and Cost. *Use the most effective, least toxic and least expensive antibiotic for the precise duration of time needed to cure or prevent infection. Pathogens specific guidance in hospital policy is encouraged.* Before prescribing consider the following:
 - a. Which organism is likely to cause the disease?
 - b. What is the clinical diagnosis and what other steps should be taken to reach diagnostic precision?
 - c. Which antimicrobial agents are available and active against the presumed cause of the illness? Is their range of antimicrobial activity appropriate and what information is available about the likelihood of drug resistance?
 - d. Check for factors, which will affect choice of drug and dose, e.g., renal function, interactions, allergy, pregnancy and lactation.
 - e. Check that the appropriate dose is prescribed. If uncertain, contact Infectious Diseases Physician or clinical microbiologist. Alternatively, check in the formulary.
 - f. What is the duration of treatment?
 - g. Is treatment working?
6. **Clinical Diagnosis:** The antibiotic treatment chosen must be based on presumptive diagnosis made on some assumption regarding the nature of disease. The treating doctor may not have difficulty in choosing the appropriate antibiotic to treat a disease caused by a single microorganisms e.g scarlet fever, typhoid, anthrax, as microbiological diagnosis is implicit in clinical diagnosis. However, diseases such as pneumonia, meningitis and urinary tract infection can be caused by spectrum of bacterial species and doctor may be wrong if he has to guess which antimicrobial agent to use. In such instances one should seek a bacteriological diagnosis.
7. **Empiric Therapy** – If the causative agent is not known and where delay in initiating therapy would be life threatening or risk serious morbidity, antimicrobial therapy based on a clinically defined infection is justified and the following points should be taken into consideration :
 - a. Do not rush to treat.
 - b. Collect the necessary specimens before commencing therapy.
 - c. Cover all possible microbial causes.
 - d. Try to attain synergy.
 - e. Consider possible interaction with other drugs.
 - f. Accuracy of diagnosis should be reviewed regularly and treatment altered/stopped when microbiological results become available.
 - g. Use less costly drugs where possible.
8. The need for antimicrobial therapy should be reviewed on a daily basis. For most infections 5 – 7 days of antimicrobial therapy is sufficient (simple UTI can be adequately treated with 3 days of antibiotic).
9. All IV antibiotics may only be given for 48 – 72 hours without review and consideration of oral alternatives. New microbiological or other information (e.g. fever defervescence for at least 24h, marked clinical improvement; low CRP) should at this stage often permit a switch to oral antibiotic(s), or switch to an IV narrow spectrum alternative, or cessation of antibiotics (no infection present).
10. Once culture reports are available, the physician should step down to the narrowest spectrum, most efficacious and most cost effective option. If there is no step down available, the reason shall be documented and is subjected to clinical audit.
11. Some guiding principles for de-escalation /Escalation:
 - a. If ESBL +ve: drug choice is monotherapy with carbapenems. Preferably choose group I carbapenem. Piperacillin –Tazobactam and Cefoperazone –Sulbactam can be used if in-vitro sensitive and for mild infections.
 - b. Vancomycin should be used only for confirmed MRSA infections and not in MSSA infections.
 - c. In case of Pan drug resistant Pseudomonas /Acinetobacter spp. combination therapy using colistin along with beta-lactams (using PK/PD principles) should be discussed with microbiologist / physician.
12. **Treatment with antibiotic combinations:** In order to avoid antagonism between drugs and undesirable side effects of several antibiotics it is advisable to use a single drug where ever possible. There are situations however, when the use of antibiotic combination is desirable. The situations are:

- a. A temporary expedient during the investigation of an obscure illness.
- b. To prevent the development of bacterial resistance in long term therapy e.g treatment of tuberculosis.
- c. To achieve synergistic effect, e.g. in treating infective endocarditis.
- d. Mixed infection, when one drug is not effective against the pathogen.
- e. To permit a reduction of the dose of potentially toxic drug.

The choice of the drug should be that they act synergistically. The following combinations are synergistic

1. Aminoglycoside and beta-lactam antibiotic.
 2. Beta-lactam antibiotic and beta-lactamase inhibitor.
 3. Beta-lactam antibiotic and Glycopeptide (vancomycin/teicoplanin)
 4. Sulphamethoxazole and Trimethoprim.
14. **Is Treatment working?:** Where treatment is apparently failing, advice from an ID physician/clinical microbiologist should normally be sought rather than blindly changing to an alternative choice of antimicrobial agent. Antimicrobial drug therapy cannot be considered in isolation and other aspects of therapy must be taken into account in judging the effect of treatment. Even an appropriate antibiotic may be ineffective unless pus is drained, septic shock treated and hypoxia and anemia corrected. There are several conditions in which chemotherapy alone cannot eliminate an infection. Obstructive lesions can cause infection to recur, unless they can be dealt with surgically. Also, chemotherapy cannot obviate the necessity for draining an abscess or removing sequestra or calculi. Failure of treatment can also be due to a super-added infection, e.g. phlebitis, development of resistance during therapy or poor tissue penetration.
13. **Laboratory control of the effects of treatment:** Whether treatment has been successful or not is best judged by clinical criteria, but it is useful to know whether the infecting organism has been eliminated. Repeated cultures are, therefore sometimes indicated.

B. Reserve Antimicrobials

These reserve antimicrobials will be made available following a recommendation from the Microbiology Department as per culture report or if included in an antimicrobial policy for a clinical specialty that has been agreed with antibiotic management team. They are held in reserve to maintain their effectiveness in treating certain difficult infections by reducing the spread of microbial resistance and to encourage cost effective prescribing. Before a reserve antibiotic is issued to the ward, the pharmacist is instructed to ascertain the indication and if this falls outside the approved policy, to request that the prescriber consult the ID Physician/clinical microbiologist.

The following criteria has been proposed to protect the Carbapenems and Linezolid from overuse –

1. Severe sepsis as defined by more than one organ failure of new onset and/or elevated serum lactate.
2. Clinical failure of other classes of antibiotics over 48 hours in terms of worsening inflammatory markers, unresolving fever and new/worsening hemodynamic instability.
3. Underlying severe immuno-suppression – Neutropenia, immuno-suppressive therapy, Diabetic Ketoacidosis (DKA) etc.
4. The organism is susceptible to only carbapenems / linezolid, as per culture report.

The following criteria has been proposed for initiating Colistin –

1. Pan-resistant organism as per culture report with evidence of invasive disease – fever/ leucocytosis/elevated procalcitonin (PCT) or culture from a sterile site.
2. Clinical failure of all other classes of antibiotics over 72 hours.

The following criteria has been proposed for initiating Rifampicin –

1. Empiric or proven TB as a part of ATT (4 drug regimen)
- Rifampicin should not be prescribed in our country for any treatment other than for Mycobacteria and for chemoprophylaxis of meningococcal meningitis in clinically indicated population**

Rifampicin should not be prescribed alone as an anti-bacterial.

The following criteria has been proposed for initiating Aminoglycosides –

- I. The focus of infection is not lung or an anaerobic abscess.
- II. Only as a part of initial empiric regimen of a combination therapy – shall step down to single drug after culture report.
- III. Other safer drug options have been ruled out in a culture report.

C. Hypersensitivity

All patients should be asked about drug allergies. This is the responsibility of the doctor caring the patient. If a patient reports a drug allergy clarify whether this is an allergy or drug intolerance. In some cases there will be an overlap between drug allergy and drug intolerance.

- Clinical features suggestive of drug allergy:
One or more symptoms developed during or following drug administration including difficulty breathing, swelling, itching, rash, and anaphylaxis, swelling of the lips, loss of consciousness, seizures or congestion involving mucous membranes of eyes, nose and mouth.

- Clinical features suggestive of drug intolerance:
One or more symptoms developed during or following drug administration including gastrointestinal symptoms e.g. nausea, vomiting, diarrhoea, abdominal pain and feeling faint.

If patients are unable to give an allergy history, the doctor caring in the patient should take reasonable steps to contact someone who can provide a reliable allergy history. It is the prime responsibility of the prescribing doctor to ensure that:

- The allergy box on the patient's drug chart is completed, when a new prescription chart is written or transcribed. If no allergy - specify "No known allergy". The box should be signed and dated. If allergy history cannot be obtained, then specify "history not available." Under no circumstances should the allergy box be left blank. A pharmacist or nurse may complete the allergy box if the allergy status is documented in the clerking in notes.
- The allergy box is completed before prescribing a new drug, except in exceptional circumstances. If patients have a suspected drug allergy then the drug and suspected reaction. Should be documented in the clerking-in notes and the drug chart.

D. Alert Antimicrobials

To Prevent and Control the Emergence and Spread of Antimicrobial-Resistant Micro-organisms in Hospitals" one major strategic goal is to "define guidelines for use of key antibiotics", ("Alert" antibiotics) targeted in these guidelines are **ciprofloxacin, ceftazidime, cefotaxime, ceftriaxone, vancomycin (or teicoplanin), imipenem, levofloxacin, meropenem, moxifloxacin, piperacillin-tazobactam, linezolid (oral/IV), voriconazole, caspofungin, valganciclovir, ertapenem and newer preparations of amphotericin.**

Collectively, these are among the drugs most frequently prescribed irrationally which is largely responsible for the current escalation of antibiotic costs. They also account for a significant proportion of serious antibiotic toxicity including *Clostridium difficile* diarrhoea and CNS toxicity/seizures as well as the emergence of major antimicrobial resistance. Safer, cheaper and equally effective alternatives are often available which allow such agents to be kept in reserve for occasions when there are clear cut microbiological indications. It is critical, therefore, that these Alert antibiotics be prescribed only on the recommendation of senior medical staff or after discussion with the on-call Clinical Microbiologist or ID physician.

E. Alert Antibiotics And Their Indications

1. CIPROFLOXACIN, INTRAVENOUS

Oral ciprofloxacin is well absorbed and this is therefore the preferred route of administration. **Intravenous therapy is only indicated** in the following situations:

- When the patient is unable to swallow or the oral route is otherwise compromised.
- In serious sepsis (e.g. nosocomial pneumonia in ITU) when the recommended dose is 400mg 8 hourly.

Common indications for ciprofloxacin in the Antibiotic Policy, either alone or in combination, are as follows:

- second line therapy in exacerbation of chronic bronchitis
- pyelonephritis
- acute inflammatory infective diarrhoeas
- serious infected diabetic ulcers infected burn wounds with coliforms or Pseudomonas infection present
- treatment of documented or presumed gram-ve bacilli resistant to penicillins or cephalosporins or when the patient is allergic (**history of anaphylactic reaction or rash**) to these agents
- selected haematology patients requiring prophylaxis
- severe acute pelvic inflammatory disease

2. CEFTAZIDIME

Limited use only. Main indication is documented or suspected *Pseudomonas aeruginosa* infection. Other indications currently listed in the Antibiotic Policy are as follows:

- Second line agent in neutropenic patients with septicaemia or pneumonia
- Empiric therapy of CAPD associated peritonitis (not children), 1g IV stat then 125mg/litre in each bag
- Empiric therapy of post operative, post traumatic or shunt associated meningitis
- Empiric therapy of infective exacerbation of cystic fibrosis

3. PIPERACILLIN - TAZOBACTAM

Currently listed in the antibiotic policy for the following:

- Pneumonia or septicaemia in neutropenic patients (+ Gentamicin)
- As a single agent (or in combination with Gentamicin) for treatment of sepsis which has not responded to first line treatment or if it is not appropriate for gentamicin to be added to first-line therapy.

4. CEFTRIAZONE

IV Ceftriazone is currently listed in the antibiotic policy for the following:

- Epiglottitis,
- Brain abscess,

- Bacterial meningitis,
- Pyelonephritis in children,
- Empiric therapy of septicaemia in children,
- In ascites for treatment of sub-acute bacterial peritonitis,
- Skin and soft tissue infections managed via out-patients or the home IV antibiotic programme,
- Acute septic monoarthritis if penicillin allergic,
- Spontaneous bacterial peritonitis.

5. **APPROPRIATE USE OF CARBEPENEMS**

- Very high rates (60-75%) of resistance to 3rd and 4th generation cephalosporins { due to extended spectrum beta-lactamases (ESBL) production } observed in *E. coli* and *Klebsiella* species..
- This pattern of resistance although seen primarily among nosocomially acquired infections, is also seen isolates of *E. coli* and *Klebsiella* species isolated from community acquired infections.
- These strains of bacteria are frequently resistant to other major classes of antibiotics (fluoroquinolones, β -lactam + β -lactamase inhibitor (BL + BLI) combinations and aminoglycosides)
- Carbapenems (imipenem, meropenem and ertapenem), beta-lactam antibiotics with exceptionally broad spectrum of activity, are **the only class** of antimicrobials which remain effective against ESBL-producing isolates of *E. coli* and *Klebsiella* species
- Imipenem is susceptible to degradation by the enzyme dehydropeptidase-1 (DHP-1) located in renal tubules and requires coadministration with a DHP-1 inhibitor cilastatin. Meropenem and ertapenem are administered without a DHP-1 inhibitor.

Indications for carbapenem use:

1. Infections [e.g., bacteremia, pyelonephritis, intra-abdominal infections (peritonitis, cholangitis, abscesses), nosocomial pneumonia etc.] confirmed (by appropriate culture and susceptibility studies) to be caused by Gram-negative bacteria (*E. coli*, *Klebsiella* spp., *Enterobacter* spp., *Pseudomonas aeruginosa*, other non-fermenting Gram-negative bacilli) **resistant to other classes** of antimicrobials and **susceptible only to carbapenems in-vitro**
2. Initial empiric treatment for severe, life-threatening infections (associated with multi-organ dysfunction, septic shock) caused by Gram-negative bacteria.
 - Febrile neutropenia
 - Ventilator associated / nosocomial pneumonia
 - Pyelonephritis / complicated urinary tract infections
 - Complicated intra-abdominal infections

Once the culture and susceptibility reports are available, choose the most appropriate antibiotic based on spectrum of activity, toxicity and cost ('de-escalation').

Indications for Ertapenem use:

Ertapenem has excellent in-vitro and in-vivo activity against ESBL producing Enterobacteriaceae, but lacks activity against *Pseudomonas aeruginosa*, and is therefore **not** considered appropriate for the treatment of conditions like febrile neutropenia and serious nosocomial infections. Ertapenem does not select Carbapenem-resistant *Pseudomonas aeruginosa* (at least in the short-term). Its use should be restricted to severe Gram-negative or polymicrobial community acquired infections confirmed to be caused by susceptible bacterial pathogens. Hence, this drug may be recommended as the initial choice for ESBL producing strains of *E. coli* and *Klebsiella* spp..

Indication of Meropenem and Imipenem

Meropenem and Imipenem regarded as third line agents and are reserved for:

- serious infections due to multiple resistant strains (e.g. ESBL)
- empiric use in the seriously ill patient in either ITU or Haematology
- the treatment of infective exacerbations in Cystic fibrosis (CF)
- severe acute necrotising pancreatitis
- Outside these clinical settings it should only be used after consultation with a Clinical Microbiologist or ID physician.

Unlike imipenem, meropenem has not been associated with CNS toxicity. Also, it is administered by convenient IV bolus injection. Clinicians must be aware that mechanism of resistance to meropenem and imipenem are different and hence in-vitro test for one carbapenem cannot be used to interpret the other.

Dose

Imipenem*: 500 mg i.v. Q6H

Meropenem: 1 g i.v. Q8H

Ertapenem: 1 gm i.v. /i.m. Q 24H

***Note Anti-infective sub-committee recommends use at a more frequent dosing interval. They believe that optimum plasma concentrations are more reliably maintained with 6-hourly dosing.**

6. *LINEZOLID (IV AND ORAL FORMS)*

Linezolid should only be prescribed after consulting an ID specialist or clinical microbiologist and a mandatory order form completed.

- Restricted indications including infections due to proven glycopeptide-insensitive *Staphylococcus aureus* or vancomycin-resistant enterococcus (currently uncommon).
- To enable IV/oral switch from IV vancomycin (used for MRSA or MRSE) to oral linezolid (when patient's discharge is possible and continuation treatment using combination rifampicin /trimethoprim is inappropriate).
- May be an option in surgical site infections (e.g. large bowel surgery, vascular surgery, etc).
- Poor IV access and a glycopeptide is indicated.
- Use in out-patient home parenteral antibiotic therapy for skin and soft tissue infections as an alternative to IV teicoplanin.
- Rare cases of proven hypersensitivity/allergy to the glycopeptides.

7. *VANCOMYCIN*

Vancomycin is the drug of choice for **in-patient** treatment of the following infections.

- Serious (e.g. bacteraemia, osteomyelitis) coagulase negative staphylococcal and MRSA infections and penicillin resistant enterococcal infections
- Empiric therapy in febrile neutropenic patients not responding to first line therapy
- Continuous ambulatory peritoneal dialysis (CAPD) associated peritonitis
- Prosthetic valve endocarditis

8. *TEICOPLANIN*

Teicoplanin is a suitable alternative to vancomycin for all indications for Vancomycin except meningitis:

- patients receiving **out-patient/home** parenteral therapy with glycopeptides after loading dosages
- inability to tolerate vancomycin
- oncology/haematology patients
- Rare cases of vancomycin resistant and teicoplanin sensitive strains.

Chapter 5

Preventive Strategies for Healthcare Associated Infections

A. Healthcare Associated Infections

Health Care Associated Infections or HCAI are a worldwide phenomenon. HCAI have been defined variously at different times and by different organizations. Current definitions incorporate infections which were neither incubating nor did they manifest or present, during the period of admission in patients admitted in the hospital but were present on or after the 3rd calendar day of admission, (the day of hospital admission being calendar day 1).

B. Reducing the risk of Health care associated infections

B1. Development of an effective Infection Prevention and Control Program

Infection Prevention and Control Programs are directed towards patient safety and health care professionals' safety. Reducing the preventable part of health care associated infections (HCAI) is central to any Infection Control program.

An effective Infection Prevention and Control Program would have the following components:

1. Infection Control Committee with its defined role and constituents
2. Infection Control Core Team for day to day working with defined roles
3. Infection Control Manual with policies, guidelines, recommendations and working protocols including activities and practices under the program with Hand hygiene and Standard Precautions being the mainstay
4. Annual Plan for each healthcare setup with prioritization based on risk matrix for that unit and review
5. Should incorporate Antimicrobial Stewardship programs

B2. Hand-hygiene and Standard Precautions'

Health care workers and professionals anywhere and at all levels should be well oriented to concepts of hand hygiene. Practicing 'Standard Precautions', prevents direct contact with all body fluids (including blood), secretions, excretions, non-intact skin (including rashes), and mucous membranes.

Hand hygiene in the form of tap, sink and appropriate antiseptic/ rubs for washing or hand-rub or surgical scrub should be facilitated. At least hand rubs should be available in all patient care areas including patient's bed side or easily available within vicinity.

Indications for hand washing and hand antisepsis should be made known amongst all engaged in providing patient care. Protocols and procedures of any area should always include hand hygiene as applicable and these should be mandatory step.

B3. Antimicrobial Stewardship Program

Antimicrobial Stewardship Program shall form another main focus of the Infection Prevention and Control Program. This shall include all components of antimicrobial stewardship so as to stress upon advocacy of safe use of antimicrobials, which shall be strengthened, with periodic review of antimicrobial guidelines and implementation locally in each of the health care setups.

B4. Educational Programs and Strategies

Appropriate educational material should be made available to all. These shall be based upon recent evidences and part of relevant national and international guidelines and appropriately indigenized for effective implementation. This would be augmented by periodic CME or educational interactive programs and awareness drives. Local Health care setup should provide antimicrobial susceptibility patterns, appropriate usage of antimicrobials and have updates on antimicrobials communicated to all relevant personnel in patient care, locally and periodically. Specific infectious diseases and their prevention and control awareness should be made available as and when required to relevant staff locally and may be extended to community if so desired by the health departments of that district/city/area.

B5. Notification All relevant information as required by law on communicable diseases would be notified as appropriate to relevant authority. In case of specific reports from public health agencies requiring action on their recommendations, appropriate action should be taken.

B6. Prophylaxis including Immunization

Staff should be immunized against diseases, which have risk of transmission through exposure from patients and to limit transmission of diseases from healthcare workers to patients. Immunisation in high-risk group may be required for influenza, meningococcal infections among exposure prone healthcare workers in outbreak situations, hepatitis B vaccination for all staff, varicella vaccine to high-risk group etc. Among the diseases that have potential of being transmitted from healthcare workers to patients typhoid vaccine should be included among the food handling staff. Immunise all health care workers and others involved in handling of bio-medical waste for protection against diseases including Hepatitis B and Tetanus that are likely to be transmitted by handling of bio-medical waste. All the under trainee staff including medical and nursing students should be immunized for potential occupational risk exposures (e.g. hepatitis B vaccination to the students).

Chapter 6

Monitoring Antimicrobial Use

A. Background

World Health Organization's 2014 report on global surveillance of antimicrobial resistance reveals that antibiotic resistance is no longer a prediction for the future; it is happening right now, across the world, and is putting at risk the ability to treat common infections in the community and hospitals. It is an increasingly serious threat to global public health that requires action across all government sectors and society.

There are high proportions of antimicrobial resistance (AMR) amongst bacteria that cause common infections (e.g. urinary tract infections, pneumonia, bloodstream infections) throughout the world. Resistant microorganisms (including bacteria, fungi, viruses and parasites) are able to survive attack by antimicrobial drugs, such as antibacterial drugs (e.g., antibiotics), antifungals, antivirals, and antimalarials, so that standard treatments become ineffective and infections persist, increasing the risk of spread to others.

The evolution of resistant strains is a natural phenomenon the use and misuse of antimicrobial drugs accelerates the emergence of drug-resistant strains. The evolving public health threat of AMR is driven by both appropriate and inappropriate use of antimicrobial agents. Overuse plays an important role in the emergence of AMR. Paradoxically, underuse through inappropriate choice, inadequate dosing, poor adherence to treatment, and substandard antimicrobials, also plays an important role in the emergence and spread of AMR. Hence, there is need to monitor the use of antimicrobials at all levels of health care, study the antimicrobial use practices in various infections and behavior of stakeholders for antibiotic use and resistance.

B. Need For Surveillance To Track Antimicrobial Use And Resistance

Increasing levels of antimicrobial resistance correlate with inappropriate antibiotic use as shown at the population and individual level. Therefore, our goal should be to use antimicrobials rationally and for that we need to know how antimicrobials are being used. Monitoring of antimicrobial use is a crucial component to identify targets for improving antimicrobial use and to further correlate with antimicrobial resistance surveillance programmes. World Health Organization (WHO) highlights the establishment of effective, epidemiologically sound surveillance of antimicrobial use and AMR among common pathogens in the community, hospitals and other health-care facilities as one of the key public health priorities. Surveillance systems are required to understand trends in antibiotic use and AMR, as well as the long-term temporal associations between these two in different areas. Tracking antimicrobial use, and the emergence and spread of resistant strains of bacteria provides information, insights, and tools needed to guide policy and to evaluate measures taken to promote appropriate antimicrobial use at all levels, from local to global. Data could also stimulate a sense of urgency to act. Improving antibiotic use is the key feature in efforts to contain AMR. Strategies for interventions to reduce antibiotic use have to be prioritized and customized based on local realities. Data from surveillance could help in identifying priorities and processes and in documenting a baseline for monitoring effects of interventions.

C. Standardized Methodology And Outcome Measures

The use of a standardised methodology allows meaningful comparisons over time and between different facilities or countries. Expression of antibiotic consumption should be in international accepted formats. Therefore, we need to have a methodology and a common unit of measurement in each country in order to assure the comparability of the data.

The Anatomical Therapeutic Chemical (ATC) classification and the Defined daily Dose (DDD) as a measuring unit have become **the gold standard** for international drug utilization research. ATC/DDD methodology of classification is a tool for drug utilization research in order to improve quality of drug use. It is an international language for grouping of drugs and measuring consumption of drug use. The WHO recommends this methodology of classification as their international standard for drug utilization studies. This methodology is widely used in drug catalogues, drug safety assessment and drug utilization and pharmacoepidemiology. The ATC/DDD system is a tool for exchanging and comparing data on drug use at international, national or local levels. When monitoring antimicrobial consumption in pediatric setting, total antibiotic events

C1. The ATC Classification

The ATC system was initiated in the 1970s by the Norwegian Medicinal Depot, and is now coordinated by the World health Organization (WHO) Collaborating Centre for Drug Statistics methodology, established in Oslo in 1982. The centre revises the ATC codes as necessary and maintains an online database and published index. Drugs are divided into different groups according to the organ or system on which they act and/or their therapeutic and chemical characteristics. Each drug is assigned at least one ATC code, which are classified into groups at five different levels. Table 1 below shows an illustration using amoxicillin as an example.

Table1: Classification of amoxicillin of the Anatomical Therapeutic Chemical (ATC) classification system

ATC Classification	ATC Category	Description
J	General anti-infectives for systemic use	1 st level, anatomical main group

J01	Antibacterials for systemic use	2 nd level, therapeutic main group
J01C	Beta-lactam antibacterials, penicillins	3 rd level, therapeutic/pharmacological subgroup
J01C A	Penicillins with extended spectrum	4 th level, chemical/therapeutic/pharmacological subgroup
J01C A04	Amoxicillin	5 th level, subgroup for chemical substance

C2. Defined Daily Dose

To facilitate the ability to compare consumption information across time and geography, a technical unit of measurement was created for use in conjunction with the ATC classification. It is referred as the Defined Daily Dose (DDD) and assigned to each drug at the 5th level (chemical substance) classification. It is defined by the ATC as the assumed average maintenance dose per day for a drug used for its main indication in adults. For antibiotics, the main indication is moderate to severe infections. The WHO Collaborating Centre using established principles assigns ATC and DDDs. Different DDDs may be assigned for different drug formulation (ie, parenteral versus oral). Table 2 provides some examples of DDDs for antibiotics.

Table 2: Examples of Defined Daily Doses

ATC Classification	ATC Drugs	Defined Daily Dose
J01C A04	Amoxicillin	1 g (oral or parenteral)
J01M A06	Norfloxacin	0.8 g (oral)
J01M A02	Ciprofloxacin	1 g (oral) 0.5 g (parenteral)
J01F F01	Clindamycin	1.2 g(oral) 1.8 g (parenteral)
J01C A12	Piperacillin	1.4 g (parenteral)

ATC – Anatomical Therapeutic Chemical

DDDs are useful for measuring and comparing volumes of drug use. DDDs should not be considered as the “correct” dose but as an international compromise on review of available documentation.

C3. How to use the ATC/DDD classification to quantify the antibiotic consumption?

- For OPD from administrative prescription claims data,** If data are available at the individual claim level and the antibiotic is identified or mentioned, it is a fairly straightforward process to apply the ATC classification and convert into a number of DDDs. For example, if the prescription indicates that the particular patient was dispensed 14 ciprofloxacin 500 tablets from a particular pharmacy. The number of DDDs is calculated by multiplying the quantity by the DDD conversion factor. In this example, the strength of one tablet is 500 mg and the ATC/DDD is 1 g for ciprofloxacin. Each 500 mg tablet is equivalent to 0.5 DDD. Multiplication of the quantity dispensed (14 tablets) by a conversion factor of 0.5 equals to total of 7 DDDs dispensed from this prescription. Data can then be collated, expressed and evaluated based on any other prescriptions record and then merged.
- Hospital pharmacy data:** Most hospital pharmacies have the ability to express their drug dispensing information in monthly collation of numbers of drugs dispenses by type of drug. ATC/DDD system can be applied in a similar fashion to the above out-patient prescription example. The usual divisions within a hospital are wards or various departments. Consumption data can be collated for each department separately from the pharmacy records.

C4. Expressing consumption information

Most commonly, units for antibiotic consumption include DDD per 1000 inhabitant-days for out-patient data and DDD per 100 bed-days in hospitals.

Because the ATC/DDD system is continuously being modified, it is essential that the version (year) of ATC classification in use is clearly identified. The most recent classification is usually used. However, one must be aware of changes in the classification or DDD assignment when comparing with earlier information.

D. Situation In Developing Countries

There are wide variations between regions and countries, in their capacity to carry out surveillance system. In resource-poor countries with comparatively weak health systems, there are constraints related to infrastructure, trained personnel, networking and coordination. Currently it is not possible in resource-poor countries to quantify the effects of AMR on the individual or the community, because of lack of availability of good quality data in sufficient quantities. Therefore, developing validated, reproducible and sustainable surveillance methodologies to quantify AMR and antibiotic use in the community, and to inform the development of interventions and evaluate their impact is a priority.

The methods for obtaining data are often problematic, especially with regards to data on antimicrobial use. About 80% of antibiotics are used in the community and the rest are used in hospitals. There is a lack of community-based databases on AMR and antibiotic use in developing countries. Moreover, antibiotics can be obtained easily from private retail pharmacies without prescription and pharmacists also advise and dispense antibiotics to patients. Therefore, developing a methodology, which is reproducible and sustainable, is needed to measure antimicrobial use in the community for developing country.

High-end Antibiotic Monitoring Sheet

Name of the Hospital		
High End Antibiotic Monitoring Form		
Meropenem, doripenem Imipenem, ertapenem Colistin, tigecycline	linezolid daptomycin teicoplanin vancomycin	Patient details
Antibiotic used:		
Indication:		
Date started:		
REVIEW		
• Second day:		
• Fifth day:		
• Tenth day:		
Comments by Infection Control team:		
Feed back given to the doctor (if necessary):		

Surgical Prophylaxis Monitoring Sheet

Name of the Hospital	
Surgical antibiotic prophylaxis monitoring sheet	
Patient Details	Date of Admission: Name of Surgeon:
Date of Surgery:	
Type of surgery:	
Date of Discharge:	
Prophylactic antibiotic used:	
Dose:	
Duration:	
Reason if antibiotic given for more than the recommended duration:	
Signature of the Doctor	
Comments by Infection control Team	
Feed back given to the doctor (if necessary)	

Chapter 7
Dosage Guide For Commonly Used Antimicrobial Agents

ANTIBIOTICS	ADVERSE REACTION	ROUTE	PAEDIATRIC DOSE	ADULT DOSE
Amikacin	Nephrotoxicity, Ototoxicity	Intravenous	15-22.5 mg/Kg/day in 2-3 doses	15mg/Kg/day q 8-12 hours, max doses 1.5mg/Kg
Amoxicillin	Fever, rash, diarrhea, abdominal cramps, AST ALT elevation.	Oral	20-50mg/Kg/day, 3-4 doses	250-500mg q 8 hourly
Amoxicillin-clavunate (co-amoxycrav)	Rash, diarrhea, abdominal, AST ALT elevation	Oral, Intravenous	40mg/kg/day (amoxicillin) in 2 doses 90mg/kg/day if penicillin resistant <i>S. pneumoniae</i> suspected in otitis media 100mg/kg/day	375mg 8hourly 625-1000mg 12 hourly
Ampicillin	Hypersensitivity reaction, nausea, diarrhea, exfoliative dermatitis, seizures, precipitates infectious mononucleosis rash, interstitial nephritis.	Intravenous or Oral	100-400 mg/kg/day in 4 doses (IV)	500 mg-1gm q 6 hourly
Azithromycin	Leukopenia, transient elevation of liver enzymes, renal toxicity.	Oral	10 mg/kg/day once daily Enteric fever 20 mg/kg/day once daily	500mg daily
Azetronam	Rash, Diarrhoea , vomiting, AST, ALT elevation	Intravenous	30 - 120mg/kg/day Q 6-8 hourly In cystic fibrosis max dose 200 mg/kg/day	1-2g q 8 hourly, Max dose 8gm in 24 hours
Benzathine penicillin	Hypersensitivity and Jarisch Herxheimer reaction, haemolytic anemia, seizures with high doses in renal failure	Intramuscular	1,200,000 units(>30 Kg) 600,000 units (<30 Kg)	1.2-2.4 million units/dose
Cefadroxil	Rash eosinophilla	Oral	30 mg/kg/day in 2 doses	500mg bid or 1 g bid
Cefazolin	Leukopenia, eosinophilia, rash, transient elevation of liver enzymes renal toxicity	Intravenous	100 mg/kg/day 3-4 divided doses	0.52gm q 6-8 hourly
Cefepime	Same as third generation cephalosporins. Adjust dose in renal failure.	Intravenous		1-4gm/day 2-3 doses
Cefixime	Diarrhoea, Leukopenia, renal toxicity, transient elevation of liver enzymes.	Oral	15mg/kg/day in 2 divided doses, 20mg/kg/day in 2 divided doses for enteric fever.	400mg/day in 1-2 divided doses.
Cefotaxime	Arrythmia, transient elevation of liver enzymes, renal toxicity.	Intravenous	100mg/kg/day in 3-4 divided doses, 200mg/kg/day in 4 divided doses for meningitis	1-2gm 6-8 hourly
Ceftazidime	Hypersensitivity reaction, dizziness, rash, diarrhea, colitis, exfoliative dermatitis, thrombocytopenia	Intravenous Intramuscular	75-100mg/kg/day in 3 divided doses 100mg/kg/day in meningitis (IV)	1-2g q 8-12 hourly (IV)
Ceftriaxone	Gall bladder sludging , transient elevation of liver enzymes, renal toxicity	Intravenous	50-100 mg/kg/day in 2 divided doses Meningitis 100mg/kg/day in 2 divided doses	1-2gm q 12-24 hourly
Cefuroxime	Leukopenia, eosinophilia, allergic reaction, transient elevation of liver enzymes , renal toxicity	Intravenous	75-100mg/kg/day in 3 divided doses	750mg- 1.5g q 8 hourly

ANTIBIOTICS	ADVERSE REACTION	ROUTE	PAEDIATRIC DOSE	ADULT DOSE
Cefuroxime	Leukopenia, eosinophilia, allergic reaction, transient elevation of liver enzymes , renal toxicity	Oral	20-30mg/kg/day in 2 divided doses	250-500md bid
Cephalexin	Transient neutropenia, AST and ALT elevation, arthralgia, rash, eosinophilia.	Oral	30-40mg/kg/day in 3 divided doses	250-500mg q 8 hourly
Chloramphenicol	Bone marrow suppression, aplastic anaemia, grey baby syndrome, hemolysis in G6PD deficiency	Oral Intravenous	75-100mg/kg/day in 4 divided doses Avoid in infants less than 3 months	50mg/kg/day in 4 divided doses
Ciprofloxacin	Nausea, vomiting, abdominal discomfort, arthralgia, photosensitivity transient elevation of liver enzymes	Oral Intravenous	20-30mg/kg/day in 2 divided doses	250-750mg q 12 hourly
Clarithromycin	Transient elevation of liver enzymes, renal toxicity, nausea, abdominal cramps	Intravenous Oral	15mg/kg/day in 2 divided doses	250-500mg bid
Clindamycin	Diarrhea, nausea, pseudomembranous colitis, skin rash, Erythema multiforme , raised ALT AST, thrombocytopenia, leucopenia	Oral Intravenous	40-60mg/kg/day in 3-4 divided doses	150-300 mg q 6-8 hourly (oral, iv) Severe infections 300-600 mg 8 hourly IV
Cloxacillin	Dose related neutropenia, elevated AST, ALT, Cholecystitis interstitial nephritis.	Oral Intravenous	50-100mg/kg/day in 3-4 divided doses. 100-200mg/kg/day divides q 6 hourly	250-500mg/kg/day in 3-4 divided doses 1-2 gram q 6 hourly
Cotrimoxazole	Megaloblastic anaemia, disturbance, rash, erythema mutliforme major/minor	Oral	5-10mg/kg/day in 2 divided doses (5-0 mg trimethoprim) 20mg/kg/day in 4 divided doses in <i>Pneumocystis jirovecii</i> pneumonia	160mg (Trimethoprim) bid
Ertapenem	Diarrhoea, nausea, vomiting, headache, hallucination, seizures, arrhythmia, pseudomembranous colitis, dose reduction in renal failure	Intravenous Intramuscular	3-12 years: 15mg/kg/day twice daily. (not to exceed 1gm/day)	13 years and above 1gm IV infusion/ IM once daily in 3-5 ml of lidocaine CI if hypersensitivity to lidocaine/β lactam
Erythromycin	Arrhythmia Jaundice	Oral	40on 4 divided doses	250-500mg q 6 hourly
Furazolidine	Avoid alcohol, tyramine containing food, Mao inhibitors, Nausea headache, dizziness, fall in BP, urticarial, safety in pregnancy unknown	Oral	100mg 3-4 times a day 5mg/kg in 3-4 divides doses (not below one year)	100mg 3-4 times a day
Gentamicin	Nephrotoxicity ototoxicity and optic neuritis	Intravenous Intramuscular	5-7.5 mg/kg/day in 2-3 divided doses	1.3-6 mg/kg/day in 3 divided doses
Imipenemcilastin	Nausea, diarrhea, rash	Oral	Intravenous	500mg once daily
Linezolid	Peripheral and optic neuropathy, thrombocytopenia, hypertension, myelosuppression, colitis.	Oral Intravenous	10mg/kg/dose 6-8 hourly (oral, IV)	400-600 mg q 12 hourly
Meropenem	Hypotension, transient elevation of liver enzymes, renal modification in renal failure	Intravenous Oral	7.5 mg/kg/day/dose (IV) divided doses in meningitis	1.5-3gm/day in 3 divided doses 6gm/day in meningitis
Metronidazole	Nausea, metallic taste, disulfuran like reaction with alcohol, peripheral neuropathy	Intravenous Oral	7.5 mg/kg/day dose 3 times/day 30-50mg/kg/day in 3 divided doses for liver abscess	500-700 q 8 hourly
Nalidixic acid	Hepatotoxicity, myalgia, leukopenia, vertigo, rash, dizziness, pseudotumor cerebri, seizure, avoid in G6PD deficiency	Oral	8 mg/kg/day in 2 divided doses	1gm 4 times/day

ANTIBIOTICS	ADVERSE REACTION	ROUTE	PAEDIATRIC DOSE	ADULT DOSE
Nitofurantoin	Discoloration of urine, vertigo, rash, methemoglobinemia, cholestatic jaundice, hepatocellular damage and neuropathy. Avoid at term and labour.	Oral	8 mg/kg/day in 2 divided doses	50-100 mg q 6 hourly (5-7mg/kg/day in 4 divided doses max dose 400mg)
Norfloxacin	Sam as quinolones	Oral	20-30 mg/kg/day in 2 divided doses	200-400 mg twice daily
Ofloxacin	Leukopenia, transient of liver enzymes, renal toxicity. May precipitate psychosis/seizures, photosensitivity.	Oral Intravenous	20 mg/kg/day in 2 divided doses	200-400 q 12 hourly
Penicillin G	Hypersensitivity reaction like anaphylaxis rare. nonfatal reactions are like serum sickness, rash contact dermatitis seen in 1 in 1000 adults. Jarisch Herxheimer reaction, haemolytic anaemia with high doses	Oral Intravenous	50,000units/kg/dose 6 hourly (Oral) 200,000-400,000 units/kg/day in 4 divided doses (IV)	2-24 million units day in divided doses q 4-6 hours (IV)
Penicillin V	Rash, haemolytic anaemia interstitial nephritis, seizure with high doses.	Oral	20-50 mg/kg/day in 4 divided doses	250-500 mg every 6-8 hourly.
Piperacillin – Tazobactam	Leukopenia, transient elevation of liver enzymes, renal toxicity.	Intravenous	200-400mg/kg/day in 3-4 divided doses	4.5 gm q 8hourly
Teicoplanin	Hypersensitivity reactions, rash, less nephrotoxic as compares to Vancomycin	Intravenous Intramuscular	10mg/kg/day /dose every 12 hours for 3 doses the 10mg/kg/day once daily	400mg once daily (6-30mg/kg/day)
Tigecycline	Nausea, vomiting, allergic reactions, photosensitivity, pseudo tumor cerebri, pancreatitis. No dose adjustment to renal failure	Intravenous	Above 10 years	100mg followed by 50mg every 12 hourly infusion over 30-60 minutes.
Vancomycin	Red man syndrome, oto-toxicity, nephrotoxicity	Intravenous	40-60 mg/kg/day in 3-4 divided doses	0.5gm q 6 hourly or 1gm q 12 hourly

Drug doses in Pediatric Age group

Drug name	Dose	Frequency	Maximum dose	Comments
Cefepime Infants >14 days of age and Children >40 kg in weight	50 mg/kg	q 12 h		
Ceftazidime Infants and children <12 years	100–15 mg/kg/d	Divided q 8 h	6 g	
Cefotaxime Infants and children a) < 50 kg b) >12 years and >50 kg	100–200 mg/kg/d 1–2 g	Divided q6-8 h q 8 h	2 g	
Ceftriaxone Infants and children	50-75 mg/kg/d	Divided q 12 h	2 g	
Vancomycin Infants and children	40 mg/kg/d	Divided q 6-8 h	2 g	
Linezolid Infants and children <12 years Children >12 years of age and adolescents	10 mg/kg 10 mg/kg	q 8 h q 12 h		
Piperacillin	100-300 mg/kg/d	q 8 h	4 g	
Ciprofloxacin	20–30 mg/kg/d	divided every 12 h	800 mg	
Levofloxacin Children 6 months to 5 years of age Children >5 years of age	10 mg/kg 10 mg/kg	q12 h q 24 h	500 mg	

Amikacin Infants and children	15–22.5 mg/kg/d	q 24 h		
Gentamicin	5-7.5 mg/kg/d	q 24 h		If normal renal function
Meropenem Infants ≥3 months of age and children	20 mg/kg	q 8 h	1 g	
Imepenem-cilastin Infants < 3 months of age Infants > 3 months of age and children	100 mg/kg/d 60-100 mg/kg/d	Divided q 6 h Divided q 6 h	4 g	
Fluconazole	12 mg/kg/d	q 24 h		
Anidulafungin Children 2– 17 years of age	1.5 mg/kg/day			Limited experience
Micafungin Children >2 years of age	1–4 mg/kg/day		150 mg	Limited experience
Caspofungin Children 3months-17 years	loading dose of 70 mg/m ² /day on day 1 followed by 50 mg/m ² /day thereafter		70 mg; may increase to 70 mg/m ² /day if clinical response is inadequate.	
Clindamycin	10 mg/kg/dose	q 6-8 h	900 mg Q 8	

Chapter 8

Link To National Programme Current Guidelines For Treatment Of Specific Infections

(HIV, RTI& STI, Tuberculosis, Malaria, Dengue, Kala azar, Leptospirosis, Leprosy, Japanese Encephalitis, Filariasis)

National AIDS control programme (NACP):

In 1986, following the detection of the first AIDS case in the country, the National AIDS Committee was constituted in the Ministry of Health and Family Welfare. In 1992 India's first National AIDS Control Programme (1992-1999) was launched, and National AIDS Control Organisation (NACO) was constituted to implement the programme. During NACP-II (1999-2006), the free ART (Antiretroviral therapy) programme was rolled out on April 1, 2004 in eight government hospitals in six high prevalence states has since been scaled up to 400 ART centres where in a total of around 16,00,000 patients have been registered in HIV care and nearly 6,00,000 patients are currently on ART. The national programme provides free First line, alternate First line and Second line antiretroviral drugs to adults and children as per their eligibility. NACO makes available with updated related infections antimicrobial therapy guidelines on regular basis.

Following links can be referred for further details:

NACO Guidelines for Antiretroviral therapy for HIV-infected Adults and Adolescents 2013
<http://www.naco.gov.in/upload/Policies%20&%20Guidelines/Antiretroviral%20Therapy%20Guidelines%20for%20HIV-Infected%20Adults%20and%20Adolescents.pdf>

National Guidelines on Second-line and Alternative First-line ART For Adults and Adolescents 2013
<http://www.naco.gov.in/upload/Policies%20&%20Guidelines/National%20Guidelines%20on%20Second-line%20and%20Alternative%20First-line%20ART%20For%20Adults%20and%20Adolescents%20May%202013.pdf>

Guidelines for Prevention and Management of Common Opportunistic Infections/Malignancies among HIV-Infected Adult and Adolescent 2007

<http://naco.gov.in/upload/Policies%20&%20Guidelines/7-Guidelines%20for%20Prevention%20and%20Management%20of%20common%20opportunistic%20infections.pdf>

National Guidelines on Prevention, Management and Control of Reproductive Tract Infections and Sexually Transmitted Infections 2014
<http://www.naco.gov.in/upload/2014%20mslns/National%20RTI%20STI%20technical%20guidelines%20Sep2014.pdf>

Revised National Tuberculosis Control Programme (RNTCP) DOTS-PLUS:

The Revised National TB Control Programme (RNTCP), an application of the WHO recommended Directly Observed Treatment, Short Course (DOTS) strategy was launched in 1992 with the objective of detecting at least 70% of new sputum positive TB patients and curing at least 85% of such patients.

However the emergence of resistance to drugs used to treat tuberculosis, and particularly multidrug-resistant TB (MDR-TB), has become a significant public health problem in a many countries. In India, the available information from the several studies conducted in the past suggests that the rate of MDR-TB is relatively low in India. Yet this translates into a large absolute number of cases. Specific measures are being taken within the Revised National Tuberculosis Control Programme (RNTCP) to address the MDR-TB problem through appropriate management of patients and strategies to prevent the propagation and dissemination of MDR-TB.

Revised National Tuberculosis Control Programme (RNTCP) DOTS-PLUS Guidelines 2010–
<http://health.bih.nic.in/Docs/Guidelines/Guidelines-DOTS-Plus.pdf>

National Vector Borne Disease Control Programme (NVBDCP):

NVBDCP Is an umbrella programme for prevention and control of vector borne diseases viz. Malaria, Japanese Encephalitis (JE), Dengue, Chikungunya, Kala-azar and Lymphatic Filariasis. Out of these six diseases, two diseases

namely Kala-azar and Lymphatic Filariasis have been targeted for elimination by 2015. Malaria, Filaria, Japanese Encephalitis, Dengue and Chikungunya are transmitted by mosquitoes whereas Kala-azar is transmitted by sand-flies. The transmission of vector borne diseases depends on prevalence of infective vectors and human vector contact, which is further influenced by various factors such as climate, sleeping habits of human, density and biting of vectors etc.

Following links can be referred for further details:

Dengue Clinical Management Guidelines 2014
<http://nvbdcp.gov.in/Doc/Dengue-National-Guidelines-2014.pdf>

Diagnosis and Treatment of Malaria Guidelines 2013
<http://nvbdcp.gov.in/Doc/Diagnosis-Treatment-Malaria-2013.pdf>

Operational Guidelines on Kala-Azar (Visceral Leishmaniasis) Elimination in India 2015
<http://nvbdcp.gov.in/Doc/operational-guideline-KA-2015.pdf>

National Guidelines Diagnosis, Case Management Prevention and Control of Leptospirosis 2015
<http://www.ncdc.gov.in/writereaddata/mainlinkfile/File558.pdf>

Operational Guidelines on Disability Prevention & Medical Rehabilitation under National Leprosy Eradication Program 2012
[http://nlep.nic.in/pdf/Guidelines%20for%20Primary,%20Secondary%20and%20TLC%20\(Atul%20Shah%20247.2012.pdf](http://nlep.nic.in/pdf/Guidelines%20for%20Primary,%20Secondary%20and%20TLC%20(Atul%20Shah%20247.2012.pdf)

Guidelines on clinical management of acute encephalitis syndrome including Japanese encephalitis 2009
http://nvbdcp.gov.in/Doc/Revised%20guidelines%20on%20AES_JE.pdf

Guidelines on Filariasis Control in India & Its Elimination
<http://nvbdcp.gov.in/doc/guidelines-filariasis-elimination-india.pdf>

Chapter 9
Case Definitions and Diagnosis for Common Infections

DIARRHEA

“Diarrhea” is an alteration in a normal bowel movement characterized by an increase in the water content, volume, or frequency of stools. A decrease in consistency (i.e., soft or liquid) and an increase in frequency of bowel movements to ≥ 3 stools per day have often been used as a definition for epidemiological investigations.

“**Infectious diarrhea**” is diarrhea due to an infectious etiology, often accompanied by symptoms of nausea, vomiting, or abdominal cramps.

“**Acute diarrhea**” is an episode of diarrhea of <14 days in duration. “**Persistent diarrhea**” is diarrhea of >14 days in duration.

If diarrhoea present WITH vomiting, low grade fever with no mucus in stools think of **viral infection**.

If diarrhoea present WITH vomiting, abdominal cramps, blood and mucus in stools WITH fever, think of **bacterial infection**.

If diarrhoea present WITH blood and mucus in stool WITH no fever, think of **amoebiasis**.

If profuse diarrhoea present (rice water stools) WITH vomiting, think of **cholera**.

If diarrhoea present WITH excessive vomiting (especially if in more than one member of the household or group) think of **food poisoning**.

ENTERIC FEVER

Acute non-complicated disease: Acute typhoid fever is characterized by prolonged fever, altered bowel function (constipation in adults, diarrhea in children), headache, malaise and anorexia. Bronchitic cough and exanthem (rose spots on chest, abdomen, and trunk) may be seen in the early disease.

Complicated disease: Severe disease can have abdominal pain, occult blood in stools, malena, perforation peritonitis, myocarditis, pneumonitis and enteric encephalopathy.

Case definition

Confirmed case of typhoid fever

A patient with fever (38°C and above) that has lasted for at least three days, with a laboratory-confirmed positive culture (blood, bone marrow, bowel fluid) of *S. typhi*.

Probable case of typhoid fever

A patient with fever (38°C and above) that has lasted for at least three days, with a positive serodiagnosis or antigen detection test but without *S. typhi* isolation.

SPONTANEOUS BACTERIAL PERITONITIS

The diagnosis of spontaneous bacterial peritonitis (SBP) is made in transudative ascitis with increased absolute polymorphonuclear leukocyte (PMN) count (i.e., ≥ 250 cells/ mm^3 [$0.25 \times 10^9/\text{L}$]) and without an evident intra-abdominal, surgically treatable source of infection. An abdominal paracentesis must be performed and ascitic fluid must be analyzed before a confident diagnosis of ascitic fluid infection can be made.

ACUTE PANCREATITIS

Acute inflammation of pancreas, usually caused by alcohol or gallstone migrating through the common bile duct. Less commonly caused by trauma, infections like mumps, ascariasis and drugs like diuretic, azathioprine, etc.

Routine use of **prophylactic antibiotics in patients with severe AP is not recommended**. The use of antibiotics in patients with sterile necrosis to prevent the development of infected necrosis is not recommended.

Infected necrosis should be considered in patients with pancreatic or extrapancreatic necrosis who deteriorate or fail to improve after 7 – 10 days of hospitalization. In these patients, either (i) initial CT-guided fine-needle aspiration (FNA) for Gram stain and culture to guide use of appropriate antibiotics or (ii) empiric use of antibiotics after obtaining necessary cultures for infectious agents, without CT FNA, should be given.

In patients with infected necrosis, antibiotics known to penetrate pancreatic necrosis, such as carbapenems, quinolones, and metronidazole, may be useful in delaying or sometimes totally avoiding intervention, thus decreasing morbidity and mortality.

ACUTE BACTERIAL MENINGITIS

Acute bacterial meningitis (ABM) is a potentially life-threatening neurological emergency.

Patients generally presents with short history of high-grade fever with prominent headache, neck stiffness, photophobia, nausea, vomiting and altered mental status (lethargy to coma). Infants, elderly, and immunocompromised patients may show only mild behavioural changes with low-grade fever and little clinical evidence of meningeal inflammation.

Patients with ABM should be rapidly hospitalized and assessed for consideration of lumbar puncture (LP) if clinically safe. Ideally, patients should have fast-track brain imaging before LP, but initiation of antibiotic therapy should not be delayed beyond 3 h after first contact of patient with health service.

CSF examination reveals elevated pressure (200-500 mm H₂O) and protein (100- 500 mg/dl, normal 15-45 mg/dl), decreased glucose (<40% of serum glucose) and marked pleocytosis (100-10,000 white blood cells/μl, (normal <5) with 60% or greater polymorphonuclear leucocytes.

Pyogenic meningitis should be differentiated from tubercular meningitis, which has relatively longer history of low to high grade of fever, constitutional symptoms, and CSF shows lymphocytic predominance, normal to mildly reduced sugar and raised proteins.

BRAIN ABSCESS

Brain abscess is defined as a focal suppurative infection within the brain parenchyma, typically surrounded by a well-vascularized capsule. The most important investigation to diagnose brain abscesses is cranial imaging, either cranial tomography (CT) or magnetic resonance imaging (MRI).

Headache is the most common presenting symptom of brain abscess. Fever is generally present but its absence does not rule out the diagnosis. Mostly patients have a focal neurologic deficit such as hemiparesis, aphasia, visual field defects depending on the location of abscess.

INFECTIVE ENDOCARDITIS

Bacterial endocarditis is a life-threatening infectious disease. Clinical manifestations of bacterial endocarditis include fever, toxemia, clubbing, splenomegaly, anaemia, microscopic haematuria, a new onset or changing murmur, evidence of immune phenomena such as roth spots, osler nodes.

The diagnosis of bacterial endocarditis is based on Modified Duke s criteria which involves clinical, laboratory and echocardiographic findings.

Definite IE

Pathological criteria

- Microorganisms demonstrated by culture or on histological examination of a vegetation, vegetation that has embolized, or an intracardiac abscess specimen; or
- Pathological lesions; vegetation or intracardiac abscess confirmed by histological examination showing active endocarditis

Clinical criteria

- 2 major criteria; or
- 1 major criterion and 3 minor criteria; or
- 5 minor criteria

Possible IE

- 1 major criterion and 1 minor criterion; or
- 3 minor criteria

Rejected IE

- Firm alternate diagnosis; or
- Resolution of symptoms suggesting IE with antibiotic therapy for ≤4 days; or
- No pathological evidence of IE at surgery or autopsy, with antibiotic therapy for ≤4 days; or
- Does not meet criteria for possible IE, as above

Modified Duke s criteria for diagnosis of endocarditis

Major Criteria

1. Blood cultures positive

- a. Typical microorganisms consistent with IE from 2 separate blood cultures

- Viridans streptococci, *Streptococcus gallolyticus* (*Streptococcus bovis*), HACEK group, *Staphylococcus aureus*; or
 - Community-acquired enterococci, in the absence of a primary focus; or
- b. Microorganisms consistent with IE from persistently positive blood culture
 - ≥ 2 positive blood cultures of blood samples drawn >12 h apart; or
 - All of 3 or a majority of ≥ 4 separate cultures of blood (with first and last samples drawn ≥ 1 h apart); or
 - c. Single positive blood culture for *Coxiella burnetii* or phase I IgG antibody titre $>1:800$
- 2. Imaging positive for IE**
- a. Echocardiogram positive for IE
 - Vegetation;
 - Abscess pseudoaneurysm, intracardiac fistula
 - Valvular perforation or aneurysm;
 - New partial dehiscence of prosthetic valve
 - b. Abnormal activity around the site of prosthetic valve implantation detected by “F-FDG PET/CT (only if the prosthesis was implanted for >3 months) or radiolabelled leucocytes SPECT/CT
 - c. Definite paravalvular lesions by cardiac CT
- Minor Criteria**
1. Predisposition such as predisposing heart condition, or injection drug use
 2. Fever defined as temperature $>38^{\circ}\text{C}$
 3. Vascular phenomena (including those detected by imaging only): major arterial emboli, septic pulmonary infarcts, infectious (mycotic) aneurysm, intracranial haemorrhage, conjunctival haemorrhages, and Janeway’s lesions
 4. Immunological phenomena: glomerulonephritis. Osler’s nodes, Roth’s spots, and rheumatoid factor
 5. Microbiological evidence: positive blood culture but does not meet a major criterion as noted above or serological evidence of active infection with organism consistent with IE

CELLULITIS

Cellulitis is an acute spreading infection that involves subcutaneous tissue, most commonly caused by group A streptococcus and staph aureus. Trauma and underlying skin lesion can lead to the development of cellulitis. Cellulitis may also develop due to the spread of adjacent infections like osteomyelitis.

Clinical findings: Clinically rapidly intensifying pain and redness is a common presentation. Fever and lymphadenopathy may be present. The borders in cellulitis are not well demarcated. Though group A streptococci and staphylococcus are the most common organisms rarely organisms like H influenza, pneumococcus may also cause cellulitis.

FURUNCULOSIS

Furunculosis is a deep infection of the hair follicle leading to abscess formation with accumulation of pus and necrotic tissue. Furuncles appear as red, swollen, and tender nodules on hair-bearing parts of the body, and the most common infectious agent is *Staphylococcus aureus*, but other bacteria may also be causative. Furunculosis often tends to be recurrent and may spread among family members.

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

URINARY TRACT INFECTIONS

The term UTI encompasses a variety of clinical entities viz asymptomatic bacteriuria (ASB), cystitis, prostatitis and pyelonephritis.

Uncomplicated UTI refers to acute cystitis or pyelonephritis in non pregnant outpatient women without anatomic abnormalities or instrumentation of urinary tract. *Complicated UTI* includes all other types of UTI.

Cystitis: The typical symptoms of cystitis are dysuria, urinary frequency, and urgency. Other symptoms are nocturia, hematuria, suprapubic discomfort, and hesitancy.

Pyelonephritis : severe pyelonephritis present as high fever, rigors, nausea, vomiting, flank or loin pain. symptoms are acute in onset and symptoms of cystitis may not be present. Fever is the main distinguishing feature between cystitis and pyelonephritis.

Prostatitis: Acute bacterial prostatitis presents as dysuria, frequency and pain in pelvis or perineal area. Fever and chills are usually present and symptoms of bladder outlet obstruction are common.

PNEUMONIA

Pneumonia is an inflammation in alveolar tissue, most often caused by a microbial agent. The community acquired pneumonia is most commonly caused by *Streptococcus pneumoniae* (typical) and less frequently by *Mycoplasma pneumoniae*, *H. influenzae*, *Chlamydia pneumoniae*, *Staphylococcus aureus* or *Legionella pneumoniae* (atypical). *Haemophilus influenzae* infection is seen mostly in patients with chronic bronchitis. Nosocomial pneumonia is likely to be caused by Gram-negative bacilli or *Staphylococcus aureus*.

Sudden onset of fever, productive cough, chest pain, shortness of breath and (in some cases) pleuritic chest pain; systemic symptoms like headache, bodyache and delirium are more severe with atypical pneumonia.

For assessment of the severity of pneumonia “**CURB- 65**” severity score can be used-

Confusion,

Urea >7 mmol/l,

Respiratory rate ≥ 30 /min,

low **B**lood pressure (diastolic blood pressure (DBP) ≤ 60 mm Hg or systolic BP ≤ 90 mm Hg) and

Age ≥ 65 years

Patients with scores 0 and 1 are at low risk of mortality (1.5%) might be suitable for management as hospital outpatients.

Patients with a score of 2 are at intermediate risk of mortality (9%) and should be considered for hospital supervised treatment.

Patients with a score of >2 are at high risk of mortality ($>19\%$) and requires ICU care.

ABBREVIATIONS

AIDS Acute Immuno Deficiency Syndrome	GBS- Guillain Barre syndrome
ALT- Alanine Amino Transferase	GI-Gastro-Intestinal
AM-CL- Amoxicillin/clavulanate	HIV-Human Immunodeficiency Virus
AMR – Antimicrobial Resistance	HSV- Herpes Simplex virus
ANC- Antenetal Care	ICU-Intensive Care Unit
AOM- Acute otitis media	ID- Infectious disease
ART- Anti retroviral treatment	IU- International unit
AST- Anti microbial susceptibility test	IUD- Intra Uterine Device
ATT- Anti Tubercular Treatment	IV-Intra Venous
BAL- Broncho Alveolar lavage	LBW-Low Birth Weight
BCG- Bacillus Calmette Guerin	MDR-Multi Drug Resistant
BD- Bis in Die (12 hourly)	MIC- Minimum Inhibitory Concentration
BL-BLI- Beta lactam-beta-lactam inhibitor	MRSA- Methicillin Resistant <i>Staphylococcus aureus</i>
BMT- Bone Marrow Transplantation	MSSA- Methicillin Sensitive <i>Staphylococcus aureus</i>
BP- Blood Pressure	NICU- Neonatal Intensive Care Unit
CABG- Coronary Artery Bypass graft	OD- Once a day
CAPD- Continuous Ambulatory Peritoneal Dialysis	OPD-Outdoor Patient Department
CI- Confidence Interval	OT-Operation Theatre
CLSI- Clinical and Laboratory Standards Institute	PANDAS- Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections
CME- Continuing medical education	PCR- Polymerase chain reaction
CMV- Cyto Megalo Virus	PICU-Pediatric Intensive Care Unit
CNS-Central Nervous System	PJI-Periprosthetic Joint Infection
CRBSI-Catheter Related Bloodstream Infection	RNTCP-Revised National Tuberculosis Control Programme
CRP- C reactive protein	RTI- Reproductive tract infection
CRS-Congenital Rubella Syndrome	SOP- Standard operating procedure
CSF- Cerebro Spinal Fluid	STI-Sexually Transmitted Infection
CSSD- Central Stores and Supply Department	TB-Tuberculosis
CTVS- Cardio Thoracic and Vascular Surgery	TDS - Ter die sumendum (8 hourly)
CVS- Cardiovascular System	TMP-SMX- Trimethoprim sulphamethoxazole
DS- Double Strength	TMP-SMX-DS- Trimethoprim sulphamethoxazole double strength
DT-Dispersible Tablet	URI-Upper Respiratory Infection
DVT- Deep Venous Thrombosis	UTI-Urinary Tract Infection
E.T.O-Ethylene Oxide Sterizilation	VAP-Ventilator Associated Pneumonia
ECG- Echo Cardio Gram	HAP-Hospital Acquired Pneumonia
ECHO- Echo Cardio Graphy	VDRL-Venereal Disease Research Laboratory
EGA- <i>Estimated Gestational Age</i>	VRE-Vancomycin Associated Enterococci
ENT-Ear Nose Throat	VZIG- Varicella Zoster immunoglobulin
ESBL-Extended-Spectrum Beta- Lactamase	WBC-White Blood Cell
ESRD- End Stage Renal Disease	WHO-World Health Organization
FDA- Food and Drug Authority	
FQ- Fluoroquinolone	
G6PD- Glucose 6- phosphate dehydrogenase	

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