Ministry of Health

Department of Medical Services

Naypyitaw General Hospital (1000 Bedded)

Antibiotic Guideline

First Edition 2021

Antibiotic Guideline for Adult Patient

1000-bedded Naypyitaw General Hospital

1st Edition

Prepared on behalf of the **Hospital Infection Control Committee**

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Preface

Antimicrobial Resistant (AMR) is a growing and challenging problem for public health as worldwide in current situation. Emerging antimicrobial resistance has been identified as a global challenge by World Health Organization. Many countries around the world are paying the highest attention to this problem as serious priority issues. Because of Antimicrobial Resistance (AMR), previous treatable infection diseases are changing to untreatable disease even though latest antibiotics have been used.

Antimicrobial Resistance (AMR) is invisible silent killer among the community as nationwide and many people are suffering life threating health problem without learning about AMR. In line with Global Action Plan for AMR, Myanmar National Plan for AMR as developed in 2017 with strong government commitment for National Multi-sectorial steering Committee (NMSC), National Coordinating Centre (NCC) and five Technical Working Groups such as Awareness, Surveillance, Infection Prevention and Control (IPC), Antimicrobial usage (AMU) and Research & Innovation.

National Health Laboratory (NHL) Yangon have delivered the analysis report on Hospital Antimicrobial Resistance in Myanmar yearly since 2016.

From the report of annual reviews, AMR has a negative impact on outcomes for patients and health care expenditures as well as in perspective of patient safety. There are some variations in culture and sensitivity of antibiotics region by region according to the causal microorganisms. Therefore, we developed our own antibiotics guidelines based our AMR surveillance regarding culture and sensitivity results within hospital from 2015-2020. We hope that the guidelines can assist in determining the scope of Antibiotics within our hospital and further more to national problems as an effective response and solution. Even though, it is the first time antibiotics guideline that will contribute to effective

response in combatting AMR within hospital highlighting situation analysis and capability of Surveillance.

The first edition of Antibiotics Guideline (2021) in Nay Pyi Taw General Hospital (1000-bedded) was developed with its primary aim to guide clinicians in their empirical choice of antimicrobial agents. Friendly, I would like to deliver my special thanks to Hospital Infection and Control (IPC) committee members, all Professors, all Consultants and all my colleagues for their tremendous effort for establishing our hospital Antibiotics guideline (2021). And also, I really appreciate Microbiology Team for their contribution and terminal Support on completion of this report. I make sure that without all participations, this guideline cannot be visualized.

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Chapter 1

Introduction

Antibiotics is being said the mainstay of medical science after the discovery of penicillin by Noble prize winner Sir Alexander Fleming and following discovery of various group of antibiotics bring the medical science to “back from the dead” era, making once lethal infections and severe sepsis readily treatable and making other medical advances, like cancer chemotherapy and organ transplants. As human beings are living in the microbe world, antibiotics make us to dream the world with freedom of infection.

When microorganisms acquired antimicrobial resistance (AMR) by means of normal evolutionary process, and it is accelerated by the selective pressure exerted by widespread use of antibacterial drugs. Resistant strains are able to propagate and spread where there is non-compliance with infection prevention and control measures. The susceptibility pattern of microorganism to the specific antibiotic is gradually decreasing while the resistance pattern including minimal inhibitory concentration, resistant strains and species population and emerging infectious diseases is increasing.

The pipeline for the development of new antibacterial drugs is now virtually empty, particularly for the treatment of Gram-negative enteric bacteria, and research on treatments to replace antibacterial drugs is still in the early stages. Situations are increasingly arising where bacteria that are resistant to most, or even all, available antibacterial drugs are causing serious infections that were readily treatable until recently. This means that progress in modern medicine, which relies on the availability of effective antibacterial drugs, is now at risk. The superbugs and *Mycobacterium tuberculosis* infections, once treatable infections threaten the medical practices as they are “back from the dead”.

An effective strategy to limit the effect of multidrug resistance must be multifaceted and must include the education of patients and doctors about appropriate drug, dose and duration, surveillance of antimicrobial resistance and antimicrobial use, improved use of immunization. and use of effective infection control practices such as hygienic life style and universal precautions in various infection handle settings.

Improving the use of antibiotics is an important patient safety and public health issue as well as a national priority. This book hopes to provide the basics about appropriate drug, dose and duration of antibiotics for common infectious diseases in 1000-bedded Naypyitaw General Hospital. Hospital Infection Control Committee tried to establish this first edition and hope that coming editions will be reviewed yearly according to the latest information of AMR and hospital needs.

Chapter 2

Principles of rational antibiotic prescribing

The Antibiotics is the one of the most commonly used group of drugs in the world. In our country we didn't know exact data how much we use in daily clinical practice. It may be underuse, misuse and over-use. Globally within last 50 years it has been seen as a golden age of antibiotics discovery which have been used widely both in hospital and community settings. Inappropriate usage of antibiotics shouldn't be allowed. However, there is a limited tool for its usage till now in human, animal and other sectors.

Usage of antibiotics should be recorded in some data system. For example, a global point prevalence survey method [Global PPS-http://www.global-pps.com] reveals quality of antimicrobial prescribing in hospitals. GPPS reveals significant variation in practice against commonly used metrics of the quality of prescriptions.

World Health Organization try to start AWaRe Policy for usage of antibiotics, antibiotics stewardship, which is a key intervention necessary to curb the further emergence and spread of antimicrobial resistance (AMR).

There are two definition help to understand the objectives of antimicrobial stewardship. In the system level it is defined as antimicrobial stewardship (AMS) is an organizational or healthcare system-wide approach to promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness. For the individual/team level, it is an inter-professional effort, across the continuum of care. It also involves timely and optimal selection, dose and duration of an antimicrobial, for the best clinical outcome for the treatment or prevention of infection, with minimal toxicity to the patient, and minimal impact on resistance and other ecological adverse events such as *C. difficile*.

From the Ecological and Societal point of view, antibiotics differ from other classes of drugs and the way in which a physician and other professionals use it can affect the response of future patients. Its practice is the one of the responsibilities to society. The AMR can spread from bacteria to bacteria, patient to patient and animals to patients. Rationalizing antibiotic use should be primarily on hospitals and then followed by community setting. On the other hand, there were alarming reports of community-onset infections by resistant bacteria related to the overuse of antibiotics outside hospitals eg., MRSA infection. Therefore, the urgency of promoting appropriate antibiotic use in community-settings also emphasized.

An antibiotic is not always necessary in clinical setting. It is only useful for the treatment of bacterial infections. Not all infections are due to bacteria therefore we should have definite indication for usage. There is no strong evidence that antibiotics will prevent secondary bacterial infection in patients with viral infection.

Moreover, not all bacterial infections require antibiotics alone and should consider other measure like usage of antiseptics and surgery appropriately. The rational use of drugs requires that patients receive

medications appropriate to their clinical needs, in doses that meet their own individual requirements for an adequate period of time, and at the lowest cost to them and their community.

Process of rational prescribing can be initially started by steps to procedures such as clinical diagnosis, identification, sensitivity test of bacteria, pharmacodynamics, pharmacokinetics and host factors. Then if we think of rational use of antibiotics, it is to be define the patient problems, to specify the therapeutic objectives, to verify the suitable of your personal treatment, start the treatment and to give information such as instruction and warning and finally to monitor and stop the treatment. Choice of antibiotic depends on the etiological agent and patient factors and antibiotic factors.

Choice of antibacterial therapy would be definitive therapy or empirical therapy or Prophylactic therapy. Education at all levels, from the public and medical students to senior doctors, is essential but has often been neglected. Good quality antibiotic prescribing should be part of doctors' continuous professional development, accreditation and clinical governance programs. The quality of antibiotic prescribing can and should be an issue for assessment of performance.

For pharmacy, electronic systems to monitor stock-taking and prescribing for easier auditing amount and quality of antibiotic. The Hospital pharmacy should be established.

For microbiology laboratory, C&S results should be reported with minimum delay. *Only report first line antibiotics if isolate is sensitive* and only on those agents which appear in their formulary and policy. It should regularly make local sensitivity patterns widely known. The situation is favorable for ward visit and eyeball contact with prescribers by laboratory personnel.

Antibiotic Policy

Aim of antibiotic policy is to minimize the morbidity and mortality due to antimicrobial resistant infection and to preserve the effectiveness of antimicrobial agents. The objectives are to improve patient outcomes, to minimize unintended consequences of antimicrobials improving patient safety, to reduce AMR and to reduce health care costs.

Generally, the hospital antibiotic policy should concur or align with the national antibiotic policy except for a few changes as warranted by the local antimicrobial resistance profiles. If there is a wide variation from national to hospital, and hospital to hospital then the desired purpose is defeated i.e., to minimize the morbidity and mortality due to antimicrobial-resistant infections; to preserve the effectiveness of antimicrobial agents in the treatment and to prevent microbial infections.

Maximizing clinical outcomes and minimizing selection of resistant organisms

A. What should be done

1. Appropriate empirical antimicrobial therapy, with right dose, for right duration and at right time.
2. Delayed therapy or modifying the initial antimicrobial therapy does not improve the outcome.
3. Multidrug-resistance organism predisposes for inappropriate therapy.

4. Early and accurate identification of the pathogen and susceptibility.
5. Combination or mono-therapy chosen on the basis of the pathogen identified.
6. De-escalation of initial broad-spectrum therapy after definitive diagnosis (generally based on microbiology reports).

B. What should not be done

1. Treat non-infectious or nonbacterial syndrome.
2. Treat colonization or contamination.
3. Treat longer than necessary.
4. Fail to make adjustment in a timely manner.
5. Prescribe antibiotic with spectrum of activity not indicated.

C. The hospital antibiotic policy shall be based upon:

1. spectrum of antibiotic activity,
2. pharmacokinetics/pharmacodynamics of these medicines,
3. adverse effects,
4. potential to select resistance,
5. cost and
6. special needs of individual patient groups.

D. Principles in hospital antibiotic policy

The following facts should be considered as principles in hospital antibiotic policy.

1. Empiric antimicrobial treatment should be limited to conditions where immediate / early initiation of antimicrobials has been shown to be beneficial. Some examples are:
   a. Severe sepsis (sepsis-induced tissue hypo-perfusion or organ dysfunction) and septic shock
   b. Acute bacterial meningitis
   c. Community acquired pneumonia
   d. Ventilator associated pneumonia
   e. Necrotizing Fasciitis
   f. Febrile neutropenia
2. Fever, leukocytosis or elevated c-reactive protein (CRP) levels by themselves should not be considered indications for starting empiric antimicrobials, as these have been shown to have very poor specificity to diagnose bacterial sepsis. Always consider multiple data points (history, physical findings and investigation reports) together to make an accurate diagnosis.
3. Incomplete or inaccurate diagnosis is the most important reason for inappropriate use of antimicrobials.

4. Always obtain cultures (two sets of blood cultures and other appropriate samples as clinically indicated – e.g. normally sterile body fluids, deep pus etc.) before starting empiric antimicrobial treatment.
    - ❖ Avoid the practice of obtaining "pan cultures" unless clinically indicated.
5. Avoid sending cultures from superficial wounds, decubitus ulcers, and chronic wounds and draining sinuses. Surface swab cultures are either inadequate or provide misleading information regarding diagnosis (as they cannot differentiate infection from colonization / contamination).
6. When starting antimicrobials, use full therapeutic doses, paying close attention to dose, frequency, and route of administration and duration of treatment.
7. Review all antimicrobial prescriptions after 48 to 72 hours ("antimicrobial timeout") with a view to modify or stop the initial empiric therapy.
8. De-escalate (pathogen-specific therapy) the antimicrobial regimen once culture and susceptibility reports are available, and the patient is showing signs of improvement with the initial empiric broad-spectrum antimicrobials. Examples of optimization include switch
    a. To a narrow-spectrum antimicrobial,
    b. From combination to single agent,
    c. To less toxic or expensive drug, or
    d. From i.v. to an oral formulation.
9. Stop antimicrobials if the cause of initial symptoms is found to be non-infectious.
10. The doses mentioned in these guidelines are for patients with normal renal function. The doses have to be modified for those with renal insufficiency.

E. Followings should be Key Prescribing Principles;

1. Therapeutic decision - prescription based on best available evidence.
2. The narrowest spectrum if possible.
3. Dosage, route, frequency - appropriate.
4. Duration of antimicrobial therapy – defined & regularly reviewed.
5. Monotherapy- in most cases.
6. "Start Smart Then Focus" approach is recommended for all antimicrobial prescriptions.
    a. Indication for antibiotic,
    b. Choice of agent with right dosage and route of administration of treatment,
    c. Writing a prescription
    d. Interpretation of microbiology with a view to de-escalation or stopping therapy,
    e. duration of therapy.

AWaRe classification

Antimicrobial stewardship (AMS) committee determines the restriction status and access rules for each antimicrobial agent (or specific formulations). The **AWaRe** classification groups antibiotics into the following categories:

Access – antibiotics that represent first or second-line for empirical treatment of common infectious syndromes based on a systematic assessment of the available evidence and that have a favorable safety profile with a low propensity to further aggravate AMR. All Access antibiotics are part of the essential medicine list (EML) core list, meaning that these antibiotics should be widely available in all settings (while still making efforts to ensure their appropriate use). Many penicillins belong to this class. Antibiotics in this category do not require an approval but are to be used in accordance with locally endorsed guidelines or the Therapeutic Guidelines. Antibiotic prescriptions are still subject to monitoring and review by the AMS team.

Watch – antibiotics that present a higher potential to negatively impact AMR. Some Watch group antibiotics are also included in the EML core list since they are the most effective options for a limited group of well-defined clinical syndromes, but their use should be tightly monitored and restricted to the limited indications. Fluoroquinolones, which are unfortunately commonly used in many settings, belong to the Watch group as their use should be avoided for indications for which they are no longer first or second choice. Usage of antimicrobials in this category are automatically approved if prescribed for selective indications or for a limited duration. If a prescription is not suitable for automatic approval, it must be reviewed by the AMS team.

Reserve – "last-resort" antibiotics, that have activity against multi (MDR)- or extensively (XDR) resistant bacteria, and therefore represent a valuable, non-renewable resource that should be used as sparingly as possible. Some of the newly approved antibiotics (e.g. ceftazidime-avibactam) fall into this class, as do some of the older "rediscovered" antibiotics (e.g. polymyxins). Prescription review or consultation is required with an Infectious Diseases physician and/or Clinical Microbiologist prior to use. - These antimicrobial prescriptions will always be flagged for review by the AMS team.

Discouraged antibiotics – this fourth category – mostly including antibiotic combinations - was developed in the 2019 EML update. Some antibiotics, such as certain fixed dose combinations of antibiotics, do not have any reasonable indications for the treatment of infectious diseases in humans and may negatively impact AMR and patient safety.

A prescription should include-

1. Name of the patient
2. Hospital No
3. The indication
4. Medicine (Approved name)
5. Dose

6. Route
7. Start Time
8. Allergy Checked
9. Prescriber Name & Sign
10. Stop/review date on the drug chart for all antibiotic prescriptions (prefer after 48 hours). See Annex-I. Antimicrobial Steward Review Form.

Role of the Nurse:

(1) Request the doctor to write the indication and stop/review date on the drug chart for all antibiotic prescriptions.
(2) Request the doctor to update the clinical plan, alter the route if necessary.
(3) Ensure prompt administration of prescribed treatments.
(4) If a patient has missed any antibiotic dose(s) identify the reason, document and escalate the problem.
(5) Query all prescriptions beyond the review date

The process of rational treatment

Step 1: define the patient's problem

Step 2: Specify the therapeutic objective: what do you want to achieve with the treatment?

Step 3: verify the suitability of your personal treatment: check effectiveness and safety

Step 4: start the treatment

Step 5: give information, instructions and warnings,

Step 6: Monitor (and stop?) treatment

Antibiotics should not be given routinely, especially early in the disease course of pancreatitis even presenting with fever. The symptom is almost universally secondary to the inflammatory response and typically does not reflect an infectious process.

Surveillance of antimicrobial use and resistance should be according to hospital guideline and national guideline.

References

World Health Organization, Step-by-step approach for development and implementation of hospital antibiotic policy and standard treatment guidelines, 2011.

Chapter 3

Initial Empiric Antibiotics for Common Infections

3.1. Gastrointestinal and Intra-Abdominal Infections

Condition	Most likely microbial etiology	First choice	Alternatives	Comments
1. Acute gastroenteritis (acute onset nausea, vomiting, watery diarrhea)	• Viral (calciviruses, rotaviruses) • Entero-toxigenic and entero-pathogenic *E. coli* • *Salmonella* spp.	PO Ciprofloxacin 500mg BD x 3D	PO Azithromycin 500mg OD x 3D	Usually not needed
2. Acute watery diarrhea, cholera suspected	• *Vibrio cholerae*	PO Doxycycline 300mg once	PO Ciprofloxacin 500mg BD x 3DOR 2g once	
3. Bacillary dysentery (acute onset fever and bloody diarrhea)	• *Campylobacter* spp. • *Shigella* spp.	PO Ciprofloxacin 500mg BD x 3-5DOR 2 g once	PO Azithromycin 1g once OR PO Ceftriaxone 2g OD x 3D	
4. Enteric fever – suspect if AFI ≥7 days, other etiology ruled out	• *Salmonella* Typhi • *Salmonella* Paratyphi A	PO Ciprofloxacin 500 mg BD x 10D	IV Ceftriaxone 2g OD x 14D OR PO Azithromycin 1g stat & 500mg OD x 6D OR PO Cefixime200mg BD x 14D	
5. Cholangitis	• *Enterobacteriaceae* • Anaerobes	IV Ceftriaxone 2g OD + IV Metronidazole 500mg/8Hx	(IV Ceftazidime 2g/8H + IV Metronidazole 500mg/8H) OR IV Imipenem 500mg/8H x 3-7D	Duration depends on whether adequate biliary drainage can be done or not
6. Acute cholecystitis	• *Enterobacteriaceae*	IV Ceftriaxone 2g OD + IV Metronidazole 500mg/8H x	(IV Ceftazidime 2g/8H + IV Metronidazole 500mg/8H) OR IV Imipenem 500mg/8H x 3-7D	

Condition	Most likely microbial etiology	First choice	Alternatives	Comments
7. Spontaneous bacterial peritonitis	• *E. coli*	IV Ceftriaxone 2g OD x 7D	IV Piperacillin-Tazobactam 4.5g/8H x 7D Ciprofloxacin 500mg BD x 7D	
8. Secondary peritonitis (bowel perforation)	• *Enterobacteriaceae* • Anaerobes (Bacteroides species)	IV Ceftriaxone 2g OD + IV Metronidazole 500mg/8H x	(IV Ceftazidime 2g/8H + IV Metronidazole 500mg/8H) OR IV Imipenem 500mg/8Hx5-7D	
9. Intra-abdominal abscess	• *Enterobacteriaceae* • Anaerobes (Bacteroides species)	IV Ceftriaxone 2g OD + IV Metronidazole 500mg/8H x	(IV Ceftazidime 2g/8H + IV Metronidazole 500mg/8H) OR IV Imipenem 500mg/8Hx10-14D	
10. Amoebic liver abscess (suspect in patients with single abscess in right lobe of liver with no IHBRD and no primary intra- abdominal source)	• *E. histolytica*	PO Metronidazole 800 mg TDS x 7-10D	PO Tinidazole2g OD x 3D PO Ornidazole 1.5-2.0g OD x 3D PO Nitazoxanide 500mg TDS x 3D	
11. Acute pancreatitis		IV Imipenem 500mg/8H x	IV Ceftazidime 1g/8H + IV Metronidazole 500mg/8Hx7-14D	Only indicated if necrosis is suspected.

3.2. Central Nervous System Infections

Condition	Most likely microbial etiology	First choice	Alternatives	Comments
1. Bacterial Meningitis				a. All patients should receive the first dose of antimicrobials as soon as the diagnosis of acute bacterial meningitis is suspected. b. DO NOT delay antimicrobials if there is a delay in obtaining a CSF sample. c. Prior administration of antimicrobials tends to have minimal effects on the chemistry and cytology findings, but can reduce the yield of Gram stain and culture.
a. Age 13-50 year	○	IV Ceftriaxone 2g/12H OR IV Cefotaxime 2g/8H 10-14D		
b. Age 13-50 year (in area with a significant incidence of penicillin resistance in community)	○	(IV Ceftriaxone 2g/12H OR IV Cefotaxime 2g/8H) + IV Vancomycin 1g/12H x 10-14D		
c. Age >50 year	○	(IV Ceftriaxone 2g/12H OR IV Cefotaxime 2g/8H) + IV Vancomycin 1g/12H + (IV Ampicillin 2g/6H OR IV Benzyl Penicillin 2.4g/6H) x 10-14D		
d. Impaired cellular immunity	○	IV Vancomycin 1g/12H + (IV Ampicillin 2g/6H OR IV Benzyl Penicillin 2.4g/6H) + (IV Cefepime 2g/12H OR IV Meropenem 1g/12H) x 10-14D		
e. Recurrent meningitis	○	IV Vancomycin 1g/12H + (IV Ceftriaxone 2g/12H OR IV Cefotaxime 2g/8H) x 10-14D		
f. Head trauma, neurosurgery or CSF shunt	○	IV Vancomycin 1g/12H + IV Ceftazidime 2g/12H) OR		

Condition	Most likely microbial etiology	First choice	Alternatives	Comments
		(IV Cefepime 2g/12H OR IV Meropenem 1g/12H) x 10-14D		
g. Patient with typical meningococcal rash		IV Benzyl Penicillin 2.4g/6H) x		
2. TB Meningitis	Mycobacterium tuberculosis			Targeted therapy as in NTP Guideline.
3. Viral Encephalitis				
a. CSF finding and/or imaging finding suggest Viral Encephalitis, or patient is very unwell or deteriorating	• Enteroviruses ○ echoviruses, coxsackieviruses A and B, polioviruses, etc., • Mumps virus, • Herpes family viruses ○ Herpes simplex virus (HSV)-1, HSV-2, varicella-zoster virus (VZV), Ebstein-Barr virus (EBV), cytomegalovirus (CMV), and human herpesvirus-6. • Arboviruses ○ Equine encephalitis viruses, West Nile virus, Japanese B virus, and Murray Valley viruses,	IV Acyclovir 10mg/kg/dose(over 1hr infusion)/8H x 1-2W	PO Valacyclovir 1g TDS x 1-2W	
b. If CSF or imaging is normal but clinical suspicious of Herpes encephalitis		IV Acyclovir 10mg/kg/dose(over 1hr infusion)/8H x 1-2W	PO Valacyclovir 1g TDS x 1-2W	
c. PCR is negative for HSV but positive for other organisms				Treatment according to PCR results
d. If CSF PCR is negative for any virus		PO Acyclovir 800mg 5times/day x 1-2W	PO Valacyclovir 1g TDS x 1-2W	

Condition		Most likely microbial etiology	First choice	Alternatives	Comments
		Jamestown Canyon viruses, Coltivirus, etc.			
e.	If CSF PCR cannot be done		PO Acyclovir 800mg 5times/day x 1-2W	PO Valacyclovir 1g TDS x 1-2W	
4.	**Cryptococcal meningitis**	• *Cryptococcus neoformans*	IV Amphotericin B 0.7-1mg/kg/day (over 2-6 hr) x 2W	PO Fluconazole 800mg/day x 8W	
5.	**Syphilitic Meningitis**	• *Treponema pallidum*	IV Benzyl penicillin 2.4g/6H x 2W	IV Ceftriaxone 2g/day x 2W	
6.	**Lyme Meningitis**	• *Borrelia burgdorferi*	IV Ceftriaxone 2g/day x 2-4W	PO Doxycycline 100mg BD x 2-4W	
7.	**Brain Abscess**				
a.	Brain abscess arising from an oral, otogenic or sinus source		IV Ceftriaxone 2g/12H + IV Metronidazole 500mg/8H x 6W		Duration could be injection 2-6 weeks or could be de-escalated to oral till 6th week
b.	Brain abscess from hematogenous spread (e.g. Bacteremia or Endocarditis)		IV Vancomycin 1g/12H + IV Metronidazole 500mg/8H + IV Ceftriaxone 2g/12H x 6W		Same as above
c.	Brain abscess in postoperative neurosurgical patients		IV Vancomycin 1g/12H + IV Meropenem 1g/12H x 6W		Same as above
d.	Brain abscess following penetrating trauma		IV Vancomycin 1g/12H + IV Ceftriaxone 2g/12H x 6W		Same as above
e.	Brain abscess without an unknown source		IV Vancomycin 1g/12H + IV Metronidazole 500mg/8H + IV Ceftriaxone 2g/12H x 6W		Same as above

3.3. Cardiovascular System Infections

See section in definitive therapy (P-32).

3.4. Skin and Soft Tissue Infections

Condition	Most likely microbial etiology	First choice	Alternatives	Comments
A. Infections				
1. Bacterial infections		•Acute staphylococcal infections Topical - Fusidic acid, Mupirocin Systemic - Flucloxacillin, Dicloxacillin, Clindamycin, Primary Cephalosporin •Carbuncles often need prompt surgical drainage. •Carrier sites (e.g. nostril) Topical antibiotic - Mupirocin) •Gram-negative folliculitis (e.g. Acneiform eruptions) Topical – Benzoyl peroxide wash, Clindamycin, Nalidixic acid Systemic – Doxycycline, Minocycline, erythromycin, azithromycin, Isotretinoin •Streptococcus pyogenes is always sensitive to penicillin and erythromycin in penicillin allergy. •Recurrent erysipelas required long term penicillin V (250mg twice a day),		•Wound swabs for bacterial culture are usually taken from the lesions and from carrier sites before topical or systemic antibiotics. •General measures such as improved personal hygiene, regular bathing, use of soap and shower cream, avoidance of rubbing and scratching. •Cold compression with KMnO4 can reduce the presence of discharge, tenseness due to crusts, pruritus and the foul smelling.
b) Commensals Erythrasma, pitted keratolysis				
b) Staphylococcal – Impetigo, Ecthyma, folliculitis, secondary infections			Alternatives – Minocycline, Cotrimoxazole, Quinolones	
c) Streptococcal – Erysipelas, Cellulitis, Impetigo, Ecthyma, Necrotizing fasciitis				
d) Gram-negative - folliculitis, secondary infections, Cellulitis				
e) Mycobacterial – Lupus vulgaris, Scrofuloderma, Fish tank granuloma, Buruli ulcer, Leprosy				
f) Spirochaetal – Syphilis, Lyme disease				
g) Neisseria – Meningococcemia				

Condition	Most likely microbial etiology	First choice	Alternatives	Comments
h) Others – Anthrax, Erysipeloid		with attention to hygiene at potential sites of entry.		
2. Viral infections				
a) Molluscum contagiosum		•Topical – Imiquimod 5% cream •Enucleation, Curettage, Cryosurgery, Electrodessication		
b) Warts: Verruca vulgaris		•Patient - initiated therapy Topical – Salicylic acid 17-40% daily up to 12 weeks OR Imiquimod 5% cream three times per week OR Hyperthermia with hot water 45'C/ 113'F •Clinician - initiated therapy Cryosurgery, Electro-surgery, CO2 laser surgery		
c) Herpes Simplex infection		•Topical – 5% Acyclovir cream 6 times daily x 7D •Systemic - Acyclovir 400mg TDS x 7-10D	Valacyclovir BD x 7-10D OR Famciclovir 250mg TDS x 5-10D	
d) Varicella / Chicken Pox Infection		•Topical – Antibiotic (e.g. Mupirocin) cream for secondary bacterial infection •Systemic Children - Acyclovir 20mg/kg/6H x 5D Adult - Acyclovir 800mg 5 times daily x 5-7D	Children - Valacyclovir 20mg/kg TDS x 5D Adult - Valacyclovir 1G TDS x 1W	•Antihistamines to relieve pruritus •Avoid antipyretics due to risk of Reye syndrome

Condition	Most likely microbial etiology	First choice	Alternatives	Comments
e) Herpes zoster		•Topical – Antibiotic (e.g. Mupirocin) cream for secondary bacterial infection •Systemic – Acyclovir 800mg 5 times daily x 7D	Valacyclovir 1G TDS x 1W OR Famciclovir 500mg TDS x 1W	•Antihistamines to relieve pruritus
3. Fungal infection				
a) Dermatophytosis		•Topical – Azole cream (Clotrimazole/ Miconazole/ Ketoconazole), Allylamines (Terbinafine), Naphthionates (Tolnaftate)	•Systemic – Fluconazole, Itraconazole, Terbinafine	
b) Onychomycosis		•Topical - Naphthionates (Tolnaftate)	•Systemic – Itraconazole, Terbinafine	
c) Candidiasis (Cutaneous/ Oropharyngeal/ Genital)		•Topical – Azole cream (Clotrimazole/ Miconazole/ Ketoconazole) •Nystatin, Clotrimazole oral suspension in oropharyngeal candidiasis	•Systemic – Fluconazole, Itraconazole Amphotericin B in severe candidiasis	
d) Tinea versicolor		•Topical – Azole cream (Clotrimazole/ Miconazole/ Ketoconazole)	•Systemic – Fluconazole, Itraconazole	•Antifungal shampoo for secondary prophylaxis
4. Infestation				
Scabies		•Topical salicylic acid in crusted scabies	•Systemic – Ivermectin 200ug/ kg single dose and	Topical – not after bath or shower, and washed

Condition	Most likely microbial etiology	First choice	Alternatives	Comments
		•Permethrin 5% cream all areas of body (neck down) OR •Benzoyl benzoate lotion (which is not suitable for extensive dermatitis, pregnant or lactating mother, children under 2yr) OR •Crotamiton 10% cream, lotion, Sulphur 2-10 % in petrolatum	second or third doses separated by 1-2 weeks in heavy infestation (which is contraindicated in children with less than 15kg body weight, pregnant or lactating mother, asthma, immunosuppression, and significant hepatic disease).	off after 8hr of application
B. Immunobullous diseases		•Topical - Fusidic acid, Mupirocin •Systemic – Flucloxacillin OR amoxicillin OR Cephalosporins	Amoxicillin-clavulanic acid OR Cefoperazone-sulbactam etc.	•Be careful the antibiotics and analgesics given in case of drug eruptions. •Wound swabs for bacterial culture are usually taken from the weepy and excoriated lesions.
C. Generalized exfoliative dermatitis		•Topical - Fusidic acid, Mupirocin •Systemic – Flucloxacillin OR amoxicillin OR Cephalosporins	Amoxicillin-clavulanic acid OR Cefoperazone-sulbactam etc. •Oral antifungal in case of seborrheic dermatitis.	
Bites (cat, dog, human, rat)	• *Pasteurella multocida,* • *Capnocytophaga,* • *Eikenella, Strep viridans,* • *Spirillum minus,* • *Streptobacillus moniliformis*			

3.5. Bone and joint infections

Condition	Most likely microbial etiology	First choice	Alternatives	Comments
1. Acute osteomyelitis	*Staph aureus*	IV Coamoxiclav **1.2G/8H x ?D**	IV Imipenem 500mg/8H x D	According to C&S Later on
2. Chronic osteomyelitis a. Secondary to a contiguous focus of infection (e.g., decubitus ulcer), b. Osteomyelitis that develops as a result of contaminated open fractures or surgical treatment of closed fractures	• Staphylococci • Aerobic GNB • Streptococci • Anaerobes	IV Coamoxiclav IV Levofloxacin IV Metronidazole	IV Imipenem 500mg/8H x D AND IV Metronidazole 500mg/8H x D	According to C&S Later on
3. Chronic osteomyelitis with orthopedic implants		IV Coamoxiclav IV Levofloxacin	IV Imipenem 500mg/8H x D	According to C&S Later on
4. Osteomyelitis associated with diabetic foot infection		IV Coamoxiclav IV Metronidazole	IV Imipenem500mg/8H x D AND IV Metronidazole500mg/8H x D	According to C&S Later on
5. Septic arthritis	Staph aureus	IV Coamoxiclav IV Levofloxacin	IV Imipenem 500mg/8H x D	According to C&S Later on
6. Diabetic foot				Usually systemic antimicrobial therapy is not indicated.

3.6. Respiratory Tract infections

Condition	Most likely microbial etiology	First choice	Alternatives	Comments
1. **Community Acquired Pneumonia (CAP)**				
a. Mild pneumonia		Amoxicillin 500mg tds or PO Clarithromycin 500mg bd or PO Azithromycin 500mg od		Treat as out-patient Duration is 5 days.
b. Moderately severe pneumonia		IV Ceftazidime 1G/12H or IV Cefoperazone-sulbactam1G/12H PLUS PO Clarithromycin 500mg bd or IV Levofloxacin 500mg od		Duration is 5 days.
c. Severe pneumonia		IV Co-Amoxiclav 1.2G/8H or IV Cefoperazone-Sulbactam1G/12H or IV Ceftazidime 1G/12H PLUS		Duration is 5 days.

Condition	Most likely microbial etiology	First choice	Alternatives	Comments
		PO Clarithromycin 500mg bd or IV Levofloxacin 500mg 12hrly PLUS IV Cefuroxime 1.5G/8H or IV Cefotaxime 1G/8H IV Flucloxacillin (if Staph. suspected) IV Vancomycin or Teicoplanin (if MRSA suspected)		
2. **Aspiration pneumonia**		PO Moxifloxacin 400mg OD or IV Amoxicillin-clavulanate1.2G/8H or Ceftriaxone 1G/12H PLUS IV Metronidazole 500mg/8H	PO Clindamycin300mg qid as second line (in place ofMetronidazole)	Duration 7-10 days
3. **Exacerbation of bronchiectasis** **(No risks of pseudomonas spp.)**		PO Amoxicillin-Clavulanate625mg tds or Moxifloxacin 400mg od or Levofloxacin 500mg od or		Duration 7-10 days

Condition	Most likely microbial etiology	First choice	Alternatives	Comments
		Ciprofloxacin 500mg bd IV Ceftazidime 1G/12H or IV Carbapenem–G/-H or IV Piperacillin Tazobactam4.5G/12H		
4. **Acute exacerbation of COPD** **a. Mild**				No Antibiotic
b. Moderate (or) Severe (Uncomplicated) At least 2 of the 3 cardinal symptoms		PO- macrolide PO- 3rd generation Cephalosporin PO- Doxycycline PO- Cotrimoxazole		
c. Moderate (or) Severe (Complicated) At least 2 of the 3 cardinal symptoms		IV Fluoroquinolone(Moxi, Gemi, Levo) IV Amoxicillin-clavulanate X7-10D		If risk of pseudomonas, consider Ciproflox and obtainsputum culture.
5. **Aspiration pneumonia**		IV Amoxicillin-clavulanate1.2G/8H or Ceftriaxone 1G/12H PLUS IV Metronidazole 500mg/8H	PO Clindamycin300mg qid as second line (in place ofMetronidazole)	Duration 7-10 days
6. **Sinusitis** **a. Acute** **b. Chronic**				
7. **Tonsillitis** **a. Acute**	Group A streptococcus (GAS) Respiratory viruses			

Condition	Most likely microbial etiology	First choice	Alternatives	Comments
b. Chronic				
8. **Pharyngitis** **a. Acute** **b. Chronic**	Group A streptococcus (GAS) Respiratory viruses			
9. **Acute epiglottitis**	H. influenzae			
10. **Ludwig's angina, Vincent's angina**	Polymicrobial (oral anaerobes)			
11. **Acute bronchitis**	Viral			None needed
12. **Lung abscess**	• Oral anaerobes (*Peptostreptococcus, Prevotella, Bacteroides* (usually not *B. fragilis*),and *Fusobacterium* spp.)			
13. **Empyema thoracis**	• *Streptococcus milleri* • *Strep. pneumoniae* • Oral anaerobes			

3.7. Genitourinary infections

Condition	Most likely microbial etiology	First choice	Alternatives	Comments
Asymptomatic bacteriuria (positive urine culture from an individual without symptoms and signs of UTI)	*E.coli*	PO Ciprofloxacin 250 mg BD x 5-7 days	PO Levofloxacin 250 mg BD x 5-7 days	according to C&S result
Acute uncomplicated cystitis in women - dysuria and frequency in healthy, adult, non-pregnant women with normal urinary tract	*E.coli*	PO Levofloxacin 250 mg BD x 5-7 days	PO Linezolid acid 300 mg BD x 7-10 days	according to C&S result
Pyelonephritis - uncomplicated (no underlying GU disease)	*E.coli*	PO Amoxicillin-Clavulanic acid 625 mg TDS x 7-10 days	PO Levofloxacin 250 mg BD x 5-7 days PO Linezolid acid 300 mg BD x 7-10 days	according to C&S result
Complicated UTI (underlying GU disease e.g. neurogenic bladder, renal stones, hydronephrosis, etc.)	*E. coli,* *Proteus spp,* *Pseudomonas aeruginosa*	IV Cefoperazone-Sulbactam 1G/12H x at least 4 days	IV Cefoperazone-Sulbactam 1G/12H x at least 4 days and IV amikacin 500mg/12H x at least 4 days	according to C&S result
Foley catheter associated UTI	*E. coli,* *Proteus spp,* *Pseudomonas aeruginosa,* *Acinetobacter spp*	for mild case- PO Levofloxacin 250 mg BD x 5-7 days PO Amoxicillin+ Clavulanic acid 625 mg TDS x 7-10 days	for severe case- IV Levofloxacin 500mg/24H x at least 4 days IV Amoxicillin 1G + Clavulanic acid 100mg/12H for at least 4days	according to C&S result

3.8. Neutropenic fever

Neutropenia

- Absolute neutrophil count (ANC) <500/µL, or
- ANC <1000/µL and a predicted decline to ≤500/µL over the next 48 hours

And Fever

- A single oral temperature measurement of ≥ 38.3°C(101°F) or
- a temperature of ≥38.0°C(100.4°F) sustained over 1 hour.

Empirical antibiotic regimens in neutropenic fever

Condition	Most likely microbial etiology	First choice	Alternatives	Comments
1. Low risk		PO Amoxicillin/Clavulanic acid 500mg/125mg TDS PLUS PO Ciprofloxacin 500mg BD Or PO Moxifloxacin 400mg OD x 7D	If penicillin allergic, PO Clindamycin 300mg QID plus PO Ciprofloxacin 500mg BD x 7D	
2. High risk First dose broad spectrum antibiotic should be administered immediately (within 1 hour of presentation)		<u>First- line monotherapy</u> IV Piperacillin-tazobactam 4.5G/6H Or IV Meropenem 1G/8H Or IV Imipenem-cilastatin 500mg/6H Or IV Cefepime 2G/8H x 2W (or until resolution of neutropenia)	<u>Second- line dual therapy</u> Add aminoglycoside IV Gentamycin 2mg/kg/8H or 5mg/kg/24H Or IV Amikacin 15mg /kg/24H x 2W	Adjust according to culture result and/or infection site Consider antifungal therapy after 4-7 days of empiric antibiotic therapy <u>Indication</u>

Condition	Most likely microbial etiology	First choice	Alternatives	Comments
				1. complicated patients (hypotension or pneumonia) or 2. suspected or proven antimicrobial resistance)
3. Additions to initial empirical therapy that may be considered for patients at risk for infection with **antibiotic resistant organisms:**	(1) MRSA	Consider Vancomycin, linezolid, daptomycin (in the absence of pneumonia)		
	(2) VRE	Consider Linezolid or daptomycin		
	(3) Extended-spectrum beta-lactamase(ESBL) producing gram negative bacteria	Consider Carbapenem		
	(4) Carbapenemase producing organism (eg. *Pseudomonas aeruginosa, Acinetobacter baumanii*)	Consider polymyxin-colistin or tigecycline		

Chapter 4

Targeted (Definitive) Therapy of Common Infections

4.1. Infective endocarditis (IE)

Definition of infective endocarditis according to the modified Duke criteria

Definite IE
Pathological criteria -Microorganism demonstrated by culture or on histological examination of a vegetation, a 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 -Dose not meet the criteria for possible IE, as above
Relapse IE
-Recurrence caused by the same species within 6 months following the initial infection
Reinfection IE
-An infection caused by a different organism/ recurrence caused by the same species later than 6 months

Definition of the terms used in the European Society of Cardiology 2015 modified criteria for the diagnosis of infective endocarditis

Major criteria
1. Blood culture positive for IE a. Typical microorganisms consistent with IE from 2 separate blood cultures - Viridans Streptococci, *Streptococcus gallolyticus* (*Streptococcus bovis*), HACEK group, *Staphylococcus aureus*; or - Community acquired enterococcus, 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 hours apart; or - All of 3 or a majority of ≥ 4 separate cultures of blood (with first and last samples drawn ≥1 hour apart); or c. Single positive blood culture for *Coxiella burnetti* or phase I Ig 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. Abnormality activity around the site of prosthetic valve implantation detected by ^{18}F –FDG PET/CT (only if the prosthesis was implanted for > 3 months) or radio-labelled leukocytes SPECT/CT c. Definite paravalvular lesions by cardiac CT
Minor criteria
1. Predisposition such as predisposing heart conditions, or injection drug use 2. Fever defined as temperature > 38 °C 3. Vascular phenomenon (including those detected by imaging only): major aterial emboli, septic pulmonary infarcts, infectious (mycotic) aneurysm, intracranial hemorrhage, conjunctival hemorrhages, and Janeway's lesions. 4. Immunological phenomenon: glomerulonephritis, Osler's nodes, Roth's spots and rheumatic factor 5. Microbiological evidence: positive blood culture but dose not meet a major criterion as noted above or serological evidence of active infection with organism consistent with IE.

Proposed antibiotic regimens for initial empirical treatment of infective endocarditis in acute severely ill patients (before pathogen identification)

Condition	Most likely microbial etiology	Antibiotic Treatment	Comments
1. Community-acquired native valves or late prosthetic valves (≥12 months after surgery) endocarditis		Standard treatment: 4-week duration Ampicillin 12 g/day IV in 4-6 doses With (Flu)cloxacillin or oxacillin 12 g/day IV in 4-6 doses With Gentamicin 3 mg/kg/day IV or IM in 1 dose x 2-week	
		In beta-lactam allergic patients Vancomycin 30 mg/kg/day IV in 2 doses x 4-week With Gentamicin 3 mg/kg/day IV or IM in 1 dose x 2-week	
2. Early prosthetic valve endocarditis (<12 months after surgery) or nosocomial and non-nosocomial healthcare associated endocarditis		Vancomycin 30 mg/kg/day IV in 2 doses x 4-week With Gentamicin 3 mg/kg/day IV or IM in 1 dose x 2-week With Rifampicin 900-1200 mg IV or PO in 2-3 divided doses x 4-week	
3. Antibiotic treatment of infective endocarditis due to oral Streptococci and *Streptococcus bovis* group	Strains penicillin-susceptible (MIC ≤ 0.125 mg/L) oral and digestive streptococci	Standard treatment: 4-week duration Penicillin G12-18 million U/day IV in 4-6 doses Or Amoxicillin 100-200 mg/kg/day IV in 4-6 doses Or Ceftriaxone 2 g/day IV or IM in 1 dose	

Condition	Most likely microbial etiology	Antibiotic Treatment	Comments
		Standard treatment: 2-week duration Penicillin G 12-18 million U/day IV in 4-6 doses Or Amoxicillin 100-200 mg/kg/day IV in 4-6 doses Or Ceftriaxone 2 g/day IV or IM in 1 dose Combined with Gentamicin 3 mg/kg/day IV or IM in 1 dose	
		In beta-lactam allergic patients Vancomycin 30 mg/kg/day IV in 2 doses x 4-week	
	Strains relatively resistant to penicillin (MIC 0.250 – 2 mg/l)	Standard treatment: 4-week duration Penicillin G 24 million U/day IV in 4-6 doses Or Amoxicillin 200 mg/kg/day IV in 4-6 doses Or Ceftriaxone2 g/day IV or IM in 1 dose Combined with Gentamicin 3mg/kg/day IV or IM in 1 dose x 2-week	
		In beta-lactam allergic patients Vancomycin 30 mg/kg/day IV in 2 doses x 4-week With Gentamicin 3mg/kg/day IV or IM in 1 dose x 2-week	
4. Antibiotic treatment of infective endocarditis due to	Methicillin-susceptible staphylococci	(Flu)cloxacillin or oxacillin 12 g/day IV in 4-6 doses x 4-6 week	

Condition	Most likely microbial etiology	Antibiotic Treatment	Comments
Staphylococcus species (Native valves)	Penicillin-allergic patients or methicillin – resistant staphylococci	Vancomycin 30-60 mg/kg/day IV in 2-3 doses x 4-6 week	
5. Antibiotic treatment of infective endocarditis due to Staphylococcus species (Prosthetic valves)	Methicillin-susceptible staphylococci	(Flu)cloxacillin or oxacillin 12 g/day IV in 4-6 doses x ≥ 6 week With Rifampicin 900-1200 mg IV or orally in 2 or 3 divided doses x ≥ 6 week And Gentamicin 3 mg/kg/day IV or IM in 1 or 2 doses x 2 week	
	Penicillin-allergic patients and methicillin-resistant staphylococci	Vancomycin 30-60 mg/kg/day IV in 2-3 doses x ≥6 week With Rifampicin 900-1200 mg IV or PO in 2-3 divided doses x ≥6 week And Gentamicin 3 mg/kg/day IV or IM in 1 or 2 doses x 2 week	
6. Antibiotic treatment of infective endocarditis due to Enterococcus species	Beta-lactam and gentamicin-susceptible strains	Amoxicillin 200 mg/kg/day IV in 4-6 doses x 4-6 week With Gentamicin 3mg/kg/day IV or IM in 1 dose x 2 week	
		Ampicillin 200 mg/kg/day IV in 4-6 doses x 6 week With Ceftriaxone 4 g/day IV or IM in 2 doses x 6 week	
		Vancomycin 30 mg/kg/day IV in 2 doses x 6 week With Gentamicin 3mg/kg/day IV or IM in 1 dose x 6 week	

Condition	Most likely microbial etiology	Antibiotic Treatment	Comments
7. Antibiotic treatment for blood culture-negative infective endocarditis	*Brucella* spp.	Doxycycline (200 mg/24 hour) plus Cotrimoxazole (960 mg/12 hour) plus Rifampicin (300-600 mg/24 hour)	for ≥ 3-6 months orally
	C. burnetti (agent of Q fever)	Doxycycline (200 mg/24 hour) Plus Hydroxychloroquine (200-600 mg/24 hour)	orally (>18 months of treatment)
	Bartonella spp	Doxycycline 100 mg/12 hour orally for 4 weeks Plus Gentamicin (3 mg/kg/24 hour) IV for 2 weeks	
	Legionella spp	Levofloxacin (500mg/12 hour) IV or orally for ≥6 weeks Or Clarithromycin (500 mg/12 hour) IV for 2 weeks, then orally for 4 weeks Plus Rifampicin (300-1200 mg/24 hour)	
	Mycoplasma spp	Levofloxacin (500 mg/12 hour) IV or orally for ≥ 6 months	
	T. whipplei	Doxycycline (200 mg/24 hour) Plus Hydroxychloroquine (200-600 mg/24 hour)	orally ≥ 18 months

4.2. Treatment guidelines for Acute Rheumatic Fever

Category	*Cardiovascular Infection*
Category sub-heading	*Acute Rheumatic Fever*

Diagnosis

Modified 2015 Jones criteria for high risk population

Major Criteria	**Minor Criteria**
▪ Carditis (clinical or subclinical) ▪ Arthritis – monoarthritis or polyarthritis ▪ Polyarthralgia ▪ Chorea ▪ Erythema marginatum ▪ Subcutaneous nodules	▪ Monoarthralgia ▪ Hyperpyrexia (≥ 38.0ºC) ▪ ESR ≥ 30 mm/h and/or CRP ≥ 3.0 mg/dl ▪ Prolonged PR interval (after taking into account the differences related to age; if there is no carditis as a major criterion)

Evidence of preceding infection;

Any one of the following:

1. Increased or rising anti-streptolysin O titer or other streptococcal antibodies (anti-DNASE B).
2. Positive throat culture for group A β hemolytic streptococci
3. Positive rapid group A streptococcal carbohydrate antigen test

Diagnostic criteria

- **First episode of the disease –**Two major criteria or one major and two minor criteria with evidence of antecedent group A β-hemolytic streptococcal infection
- **Subsequent episodes -**
  - Two major criteria or
  - one major and two minor criteria or
  - three minor criteria

Aetiology

Rheumatic fever is caused by group A β haemolytic streptococcal infection

Recommended treatment for Acute Rheumatic Fever

Drug Name	Dose	Frequency/Duration
Benzathine penicillin	0.6 MIU (Paediatrics) 1.2 MIU (Adult)	Intramuscularly at a single dose
Phenoxymethyl Penicillin (Pen V)	250 mg (Paediatrics) 500 mg (Adult)	8-12 hourly for 10 days

Erythromycin	250 mg (Paediatrics) 500 mg (Adult)	12 hourly for 10 days

Secondary Prevention of Rheumatic Fever

No	Drug	Dose	Mode
1	Benzathine penicillin G	600 000 U for children <27 kg (60 lb), 1 200 000 U for those >27 kg (60 lb) every 3 wk or 4 wk	Intramuscular
2	Penicillin V	250 mg twice daily	Oral
3	Sulfadiazine	0.5 g once daily for patients <27 kg (60 lb), 1.0 g once daily for patients >27 kg (60 lb)	Oral
4	Macrolide or azalide	Variable	Oral

Duration of Secondary Rheumatic Fever Prophylaxis

No	Category	Duration After Last Attack
1	Rheumatic fever with carditis and residual heart disease	10 years or until 40 years of age (whichever is longer), sometimes lifelong prophylaxis
2	Rheumatic fever with carditis but no residual heart disease	10 years or until 21 years of age (whichever is longer)
3	Rheumatic fever without carditis	5 years or until 21 years of age (whichever is longer)

Empirical treatment guidelines for Cardiovascular Implantable Electronic Device (CIED) Infection

Category	*Surgical Site Infection (SSI)*
Category sub-heading	*CIED infection*
Diagnosis	
Infection is a serious complication of cardiovascular implantable electronic devices (**CIED**) and is associated with significant morbidity and mortality. **CIED infection** can present as generator pocket **infection** or systemic **infection** (bacteraemia or endocarditis). While diagnosis of pocket infection is typically made based on inflammatory changes (swelling, pain, erythema, drainage, erosion) at the pulse generator site, diagnosis of CIED-related systemic infection is based on positive blood cultures with or without echocardiographic evidence of vegetation on CIED leads or heart valves.	
Aetiology (likely organism)	
Coagulase-Negative Staphylococci (42%), Oxacillin sensitive Staphylococcus aureus (25%), Oxacillin resistant Staphylococcus aureus (4%), Other Gram-positive cocci (4%), Gram –negative bacilli (7%), Polymicrobial (7%), Fungal (2%), Culture-negative (7%)	
Therapy: include generic name, dose, route, frequency and duration	
Empirical	Definitive
Vancomycin 15-20 mg/kg q12h (monitor serum levels) or Linezolid (IV or PO): 600 mg q12h	According to C & S result (at least 2 weeks) Removal of CIED
Prevention of CIED infection	
Strict adherence to aseptic techniques pre-operative antibiotic prophylaxis – IV Amoxicillin/Clavulanic acid + IV Ceftazidime	

4.3. Other infections

Condition	Most likely microbial etiology	First choice	Alternatives	Comments
A. Bacterial Infection				
1. Enteric fever	• *S. Typhi* • *S.Paratyphi A*	Uncomplicated- Cefixime 200mg BD ×14D Complicated- IV Ceftriaxone 2G/12H×14D	PO Ciprofloxacin 500mg BD×10D	
2. Melioidosis	• *B. pseudomallei*	IV Ceftazidime 2G/8H×2wk + Septrin 480mg 3BD×3-6W	IV Meropenem 1G/8H× 2-3W	
3. Brucellosis	• *Brucella abortus,* • *B. melitensis*	PO Doxycycline 100mg BD×6wk + IV Gentamicin 5mg/kg/24H×2W	PO Doxycycline 100mg BD + Rifampicin 600-900mg OD ×6W	
4. *C. difficile* colitis	• *C. difficile*	PO Metronidazole 500mg TDS×10D	PO Vancomycin 125mg QID ×10D	
5. Carbapenem resistant Gram negative bacilli (CR-GNB) causing BSI, pneumonia	• *K. pneumoniae* • *A. baumannii*	High dose Meropenem+ Polymyxin B+ Aminoglycoside/Tigecycline/Fosfomycin ?mg/?Hx?D	IV Ceftazidime-avibactam?mg/?Hx?D	
B. Parasitic infection				
6.Malaria	*Plasmodium vivax*	Chloroquine 25mg base/kg onD0,1,2 F/b Primaquine 0.25mg base/kg/day ×14D		
	Plasmodium falciparum	Artemether-Lumefantrine	Artesunate-Mefloquine	

Condition	Most likely microbial etiology	First choice	Alternatives	Comments
		F/b Primaquine (0.75mg/kg) single dose	Dihydroartemisinin-piperaquine?mg/?Hx?D	
	Severe Malaria	IV Artesunate 2.4mg/kg stat F/b 2.4mg/kg after 12hr and 24hr and then daily until can tolerate PO ACT× 3D + Primaquine (0.75mg/kg) single dose	IM Artemether 3.2mg/kg stat F/b 1.6mg/kg IV Quinine 20mg/kg loading IV infusion over 4hr F/b 10mg/kg every 8hr until can tolerate PO ACT×3D	
7. Visceral leishmaniasis	*Leishmania donovani*	Antimony pentavalent antimonial 20mg/kg IV or IM ×28-30D	Amphotericin B (0.75-1mg/kg)×15-20Doses	
8. Amoebic liver abscess	*Entamoeba histolytica*	PO Metronidazole 800mg TDS ×5-10D	PO Tinidazole/Ornidazole 2G/D ×3D	
9. Neurocysticercosis	*Taenia solium*	Praziquantel 50mg/kg/day in 3 divided doses + Albendazole 15mg/kg in2 divided doses × 2W		
C. Viral infections				
10. Influenza	Influenza A and B viruses	PO Oseltamivir 75mg BD × 5D	PO Zanamivir 10mg (two 5mg inhalations) BD ×5D	
Mycobacterial infections				

Condition	Most likely microbial etiology	First choice	Alternatives	Comments
11. Tuberculosis	*Mycobacterium tuberculosis*			Targeted therapy as in NTP Guideline.
12. Surgical site infection caused by rapidly growing mycobacteria	*M. cheloniei* *M. abscessus* *M. fortuitum*	IV Imipenem 0.5-1G/12-6H + Amikacin 500mg/day x 6W + PO Clarithromycin 500mg BD ×6M		
D. Fungal infections				
13. Pneumocystis pneumonia	*Pneumocystis jiroveci*	Cotrimoxazole 960mg 2TDS ×3W	IV Pentamidine or PO Primaquine 15-30mg Base /day + Clindamycin 600mg/8H× 3W	
14. Invasive aspergillosis	*Aspergillus fumigatus*	IV Voriconazole 6mg/kg/12H for first 24hr, then 4mg/kg/12H or PO 200mg/12H (IV 10D, PO 6-12W)	Liposomal Amphotericin 3-5mg/kg/day x	
15. Invasive mucormycosis	Mucorales	Liposomal Amphotericin 3-5mg/kg/day × 3W	Posaconazole 200mgQID x	
16. Candiduria: Treatment only if patients are Symptomatic or Neutropenic or Undergoing urologic manipulation	Candida spp.	PO Fluconazole 400mg BD × 14D	PO Voriconazole 400mgBD for 2 doses then 200mgBD×14D IV Amphotericin B 0.3-0.6mg/kg OD ×14D	

Chapter 5

Infective Endocarditis Prophylaxis Guideline

Prevention of Infective Endocarditis

Population at risk

Patients with highest risk of infective endocarditis

(1) Patients with prosthetic valves or with prosthetic material used for cardiac valve repair (including trans-catheter-implanted prostheses and homografts
(2) Patients with previous IE
(3) Patients with untreated cyanotic congenital heart disease (CHD) and those with CHD who have postoperative palliative shunts, conduits and other prostheses

Patients with intermediate risk of infective endocarditis

Any other form of native valve disease (including bicuspid aortic valve, mitral valve prolapses and calcific aortic stenosis).

In the highest-risk patients, antibiotic prophylaxis should only be considered for dental procedures requiring manipulation of the gingival or periapical region of the teeth or perforation of the oral mucosa.

Antibiotic prophylaxis is not recommended for respiratory tract procedures, gastrointestinal and urogenital procedures or trans-oesophageal echo and skin and soft tissue procedures.

Recommended prophylaxis for high-risk dental procedures in high-risk patients

Situation	Antibiotic	Single dose 30-60 min before procedure	
		Adults	Children
No allergy to penicillin Or ampicillin	Amoxicillin or Ampicillin Cephalexin, Cefazolin or Ceftriaxone	2 g orally or IV 2 g IV 1 g IV	50 mg/kg orally or IV 50 mg/kg IV 50 mg/kg IV
Allergy to penicillin Or ampicillin	Clindamycin	600 mg orally or IV	20 mg/kg orally or IV

Antibacterial prophylaxis is not recommended for the prevention of IE in patients undergoing dental and dermatological procedures and patients undergoing procedures of the:

- Upper and lower respiratory tract (including, ear, nose, and throat procedures and bronchoscopy)
- Genitourinary tract (including urological, gynecological and obstetric procedures)
- Upper and lower gastrointestinal tract

If patients at risk of IE are undergoing a gastrointestinal or genitourinary tract procedure at a site where infection is suspected, they should receive appropriate antibacterial therapy that includes cover against organisms that cause endocarditis (see 4.1).

Chapter 6

Antibiotic prophylaxis in surgical operation

Preoperative antibiotics prophylaxis is defined as the administration of antibiotics prior to performing surgery to help decrease the risk of post-operative infections.

The routine administration of prophylactic antibiotics is standard in cases in which a patient will have an artificial implant or foreign body implanted as part of the procedure, and other surgeries in which large dissections and higher amounts of anticipated blood loss is expected.

The timing of antibiotic administration may vary, but the goal of administering preoperative systemic prophylactic antibiotics is to have the concentration in the tissues at its highest at the start and during surgery.

The literature supports at least 30 minutes, but no greater than 60 minutes before the skin incision is made as to the optimal timing for the pre-operative administration of most commonly used antibiotics. Special consideration is given for ideal preoperative timing when using a tourniquet, as the administration is at least effective when the antibiotic is given after the application of a tourniquet.

In general, the preoperative antibiotic selection is based on the anatomic region undergoing the specific surgical procedure. The goal when determining appropriate antibiotic selection is to have achieved a relatively narrow spectrum of activity while ensuring the most common organisms are targeted.

Additionally, preoperative antibiotics are chosen based on multitude of factors including cost, safety, ease of administration, pharmacokinetic profile, bactericidal activity, and hospital resistance patterns. By addressing all of these factors during antibiotic selection, surgical site infections (SSIs) are minimized. SSIs, in aggregate, constitute a significant factor driving negative patient-reported outcomes and independent risk factors for increasing financial burden to the entire healthcare system.

Administration

The majority of preoperative prophylactic antibiotics are administered intravenously (IV). The initial timing of administration, re-dosing if applicable, during of prophylactic therapy, and dosing in obese patients are important components in the prevention of surgical site infections as well as antimicrobial stewardship.

Antibiotics should be given within 30 to 60 minutes of a surgical incision. If a patient is already receiving an antibiotic for another infection before surgery, and it is appropriate for surgical prophylaxis, an extra dose of the antibiotic can be administered within 60 minutes of the incision.

Re-dosing antibiotics is an important factor due to the half-life of the particular antibiotic used. Unless there is a known infection, prophylactic antibiotics should be discontinued within 24 hours.

Adverse Effects

Limiting the duration of all antibiotics is important since any antimicrobial usage can alter hospital and patient bacterial flora, which can potentially lead to colonization, resistance, or *Clostridium defficile*.

Contraindications

Antibiotics are commonly used for surgical prophylaxis, so it is important to identify when these antibiotics are contraindicated. Obtaining a thorough allergy history from each patient is vital to ensure if the allergy stated by the patient is a real and significant allergy that would impact the usual preoperative surgical prophylaxis.

Monitoring

When considering antibiotic prophylaxis practices, the correct antibiotic, dosage, timing of initial dose, and timing of any applicable redosing are major factors to review to ensure best practices are always followed. When specific antibiotic in surgery or additional antibiotics are recommended, monitoring should take place to ensure no surgical site infections are occurring due to increasing local resistance.

Toxicity

No apparent toxicities are known with the recommended doses. This is partially due to the limited duration of antibiotic exposure in surgical prophylaxis.

Reference

- Clinical Practice Guidelines for Antimicrobial Prophylaxis in Surgery, ASHP Therapeutic Guidelines.
- Marsha F. Crader Matthew Varacallo. *Preoperative Antibiotic Prophylaxis* StatPearls Publishing; 2020 January.

Type of Procedure	Recommended Agents	Alternative agents in patients with β lactam allergy
Upper GI Surgery		
Procedures involving entry into the lumen of gastrointestinal tract (bariatric, pancreaticoduodenectomy)	Cefazolin	Clindamycin or vancomycin + aminoglycoside or fluoroquinolone
Procedures without entry into the gastrointestinal tract (antireflux, highly selective vagotomy) for high-risk patients	Cefazolin	
Biliary Tract		
Open procedure	Cefazolin, cefoxitin, ceftriaxone, ampicillin-sulbactam	
Laparoscopic procedure		
Elective, low-risk,	None	None
Elective, high-risk	Cefazolin, cefoxitin, ceftriaxone, ampicillin-sulbactam	Clindamycin or vancomycin + aminoglycoside or fluoroquinolones
Appendicectomy for **uncomplicated appendicitis**	Cefoxitin, Cefazolin + Metronidazole	Clindamycin or vancomycin + aminoglycosides or fluoroquinolones Metronidazole + aminoglycoside or fluoroquinolone
Small Intestine		
Obstructed	Cefazolin	Clindamycin + aminoglycoside or fluoroquinolones
Non-Obstructed	Cefazolin + Metronidazole	Metronidazole + aminoglycoside
Hernia repair **(hernioplasty and herniorraphy)**	Cefazolin	Clindamycin or vancomycin
Colorectal	Cefazolin + metronidazole Ampicillin-sulbactam Ceftriaxone + Metronidazole Ertapenem	Clindamycin + aminoglycoside Fluoroquinolone + metronidazole Aminoglycoside + Fluoroquinolones

Reference ++ ASHP therapeutic Guideline

Chapter 7

Antibiotic Therapy for Ventilator Associated Pneumonia (VAP)

VAP

A type of hospital acquired pneumonia that occurs more than 48 hours after endotracheal intubation.

Early VAP -within the first 96 hours of MV

-Common pathogens

Streptococcus pneumoniae

Haemophilus influenza

Staphylococcus aureus

Klebsiella pneumoniae

Escherichia coli

Enterobacter spp.

Late VAP -more than 96 hours after the initiation of MV, which is more commonly attributable to multidrug–resistant pathogens

-More gram negative bacteria; higher incidence of antibiotic resistance

-Common pathogens include:

Pseudomonas aeruginosa

MRSA

Acinetobacter spp.

Stenotrophomonas maltophilia

ESBL producing GNB

Carbapenemase producing GNB

Risk Factors for the Development of Ventilator-associated Pneumonia

- Increasing age (55 years)
- Chronic lung disease
- Aspiration/ micro-aspiration from being nursed in a supine position
- Chest or upper abdominal surgery
- Previous antibiotic therapy, especially broad-spectrum antibiotics
- Reintubation after unsuccessful extubation, or prolonged intubation
- Acute respiratory distress syndrome
- Frequent ventilator circuit changes
- Poly-trauma patient
- Prolonged paralysis
- Premorbid conditions such as malnutrition, renal failure, and anaemia

Risk Factors for Multidrug–resistant Ventilator-associated Pneumonia (VAP)

- Intravenous antibiotic use within the previous 90 days
- Septic shock at the time of VAP
- Acute respiratory distress syndrome (ARDS) preceding the development of VAP
- More than 5 days of hospitalization prior to the development of VAP

Patient requiring acute renal replacement therapy prior to the development of VAP

- Immuno-suppression- chemotherapy, radiotherapy, chronic systemic steroid therapy, splenectomy, autoimmune disease
- Home infusion therapy and home wound care
- Increase severity of illness
- Prolong duration of mechanical ventilation

Clinical Pulmonary Infection Score

Sign	0	1	2
Temperature, °C	36.5-38.4	38.5-38.9	< 36 or > 39
White blood cell count (cells/mm3)	4.0-11.0	< 4 or > 11	> 50% band forms
Oxygenation paO2:Fio2	> 240 or ARDS		< 240 and no ARDS
Chest radiograph findings	No infiltrate	Diffuse (or patchy) infiltrates	Localized infiltrate
Tracheal secretions score	< 14	> 14	Purulent
Culture of tracheal aspirate	Pathogenic bacteria cultured minimal or no growth	Pathogenic bacteria cultured moderate or more growth	Moderate of greater growth of pathogenic bacteria same as on original Gram stain

Score >6 = VAP

ARDS = Acute Respiratory Distress Syndrome

7.1. Antibiotic Therapy for Ventilator Associated Pneumonia (VAP)

Condition	Most likely microbial etiology	First choice	Alternatives	Comments
Early VAP		IV Ampicillin-Sulbactam 1,5-3G/6H Or IV Cefepime 2G/12H Or IV Ceftriaxone-Sulbactam-EDTA 1.5G/12H x7-10D	IV levofloxacin 500mg/12Hx7-10D	Monotherapy is recommended for early VAP.
Late VAP (based on predominant causative organism in local setting)	MDR *Pseudomonas aeruginosa*	IV Ceftazidime 1G/8Hx10-14D Or IV Cefepime 2G/12H x Or IV Piperacillin-Tazobactam 4.5G/6H x Plus IV Amikacin 500mg/12H x Or IV Levofloxacin 500mg/12H x	IV Colistin 3MU/8H x	Use combination therapy if MDR pathogen is suspected Renal adjusted dose is required.
	MDR *Acinetobacter* species	IV Cefoperazone-sulbactam 2-4G/6-8H x Or IV Ampicillin/sulbactam 3G/6H x	IV Meropenem 1G/8H x Or IV Imipenem 500mg/6H x Plus IV Amikacin 500mg/12H x	Duration of antibiotic therapy is 10-14 days.
	ESBL Producing *Klebsiella pneumoniae*	IV Meropenem 1G/8H x Or IV Imipenem 500mg/6H x		

Condition	Most likely microbial etiology	First choice	Alternatives	Comments
	MRSA	IV Vancomycin 1G/12H x OR IV/PO Linezolid 600mg/12H x		

Chapter 8

DRUGS AND THE KIDNEYS
(DOSING OF ANTIMICROBIAL AGENTS IN RENAL INSUFFICIENCY)

Drugs and The Kidneys

In patients with kidney diseases dosing of the drugs must be modified depending on the following factors;

(1) effects of impaired kidney function on drug disposition and response,

(2) assessment of the patient for drug dosing,

(3) calculating drug doses for patients with AKI and CKD, and

(4) drug removal by intermittent and continuous renal replacement therapies.

Renal function in adults is reported on the basis of estimated glomerular filtration rate (eGFR) normalized to body surface area of 1.73m^2 which is calculated by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) or Modification of Diet in Renal Disease (MDRD) formula (mL/min/1.73m^2). *Not valid in acute kidney injury, dialysis and pregnancy.

Published information on the effects of renal impairment on drug elimination has been stated in terms of creatinine clearance (CrCl). The Cockcroft-Gault formula has been used to estimate creatinine clearance for drug dosing in renal impairment. The Cockcroft Gault equation is shown below and there is a calculator on website/app.

$$\text{CrCl (ml/min)} = F \times \frac{(140\text{-age}) \times \text{weight (kg)}}{\text{serum creatinine (micromol/L)}}$$

Where,
F= 1.23 (male)
F = 1.04 (female)

- eGFR should not be used for calcul~~ating drug doses in patients at extremes of~~ body weight (BMI of <18.5 kg/m2 or > 30 kg/m2). Ideal body weight should be calculated and then used to calculate creatinine clearance using Cockcroft-Gault.
    - IBW for males = 50 + (2.3 x (height in inches - 60))
    - IBW for female = 45 + (2.3 x (height in inches - 60))
- eGFR should not be used for calculating drug doses for potentially toxic drugs of a narrow therapeutic index.
- Neither equation is a perfect marker of renal function. When using the equation, creatinine levels should be stable and the clinical picture should always be taken into account.
- Patients that are oligoanuric or dialysis dependent should be assumed to have GFR <10 ml/min and neither equation is valid.

- Dosing guidelines should not replace clinical judgement and are intended to provide initial guidance and may be modified depending on individual patient.

Patients with CKD

In patients with CKD, several pharmacokinetic factors may be altered. These include bioavailability, volume of distribution (Vd), protein binding, and biotransformation.

Assessment of renal function by the Cockcroft–Gault (CG) equation (Cockcroft and Gault 1976), the Modification of Diet in Renal Disease (MDRD)equation (Levey et al., 1999), and the most recent, Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation (Stevens and Levey, 2009; Stevens et al., 2010).

Adjustment for loading dose and maintenance doses depending on the renal function for individual drugs as shown in following tables.

Determining loading dose

In patients with normal renal function, steady-state drug concentration is achieved after approximately 3.3 half-lives. In patients with renal failure, the half-life may be significantly prolonged.

Achievement of steady-state drug levels, which ensures therapeutic efficacy, may be greatly delayed if a loading dose is not given. In general, patients with renal failure should receive the same loading dose as patients with normal renal function in order to achieve a rapid therapeutic dose.

The following formula can be used to calculate the loading dose with Vd in L/kg, IBW, and desired plasma concentration, Cp(mg/L):

LD = Vd× IBW× [Cp]

Vd = volume of distribution

IBW = Ideal body weight

Cp = desired plasma concentration

Determining maintenance dose

There are two ways to adjust the maintenance dosage in patients with renal failure: prolonging dosing interval and dosage reduction.

Increasing the dosage interval can be directly correlated to the degree of renal impairment by the following formula:

$$\text{Dosing Interval} = \frac{\text{normal Clcr x normal interval}}{\text{patient 's Clcr}}$$

With the dosing interval remaining constant, dosage reduction corresponding to the degree of renal impairment can be determined by the following formula:

$$\text{Maintenance Dose} = \frac{\text{patient s Clcr x normal dose}}{\text{normal Clcr}}$$

Dosage interval extension allows for adequate peak concentrations but may risk sub-therapeutic trough levels. Dosing reduction may provide for more constant drug levels but increases the risk of toxicity from higher plasma trough concentrations.

Drug dosing considerations for patients with AKI

- The KDIGO AKI, AKIN, RIFLE criteria should be prospectively utilized to optimize the identification of patients at highest risk of developing AKI
- High-risk medications, those with known nephrotoxicity, or other potential toxicities associated with supra-therapeutic serum concentrations should be identified proactively, for example, computerized order entry, so that the prescribing clinician can closely monitor patient response
- The volume of distribution of several medications is dramatically increased in the presence of AKI and thus larger loading doses may need to be administered to avoid sub-therapeutic responses due to the achievement of lower than desired serum concentrations.
- When possible, therapeutic drug monitoring should be utilized for those medications where serum drug concentrations can be obtained in a clinically relevant time frame.
- Trends in renal function indices such as serum creatinine and urine output along with volume status should be utilized to guide drug dosing when rapidly measurable indices are unavailable.
- For those medications where therapeutic drug monitoring is not possible, close monitoring of drug PD(Pharmacodynamics) may prove to be a useful surrogate.
- Evaluation of risk for drug–drug and drug–nutrient interactions should be facilitated by incorporating validated electronic drug interaction tools into EMRs (electronic medical records).
- A patient-centered team approach that includes an ICU pharmacist is recommended to prevent medication-related problems and enhance safe and effective medication use.
- EMRs should maintain records for discontinued medications for up to 7 days to make it possible to assess potential residual effects on the patient's current condition.

Antimicrobial	Creatinine clearance (CrCl) (ml/min)			Comments
	20-50	10-20	<10	
Aciclovir IV	CrCl 25-50 5-10mg/kg every12h	CrCl 10-25 5-10mg/kg every24h	2.5-5mg/kgevery24h	The higher dose should be used for those patients with encephalitis and those who are immunocompromised. Give doses post HD.
Aciclovir PO	CrCl 25-50 Normal	Cr-Cl10-25 Simplex:200mgqds Zoster:800mgtds Prophylaxis: Reducedoseby50%	Simplex:200mgbd Zoster:800mgbdProphylaxis: Reducedoseby50%	Give doses after HD.
Amikacin	5-6 mg/kg12h	3-4 mg/kg24h	2mg/kg24-48h	*Therapeutic drug monitoring required. Subsequent doses should be adjusted according to levels. HD:5mg/kg post each HD session.
Amoxicillin IV and PO	Normal	Normal	250mg-1G8h	Give doses after HD.
Ampicillin	Normal	250mg – 2G 6h	250mg-1G6h	Give doses after HD.
Ampicillin + Sulbactam (IM/IV)	CrCl>30 1.5-3g6-8h	CrCl 15-30 1.5-3g12h	CrCl<15 1.5-3g24h	Give doses after HD.
Amphotericin IV	Normal	Normal	Normal	Amphotericin is highly NEPHROTOXIC*.

Antimicrobial	Creatinine clearance (CrCl) (ml/min)			Comments
	20-50	10-20	<10	
				Daily monitoring of renal function is essential.
Azithromycin	Normal	Normal	Normal	Give doses after HD.
Benzylpenicillin	Normal	600mg-2.4Gevery 6hours	600mg-1.2Gevery 6hours	Give doses after HD.
Cefepime IV	0.5-2g 12-24H	0.5-2g 24h	0.25-1g 24h	For Hemodialysis: 1G on day-1, then 0.5g/24h thereafter.
Cefoperazone + Sulbactam IV	Normal	Normal	Normal Max 2G/day	
Cefotaxime IV	CrCl 20-50 Normal	CrCl 5-20 Normal	CrCl<5 Reduce dose by 50%	
Ceftazidime IV	CrCl30-50 1-2G/12H	CrCl15-30 1-2G/24H	CrCl6-15 500mg-1g24h CrCl<5 500mg-1g48h	For Hemodialysis: Give 500mg-2g every 48h or post dialysis.
Ceftriaxone IV	Normal	Normal	Normal Max2g/day	
Cefuroxime IV	Normal	750mg–1.5g12h	750mg–1.5g 24h	Give doses after HD.
Chloramphenicol	Normal	Normal	Normal	Give doses after HD.

Antimicrobial	Creatinine clearance (CrCl) (ml/min)			Comments
	20-50	10-20	<10	
Ciprofloxacin IV+PO	Normal	50-100% of normal dose	50% of normal dose	
Clarithromycin IV + PO	CrCl30-50 Normal	CrCl10-30 250-500mg12h	250-500mg12h	Give doses after HD. .
Clindamycin IV + PO	Normal	Normal	Normal	
Co-Amoxiclav IV	CrCl30-50 Normal	CrCl10-30 1.2g12h	1.2g12h	Give doses after HD.
Co-Amoxiclav PO	Normal	Normal	Normal	Give doses after HD.
Colistin (Colistimethate sodium) Standard dose: Colistin IV 3 million units/8h	CrCl 30-50 3.5millionunits/12h Normal loading dose in critical care patients	CrCl 10-30 2.5millionunits/12h Normal loading dose in critical care patients	CrCl<10 1.75millionunits/12h Normal loading dose in critical care patients	Inpatients on critical care, give a loading dose of 9 million units. The same loading dose applies to those with normal and impaired renal function, including those on renal replacement therapy. Start the maintenance dose 12hours after the loading dose in those with CrCl<50ml/min. HD patients: 1.5millionunits twice a day, where possible give post dialysis.
Co-trimoxazole IV + PO **(Treatment doses only)**	CrCl30–50 Normal	CrCl15-30	CrCl<15 PCP:30mg/kg/12h	Give doses after HD.

Antimicrobial	Creatinine clearance (CrCl) (ml/min)			Comments
	20-50	10-20	<10	
		PCP: Normalfor3days, then30mg/kg/12h Other infections: 50%of normal dose	Other infections: 50%of normal dose	
Doxycycline	Normal	Normal	Normal	
Erythromycin PO	Normal	Normal	Normal	
Flucloxacillin IV+PO	Normal	Normal	Normal uptomax4g/day	
Fluconazole(IV+PO)	50-100% of normal dose	50-100% of normal dose	50%ofnormaldose	Give doses after HD. Dose is dependent on indication. No adjustments for single doses required.
Gentamicin	CrCl 30-70 3-5mg/kg/day	CrCl 10-30 2-3mg/kg/day	CrCl 5-10 2mg/kg every 48-72h according to level	Monitor blood levels*
Imipenem	50% of normal dose	50% of normal dose	25% of normal dose	
Itraconazole(PO)	Normal	Normal	Normal	
Levofloxacin	Initial dose 250-500mg then 125mg daily to 250mg/12-24h	Initial dose 250-500mg then 125mg/12-48h	Initial dose 250-500mg then 125mg/24-48h	
Linezolid	Normal	Normal	Normal	Give doses after HD.
Meropenem	CrCl26-50 500mg - 2g 12h	CrCl10-25 500mg – 1g 12h (or) 500mg 8h	CrCl<10 500mg – 1g 24h	Give doses after HD.
Metronidazole	Normal	Normal	Normal	Give doses after HD.

Antimicrobial	Creatinine clearance (CrCl) (ml/min)			Comments
	20-50	10-20	<10	
Moxifloxacin(IV and PO)	Normal	Normal	Normal	
Ofloxacin	200-400mgod	200-400mgod	100-200mgod	Give doses after HD.
Oseltamivir(treatment dose)	CrCl 30-60 Normal75mg/12h	CrCl 10-30 75mg 24h 30mg12h	75mgsingledose	
Penicillin-V	Normal	Normal	Normal	Give doses after HD.
Piperacillin-Tazobactam	CrCl>40 Normal	CrCl 20-40 2.25g 6h	CrCl<20 2.25g 8h	Give doses after HD.
Valacyclovir	CrCl30-50 Zoster:1gbd Simplex: Normal	CrCl 10-30 Simplex: 500mg-1000mg daily Zoster: 1g daily	CrCl<10 Simplex: 500mg daily Zoster: 500mg daily	Give doses after HD.
Vancomycin	0.5-1g /every 12-24 hours	0.5-1g /every 24-48 hours	0.5-1g /every 48-96 hours	Monitor blood levels* and adjust dose as required.
Zanamivir	Normal	Normal	Normal	

Anti-tuberculous drugs and kidney disease

Ethambutol

- ✓ Cleared by the kidneys.
- ✓ Dose adjustment required for renal failure.
- ✓ Increased risk of toxicity with renal failure
- ✓ Dose: 15-25 mg/kg/dose 3 times/wk (not daily)

Pyrazinamide

- ✓ Cleared by the kidneys.
- ✓ Dose 3 times a week and after dialysis
- ✓ Dose: 25mg/kg/dose 3 times/wk(not daily)

Conclusions

Individual patient responses to drug therapy during renal insufficiency are variable, complex, and require a basic understanding of pharmacologic principles in order to maximize drug therapy and avoid toxicity. Dosage adjustment strategies should be based on several factors including not only reduction in GFR, drug level monitoring, and direct correlation with clinical picture, but clinicians must also take into account the many pharmacokinetic and pharmacodynamic parameters involved in drug therapy for patients with CKD. Every attempt has been made to provide the latest data on drug dosing in CKD in accordance with existing dosage recommendations. However, the clinical circumstances, co-morbid conditions, and drug–drug interactions should be considered to avoid drug toxicity and ensure the therapeutic benefits of each individual agent (Seyffart 2011).

Chapter 9

HOSPITAL ANTIBIOTIC PROFILE (2015-2018)

In this chapter, antibiotic profile (otherwise, cumulative antibiogram) of 1000-bedded Naypyitaw General Hospital for 4-years (2015 to 2018) could be studied. The comprehensive cumulative antibiogram may help in clinical decision-making, design infection control interventions, and antimicrobial-resistance containment strategies. This data can only show the antibiogram of only patients' clinical specimens. For microbial surveillance, fumigation swabs in operation theater and dialysis water study are routinely undergoing. There were no more environmental swabs received in microbiology laboratory since neonatal ward had shifted to Ottarathiri Township.

This antibiotic profile could reveal the resistant patterns of aerobic bacteria mainly isolated from the clinical specimens of hospitalized patients only. Antibiogram of inpatients' specimen may differ from that of all inpatients and outpatients.

Table-1. Number and type of C&S specimen (2015-2018)

Specimen Type	Specimen number				
	2015	2016	2017	2018	Total
Urine	729	696	205	213	1843
Pus	330	490	271	211	1302
Blood	506	345	159	291	1301
Sputum and respiratory specimens	345	181	238	285	1049
Wound	153	181	121	104	559
Stool and Rectal Swab	92	55	20	3	170
Fluid	37	37	30	19	123
CSF	22	18	18	23	81
Others	69	24	43	12	148
Total	2283	2027	1105	1161	6576

Others = HVS, Tissue, Liver, Bile, Urethra, Gastric, Eye, Ear & GANT,

Table-2. Isolated organisms and type of specimen (2015-20118)

Type of specimen	Escherichia coli	Klebsiella sp.	Staphylococcus aureus	Pseudomonas aeruginosa	Other Staphylococcus sp.	Enterobacter sp.	Acinetobacter sp.	Streptococcus sp.	Proteus sp.	Citrobacter sp.	Other Pseudomonas sp.	Enterococcus sp.	Burkholderia cepacia complex	Salmonella sp.	Shigella sp.	Aeromonas sp.	Serratia sp.	Burkholderia pseudomallei	Other bacteria	Candida albicans	Candida, not albicans	Culture +	Culture Positive Rate	Contaminated specimen	No growth	Total
Urine	118	40	2	16	6	26	7		17	10	13	19	1	4	5	1			13	15	21	334	18.12%	54	1455	1843
Pus	98	59	253	24	48	24	11	34	28	14	2	5	1	1	1	1	3	1	21		1	630	48.39%		672	1302
Blood	9	46	6	2	55	11	8	3	1	6	2	1	5	4		3	1	2	12	1	3	181	13.91%	12	1108	1301
Sputum and respiratory	47	139	4	95	11	49	51	45	7	14	16	4	4	1	1	5	2		24	28	12	559	53.29%	1	489	1049
Wound	60	34	39	59	38	28	33	8	18	15	9	9	1		1	1	5	1	19	1	3	382	68.34%	3	174	559
Stool and Rectal	10	1		1		3	2		1	2	1			1	3				1			26	15.29%		144	170
Fluid	5	5	4	15	1	2	6		1		4	1	2						6	1		53	43.09%	1	69	123
CSF				1	2	1																4	4.94%	1	76	81
Other specimens	13	6	12	5	19	3			2	2				1	1				6			70	47.30%	1	77	148
Total	**360**	**330**	**320**	**218**	**180**	**147**	**118**	**90**	**75**	**63**	**47**	**39**	**14**	**12**	**12**	**11**	**11**	**4**	**102**	**46**	**40**	**2239**	**34.05%**	**73**	**4264**	**6576**

Table.3 Antimicrobial Susceptibility Pattern (%) of Gram Negative Bacteria

Gram Negative Bacilli	Probable ESBL+	Sensitive to Antibiotics																			
		Ampicillin	Amoxicillin/Clavulanic acid	Cefoperazone/Sulbactam	Ampicillin/Sulbactam	Piperacillin/Tazobactam	Cefazolin	Ceftazidime	Ceftriaxone/Cefotaxime	Cefepime	Aztreonam	Ertapenem	Imipenem	Meropenem	Amikacin	Gentamicin	Tobramycin	Ciprofloxacin	Levofloxacin	Chloramphenicol	Doxycycline	Colistin
Escherichia coli (n=360)	15%			53%		54%						85%	87%	88%	85%	50%				75%		
Klebsiella spp. (n=330)	15%			60%		56%					88%	79%	82%	85%	59%			65%		67%		
Pseudomonas aeruginosa (n=218)				71%		68%		61%		66%	56%		65%	57%	82%	62%	71%	63%	62%			100%
Enterobacter spp. (n=147)				50%							78%	68%	74%	76%							53%	
Acinetobacter spp. (n=118)				50%											56%							100%
Proteus spp. (n=75)			57%		85%	75%	50%	63%	57%	50%	71%	91%	75%	94%	89%	54%			66%			

Table.3 Antimicrobial Susceptibility Pattern (%) of Gram Positive Bacteria

Gram Positive Cocci	Sensitive to Antibiotics																		
	Penicillin	Methicillin	Ceftriaxone/Cefotaxime	Gentamicin	Rifampin	Ciprofloxacin	Levofloxacin	Moxifloxacin	Cotrimoxazole	Clindamycin	Azithromycin	Clarithromycin	Erythromycin	Nitrofurantoin	Linezolid	Vancomycin	Chloramphenicol	Quinupristin/Dalfopristin	Doxycycline	Tetracycline
Staphylococcus aureus (n=320)	4%	63%		94%	82%	89%	93%	91%	53%	85%	81%	87%	58%	97%	98%	94%	93%	91%	88%	74%
Coagulase Negative Staphylococci (n=157)	6%	20%		64%	62%	36%	40%	33%	27%	57%	40%	29%	28%	98%	95%	95%	74%	84%	67%	61%
Streptococcus spp (n=91)	77%		75%				70%			70%	54%	60%	52%		100%	100%	79%		88%	27%
Enterrococcusspp (n=39)	31%					26%	30%	13%	29%				21%	82%	86%	75%	72%		38%	7%

MRSA = Methicillin Resistant Staphylococcus aureus, MRSS = Methicillin Resistant Staphylococcus species

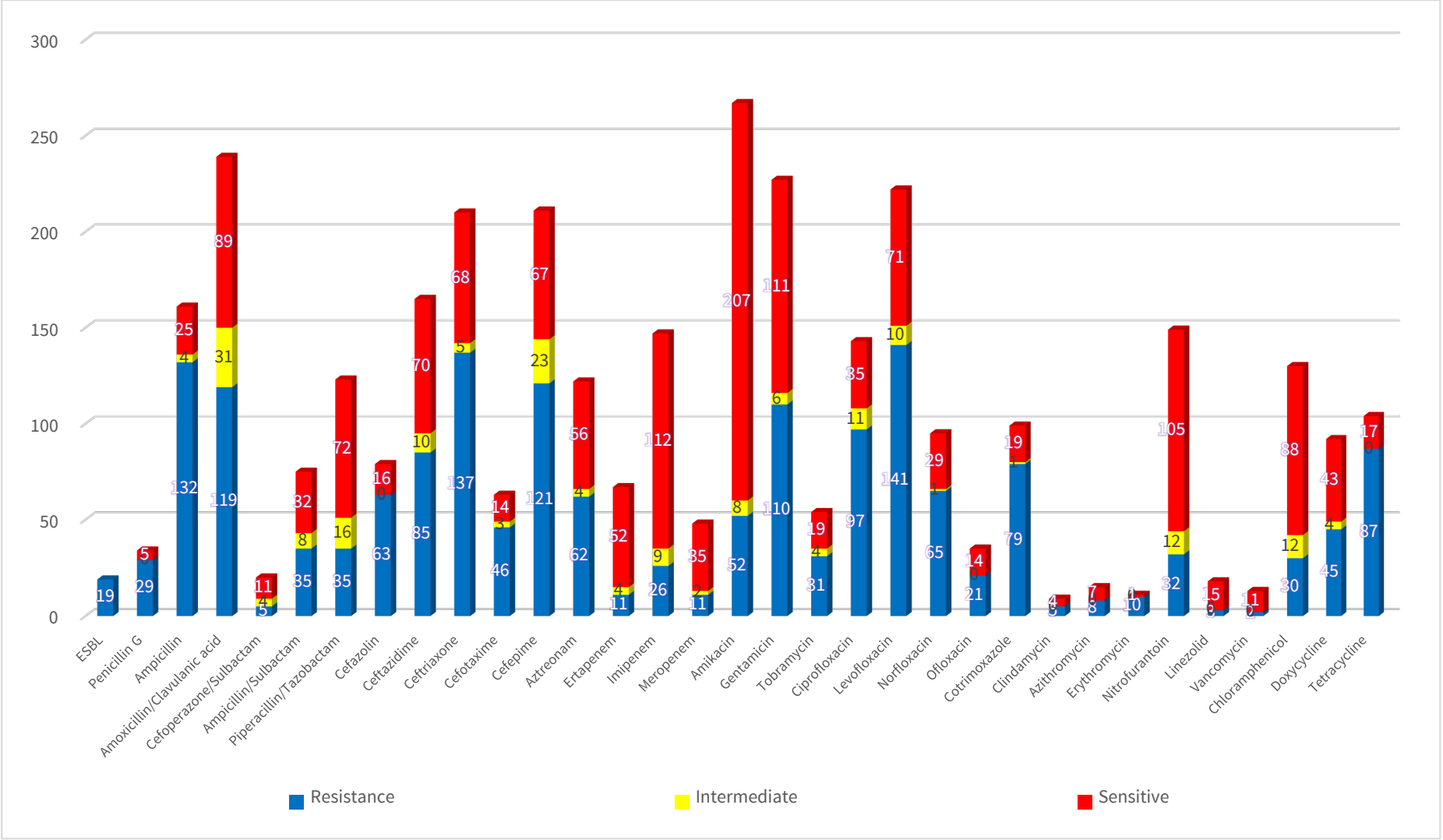

Fig-1. Antibiotic profile of Urine C&S (n=298)

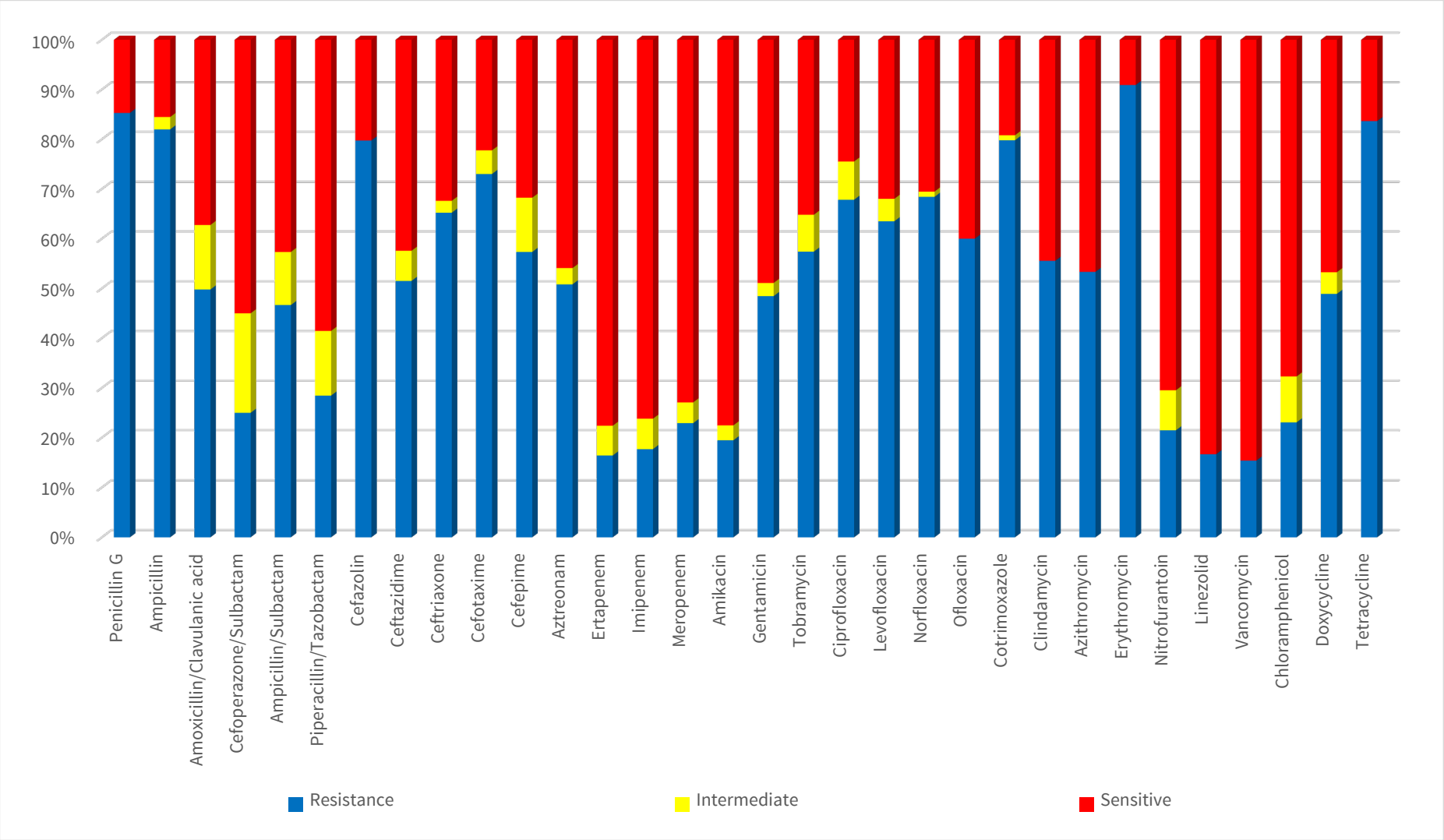

Fig-2. Antibiotic profile of Urine C&S (%)

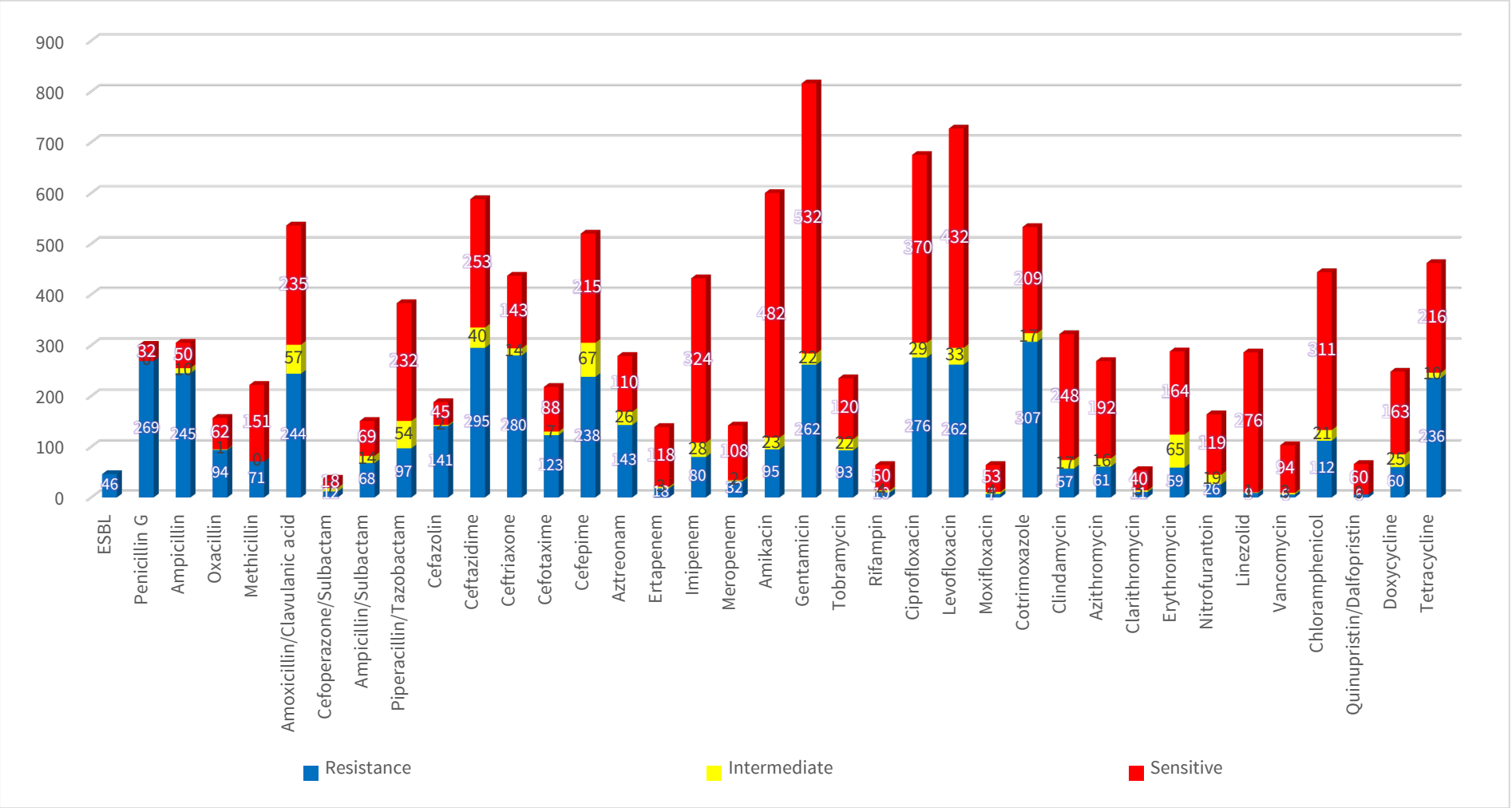

Fig-3. Antibiotic profile of Pus and Wound C&S (n=1003)

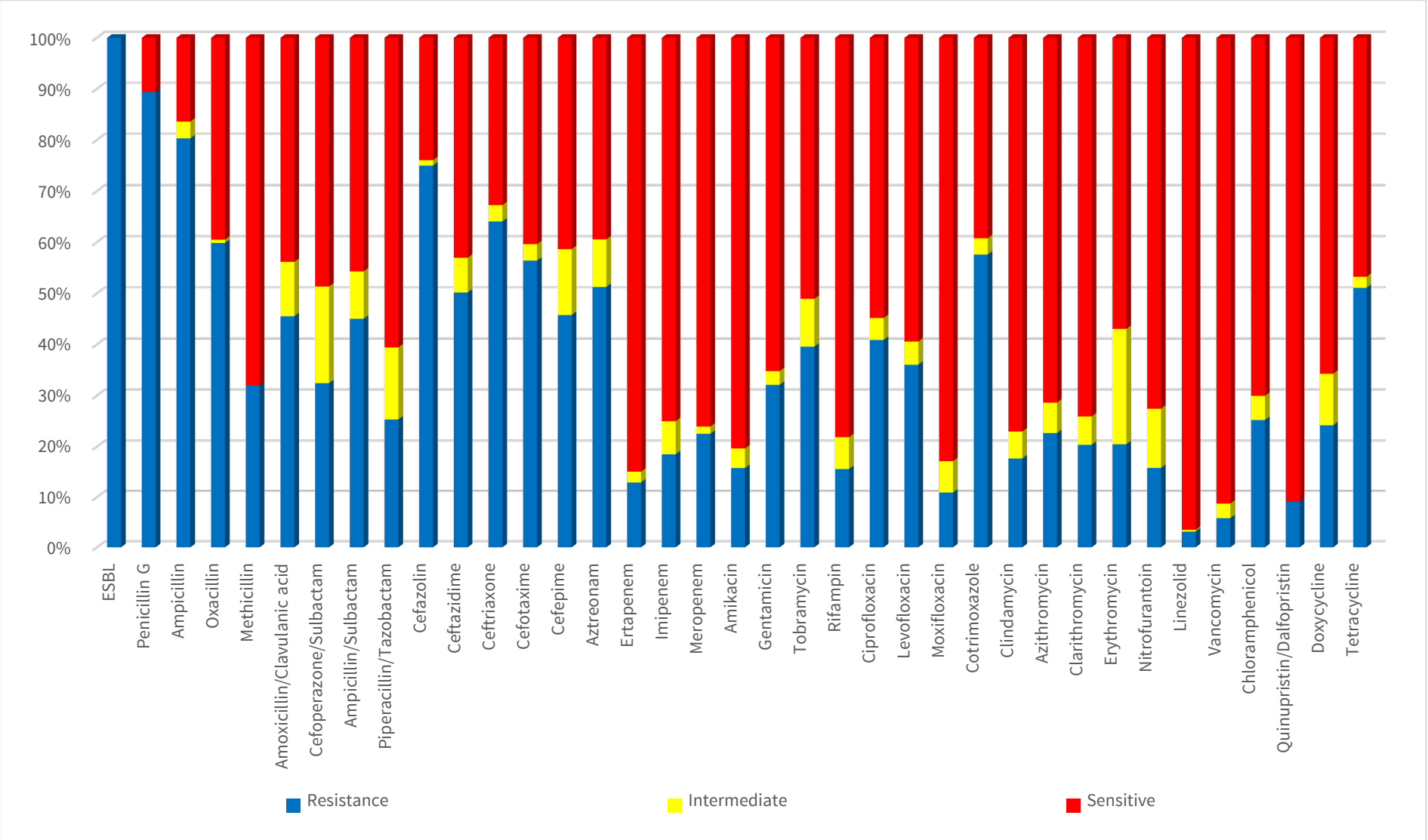

Fig-4. Antibiotic profile of Pus and Wound C&S (%)

Annexes

Annex-I. Antimicrobial Steward Review Form.

Patient Information		
Date:	Department:	Ward:
Patient name:	Age:	Sex: Male ☐ or Female ☐

Antibiotic prescriptions					
#	Antibiotics prescribed	Dose	Route	Interval	Start date

Indication for antibiotic treatment				
Prophylaxis ☐	UTI ☐	Pneumonia ☐	GI Infection ☐	Bloodstream Infection ☐
CNS infection ☐	Skin infection ☐	Bone infection ☐	Other:…….	

Initial review of antibiotic treatment		
Is indication for antibiotic treatment documented? Yes ☐ No ☐	Is antibiotic treatment prescribed according to guideline? Yes ☐ No ☐ Why not? Comment →	Comment:
Correct dose? Yes ☐ No ☐	Appropriate route? Yes ☐ No ☐	Treatment duration or review date stated? Yes ☐ No ☐

48-hour review of antibiotic treatment				
Is antibiotic treatment reviewed? Yes ☐ No ☐		If yes, what action?		
Escalate ☐	Continue ☐	De-escalate ☐	Stop ☐	IV-oral switch ☐
Why is antibiotic treatment being continued?				
Continuing clinical signs of infection ☐	Confirmed infection ☐	Other (comment):		
Microbiology specimens collected? ☐ Date:	Microbiology results received? ☐ Date:	Microbiology results acted upon? ☐ Comment:		

General Comments:
Date: ……/……/……. Name & Signature (Reviewer):

5-Moments of Hand Hygiene

7-Steps of Hand Hygiene

7 steps of hand hygiene

ဖဝါးဖမိုး လက်ခေါက်ချိုး

လက်ကြားလက်မ မကျန်ရ

ကုတ်၍ခြစ်ပါ လက္ခဏာ

လက်ကောက်ဝတ်မှာ အဆုံးသတ်ပါ။

5 moments of hand hygiene

1. Before touching a patient, (လူနာကို မထိမီ)
2. Before clean / aseptic procedure, (Procedure မလုပ်မီ)
3. After touching a patient, (လူနာကို ထိပြီး)
4. After body fluid exposure risk (After risk procedure) (Procedure လုပ်ပြီး)
5. After contact with patient surrounding. (လူနာနေရာတဝိုက်ကိုထိပြီး)

Daily Floor cleaning (Mopping) Steps

ပထမ - ကြမ်းပြင်ကို ဆပ်ပြာရည်+ရေဖြင့် သန့်ရှင်းရေး စလုပ်ပါ။

ဒုတိယ - 0.1% Chlorine solution OR 10% Aseptol (Phenol) solutionဖြင့် သန့်ရှင်းရေး လုပ်ပါ။

တတိယ - အဝတ်ခြောက်ဖြင့် သန့်ရှင်းရေး လုပ်ပါ။

Spillage Management အညစ်အကြေး (ဆီး၊ဝမ်းသွေး၊သလိပ်)များဖိတ်စင်လျှင်

လိုအပ်သော အကာအကွယ်ပစ္စည်းများ (Boot, Apron, Mask, Goggles, Cap) ဝတ်ဆင်ပြီး

၁- ဖန်ကွဲစများရှိလျှင် ညှပ်ဖြင့် ကောက်၍ sharp container ထဲသို့ စွန့်ပစ်ပါ။

၂- အရည်စုပ်သော စက္ကူ၊ အဝတ်၊ ဝါဂွမ်းဖြင့် အုပ်ပါ။

၃- Antiseptic (0.1% Chlorine OR 10% Aseptol/Phenol) solution လောင်းပါ။

၄- မိနစ်-၃၀နှန့် ထားပါ။ ဆိုင်းဘုတ်ထောင်ထားလျှင် ပိုကောင်းသည်။

၅- ပလတ်စတစ်တံမြက်စည်းနှင့် ဂေါ်ပြားကို သုံး၍ Infectious container တွင်စွန့်ပစ်ပါ။

၆- Mopping ပြုလုပ်ပါ။

၇- Incident register bookတွင် မှတ်တမ်းတင်ပါ။