राष्ट्रीय आयुर्विज्ञान आयोग

National Medical Commission

National Action Plan on Antimicrobial Resistance (NAP-AMR) Module for Prescribers

2024

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Pocket-14, Sector-8, Dwarka Phase-1, New Delhi-110077, INDIA

National Action Plan on Antimicrobial Resistance (NAP-AMR)

Module for Prescribers

राष्ट्रीय आयुर्विज्ञान आयोग

National Medical Commission

-Editor-

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Government of India
Department of Health and Family Welfare
Ministry of Health and Family Welfare

MESSAGE

Antimicrobial resistance is recognised as a serious current and future threat in the practice of modern medicine. Misuse and overuse of antimicrobials are the main drivers in the emergence of drug resistant pathogens. AMR impacts all sectors and hence is a "One health" issue. Ministry of Health and Family Welfare developed the National action Plan on AMR in alignment with the Global Action Plan with a "One Health" approach and launched it is April 2017.

One of the Strategic objectives of the NAP AMR is strengthening education and awareness and National Medical Commission is an important stakeholder to implement the activities enlisted under this objective. One such activity is to review and revise the curricula for professionals and allied services by developing an AMR module to bring together segmented knowledge imparted under different subjects.

The containment of AMR demands judicious use of antimicrobials through effective utilisation of laboratory services and continuous improvement in infection prevention and control practices to prevent transmission of AMR pathogens. I hope this AMR module developed by NMC which covers these competencies will impart practical education to medical students thereby promoting prescribing behaviours towards judicious use of antimicrobials in day to day management of patients by these young doctors and thereby sustain the gains of modern medicine over the past years in management of disease. NMC would need to ensure availability of adequate infrastructure, manpower and other resources in medical colleges for practical implementation of these modules.

I convey my best wishes to NMC for release of these modules and for implementing these modules effectively.

Place : New Delhi
Date : 10th April 2024

(**Apurva Chandra**)

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MESSAGE

Antimicrobials have served as one of the most important arsenal in modern medicine in the last century and have improved treatment outcomes across both medical and surgical practice. However, their utility is threatened due to increasing resistance of micro-organisms to antimicrobials to such an extent that bacteria resistant to almost all antibiotics are being witnessed.

To combat this increasing trend of antimicrobial resistance, the Government of India released its National Action Plan on Antimicrobial Resistance (NAP-AMR) in 2017 with a "One Health" approach, involving consultation with various stakeholders Ministries/Departments at the national level, in alignment with the Global Action Plan on Antimicrobial Resistance (GAP-AMR) by the World Health Organization (WHO). In addition to the five objectives of the GAP-AMR, India's NAP-AMR has set a target of achieving six main objectives to fulfil its commitment towards the sustainable development goals 2030.

The National Medical Commission has taken up the humungous task of achieving objective under Strategic priority no. 1 and 4 by developing curriculum for prescribers as well as non-prescribers; to improve the awareness and understanding of AMR through training and education and regarding prescription of antibiotics. The prescriber module of NAP-AMR likely focuses on educating and empowering healthcare providers mainly prescribers on appropriate antibiotic use. This may include recommendations on: When to prescribe antibiotics; choosing the right antibiotic for the specific infection; Using the correct dosage and duration of antibiotic treatment.

I am positive that the Medical Colleges and Institutions will actively participate and support National Medical Commission to achieve the objectives in this National Action Plan with enthusiasm and collectively contribute towards making this programme a success.

I assure all support and resources to the stakeholders involved and convey my best wishes.

(Dr. B.N. Gangadhar)

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Message

Modern medicine or Allopathy has contributed immensely in improving the health quotient and quality of life. Alexander Fleming's discovery of Penicillin in 1928, was a miracle that came in to save millions of lives from bacterial infections globally. Over the years the research in antimicrobials grew by leaps and bounds. Along with the fast pace of development, human beings also lost the patience of waiting to see response of antibiotics and anti-microbials. Slowly the abuse and overuse of molecular combinations and swift shift from oral to intravenous and central lines occurred by the beginning of 21st century. Thus, along with the threat of global warming that has affected the civilization and human race as also the planet, field of allopathy in the present times. It has affected the recovery from simple respiratory diseases to immunocompromised states universally, with more dire consequences in developing countries than developed countries. As per the WHO data, bacterial AMR was directly responsible for 1.27 million global deaths in 2019. Further, the World Bank estimates that AMR may result in US$ 1 trillion additional healthcare costs by 2050. India will also be hit hard if aggressive, pro-active steps are not taken to control this human-created threat to the very existence of life.

It is therefore very praise worthy effort by Dr. Vijayalakshmi Nag, member of Ethics and Registration Board (EMRB) of National Medical Commission, who is also the Chair of this committee, and her team to take up this project of 'Antimicrobial Resistance- awareness and steps to control it in India'. This compendium prepared by the team has been done by painstaking efforts of various scientists. It has emerged as an excellent hand-book. It begins with general background of the subject and moves on to describe clinical approaches for prescribing antimicrobials, stewardship, interpretation of antimicrobial sensitivities, watchdogs of the same, various drugs, and further navigates to policy

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making, dos and don'ts, including biomedical waste management and finally covers important aspects of corona pandemic era to close with biomedical waste management and beautiful illustrations obtained from prestigious medical institutions.

I would like to recommend it as a project for all undergraduate students to be taken up preferably during the phase of 'electives' as mandatory training in the end of first block, in the end of Final MBBS part 1. I congratulate the entire team for this work and wish that it achieves the desired result of educating young medical students and in controlling the abuse and overuse of anti-microbials.

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MESSAGE

Invention of anti-microbials paved way for treatment of severe infections, particularly in immuno-compromised patients. Studies have shown the utility of anti-microbial agents in preventing infections in surgeries where there is bacterial contamination. However, indiscriminate and excessive use of these agents have developed resistance mechanism in these organisms making them anti-microbial resistant organism.

Also unnecessary use of anti-microbials comes is the way of development of natural immunity apart from avoidable side effects of these drugs and financial burden on patients. So the time has come for judicious use of anti-microbial agents. Government of India has taken timely step to prepare guidelines for the judicious use of anti-microbials and steps to be taken to prevent anti-microbials resistance.

I thank the government for trusting National Medical Commission for preparing these guidelines in the form of modules and toolkits for the training of all prescribers in an attempt to combat the increasing anti-microbial resistance. Dr Vijaya Lakshmi Nag, Member, Ethics and Medical Registration Board and Professor and HoD (Microbiology), AIIMS, Jodhpur and her team has done an excellent job in preparing this module and its accompanying toolkit keeping in mind the needs of the country in early sensitization of the medical students that represent the cohort of future prescribers. I look forward to the plan being implemented efficiently in all medical colleges and institutions of the country and at all levels wherever antibiotics are used which can be achieved by continued communication, collaboration and public engagement.

Vijay. V. Oza

(Dr Vijay Oza)

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MESSAGE

Antimicrobial resistance (AMR) is one of the most serious global public health threats in this century caused due to misuse/overuse of antimicrobials. According to WHO, It is estimated that bacterial AMR was directly responsible for 1.27 million global deaths in 2019 and contributed to 4.95 million deaths. The World Bank estimates that AMR could result in US$ 1 trillion additional healthcare costs by 2050, and US$ 1 trillion to US$ 3.4 trillion gross domestic product (GDP) losses per year by 2030.

Inappropriate use of antimicrobials leads to development of drug resistance, hence making common infections difficult to treat leading to higher mortality, complications, and prolonged hospital stays. This makes it crucially important that our healthcare professionals should be well versed with the Antimicrobial stewardship program (AMSP) to ensure prudent antimicrobial prescribing focused on "4Ds", practice appropriate infection control techniques like OSHA etc. and learn effectual segregation & disposal of Biomedical Waste (BMW) as per rules.

Together we can make a difference in this fight while ensuring future generations have access to effective treatments for infections. I hope that this module would serve as a guiding light to maintain the effectiveness of antibiotics and preserve our ability to combat infectious diseases.

(Dr J. L. Meena)
22/3/2024

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From Editor's Desk

I am deeply grateful to Prof. S.C. Sharma, the founder Chairman, of the National Medical Commission (NMC) and Ex-Head of the Department of Otorhinolaryngology-Head and Neck Surgery at All India Institute of Medical Sciences, New Delhi for assigning this task, which brought me closure to my field of microbiology and providing necessary support and guidance for accomplishing this task.

Antimicrobial resistance (AMR) has been identified by the World Health Organization (WHO) as one of the top 10 global public health threats against humanity. Misuse and overuse of antimicrobials are the main drivers in developing drug-resistant pathogens. AMR being a "One Health" issue, its containment requires the active participation of various stakeholders, ministries and departments.

The Ministry of Health and Family Welfare developed the National Action Plan on AMR (NAP-AMR) in alignment with the Global Action Plan on AMR (GAP-AMR) with a "One Health" approach at the National level. The NAP-AMR sets out six strategic priorities. Under each strategic priority, specific objectives of key focus areas with elaborate interventions, activities and key outputs, responsible agencies, and expected timelines have been stated. The NMC has been assigned objectives under strategic priorities 1 and 4 of the NAP-AMR.

The National Medical Commission governs medical colleges and medical professionals. It is also responsible for maintaining the quality of medical education in India. For NAP-AMR a letter was circulated to the Directors, Principals and Deans of 606 institutions across the country to collect baseline data on ongoing AMR activities in their institutions. They were to nominate a nodal officer in each institute to facilitate the implementation of the 'national action plan on antimicrobial resistance' objectives assigned to NMC. Three hundred fifty (350) medical colleges responded through the prescribed Google form and provided the details of activities going on.

We also invited experts online among nominated nodal officers preferably from all zones of the country to discuss the objectives assigned to NMC under NAP-AMR. We conducted various online & physical meetings to discuss the objectives and ways to achieve the goal.

It's my pleasure to introduce the prescribers' module, produced with the help of subject experts, from the field of Microbiology, Medicine, Pharmacology and Community Medicine from various medical colleges and Institutions of the country. The Prescribers' module is primarily for the residents and faculties working in Government and private medical colleges and institutions across the country. The module can also be used by any medical practitioner.

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Two more modules in the series are currently in the pipeline. One of these is the 'AMR module for undergraduate medical students and interns to create an awareness of AMR. The other one is for the allied health professionals comprising of nurses, technicians & pharmacists belonging to a significant group responsible for handling anti-microbial, preparing anti-microbial reports and audits for antimicrobial use in the medical colleges and institutions.

These modules are being developed as per the NAP-AMR strategic priorities assigned to NMC and the guidelines provided under NAP-AMR. Modules and Toolkits will help medical professionals acquire the requisite knowledge and skills along with a positive shift in attitude towards responsible antimicrobial use. I am confident that this module will serve as an excellent guide for the prescribers in the fight against AMR by updating their knowledge on key aspects of antimicrobial resistance such as clinical approach for prescribing antimicrobials, microbiological diagnostic stewardship, interpretation of antimicrobial sensitivity results, antimicrobial stewardship, antimicrobial policy, infection control, biowaste management and bundle care approach for device-associated infections.

These modules are written in very simple and understandable language suitable to any cadre of health professional for their understanding or teaching purposes. The PPTs are given chapter-wise to help the nodal officers modify the imparting training and teaching in their respective workplaces according to the need. We aim to train all cadre of health professionals systematically and structured. After the release of this module, the training of nodal officers of the medical colleges will be started with the help of the experts to give them an insight into the purpose, content, utility and use of the module and help further propagate the idea to the health care professionals in the medical institutions.

With this, I acknowledge the sincere efforts of all the contributors and supporters to make this document see the light of the day.

With Regards and best wishes,

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We are thankful to Padma Shri Prof. B N Gangadhar, Officiating Chairman, NMC for providing guidance, strength and support in fulfilling this task.

We are grateful to our esteemed Presidents and Members of all four boards for their constant encouragement and continued input which has been very useful for formulating the module. We thank Dr Vijay Oza, President of PGMEB, for attending the meetings and providing on-the-spot inputs and suggestions for taking forward the program to all institutions in the country. We are also greatly appreciative of the contribution from Dr Aruna V. Vanikar, President of UGMEB, for her encouragement, valuable comments and suggestions.

We sincerely appreciate and acknowledge Dr Atul Goel, DGHS & Director, NCDC; Dr Lata Kapoor, Additional Director, NCDC, New Delhi for their valuable suggestions, cooperation and help to jointly host the two-day physical meeting of NAP-AMR in NMC.

We also acknowledge the inputs for the module from Dr Kamini Walia, Senior Scientist, ICMR, New Delhi.

We were fortunate to have a panel of esteemed Experts who, with the help of their vast knowledge, experience and skill had devoted their time and energy to giving the present shape to the module. We are grateful to them.

We sincerely appreciate and acknowledge the experts* who attended various meetings held in support of this module and provided their valuable comments and suggestions in preparing this document.

I would like to extend my great appreciation to the Media section of NMC for their unwavering support in creating and printing this module.

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National Medical Commission

National Action Plan on Antimicrobial Resistance (NAP-AMR) Module for Prescribers

- 2024 -

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List of Abbreviations

3GCEB	**:**	Third Generation Cephalosporin Resistant Enterobacterales
AMR	:	Antimicrobial Resistance
AMSP	:	Antimicrobial Stewardship Program
AST	:	Antimicrobial Susceptibility Test
AUC	:	Area Under the Curve
BMQ	:	Breakpoint to MIC Quotient
CDC	:	Centre for Disease Control & Prevention
CLSI	:	Clinical and Laboratory Standards Institute
CRAB	:	Carbapenem Resistant *Acinetobacter baumannii*
DDD	:	Defined Daily Doses
DOT	:	Days of Therapy
ESBL	:	Extended Spectrum Beta Lactamase
EUCAST	:	European Committee on Antimicrobial Susceptibility Testing
GAP-AMR	:	Global Action Plan on Antimicrobial Resistance
HBV	:	Hepatitis B Virus
HCV	:	Hepatitis C Virus
HIV	:	Human Immunodeficiency Virus
HLGR	:	High Level Gentamicin Resistance
I	:	Intermediate
ICMR	:	Indian Council of Medical Research
ICU	:	Intensive Care Unit
IV	:	Intravenous
MIC	:	Minimum Inhibitory Concentration
MoHFW	:	Ministry of Health & Family Welfare
MDRO	:	Multi Drug Resistant Organism
MDR TB	:	Multidrug Resistant Tuberculosis
MRSA	:	Methicillin Resistant *Staphylococcus aureus*
NACO	:	National AIDS Control Organization
NAP AMR	:	National Action Plan on Antimicrobial Resistance
NCDC	:	National Centre for Disease Control
OSHA	:	Occupational Safety and Health Act
PEP	:	Post Exposure Prophylaxis
PCR	:	Polymerase Chain Reaction
PK	:	Pharmacokinetics
PD	:	Pharmacodynamics
R	:	Resistant
SARS	:	Severe Acute Respiratory Syndrome
SDD	:	Susceptibility Dose Dependent
S	:	Susceptible
VRE	:	Vancomycin Resistant Enterococci
WHO	:	World Health Organization

Overview of AMR

1

Antimicrobial Resistance (AMR) occurs when microorganisms change over time and become resistant to drugs, making common infections harder, increasing the risk of disease spread, severe illness and death. This is a significant threat as it undermines the effectiveness of antibiotics and antimicrobials, which are crucial for surgeries, chemotherapy and managing chronic infections. The emergence of multi-drug resistant organisms (MDROs) further complicates the issue, as these "superbugs" are resistant to many different antimicrobials, making infections very difficult to treat.

AMR is a complex problem that requires a united multisectoral approach that considers factors like antibiotic overuse in humans and animals, hygiene practices, and development of new drugs. It is an ongoing threat to modern medicine throughout the world with a negative effect on patient treatment outcome. Pathogens are developing mechanisms of resistance, making it difficult to treat common infectious diseases like pneumonia, tuberculosis and foodborne diseases.

Antibiotic prescribing is determined by various factors, including the socio-cultural and socio-economic factors of each country and the beliefs of patients and professionals regarding antibiotic use. The shortage of appropriate diagnostic tools, the insufficient regulatory policies of country can further cause an increase in over-the-counter antibiotics. Medical professionals have to be prepared appropriately in order to face the challenges of antimicrobial use in everyday clinical practice.

Background and Objectives

In 2015, understanding the gravity of the problem of antimicrobial resistance (AMR), the World Health Assembly (WHA) has adopted the Global Action Plan on AMR (GAP-AMR) in collaboration with the World Health Organization (WHO), Food & Agricultural Organization (FAO) & World Organization for Animal Health (WOAH).

The World Health Organization (WHO) has outlined five core objectives for NAP-AMR that countries should strive towards:

1. Improve awareness and understanding: This involves educating the public, healthcare professionals, and policymakers about AMR through effective communication, education, and training programs.

2. Strengthen knowledge and evidence base: This objective focuses on improving surveillance of AMR trends, conducting research on resistant pathogens, and identifying best practices for infection prevention and control.
3. Reduce the incidence of infection: Strategies here target preventing infections in the first place, including promoting hygiene and sanitation practices, and ensuring access to clean water.
4. Optimize use of antimicrobial medicines: This objective aims to ensure antimicrobials are used appropriately in both human and animal health. This involves developing national guidelines for antibiotic use, promoting antimicrobial stewardship programs, and tackling the misuse of antibiotics in agriculture.
5. Develop economic case for investment: This objective highlights the need for sustainable investment in research and development of new diagnostics, vaccines, and antibiotics to combat AMR. It also emphasizes the economic burden of AMR and the return on investment for proactive measures.

Later in May 2017, the WHO resolution urged member states to align National Action Plans on AMR (NAP-AMR) with GAP-AMR. In India the Core Working Group as notified by MoHFW had developed "National Action Plan on AMR" involving consultation with various stakeholders Ministries/ Departments at the national level. The strategic objectives of NAP-AMR are aligned with the GAP-AMR based on national needs & priorities.

The NAP-AMR sets out six strategic priorities (**Fig 1**) and under each strategic priority, specific objectives of key focus areas with elaborate interventions, activities and key outputs along with responsible agencies and expected timelines, have been stated.

Fig 1: Six strategic priorities in national action plan for antimicrobial resistance in India

Objectives under National Medical Commission:

NMC is responsible in following specific objectives under priority 1 and 4 for human health

- **Strategic priority 1- Improve awareness and understanding of AMR through effective education and training**

The intervention activities mentioned for achieving the objectives are- Improve knowledge and capacity of key stakeholders regarding AMR and related topics- by strengthening and consolidating AMR and related topics as core components of professional education and training

Target audience:

Medical students, Doctors (Residents. Faculty, Medical officers etc.) and allied health professionals (Nurses, Pharmacist, Technicians and other allied health professionals) and the administrators,

This is to be achieved by-

- Reviewing and revising curricula of undergraduate medical professionals-**Undergraduate module.**
- Reviewing and developing training modules for in-service medical professionals – **Prescribers' module.**
- Reviewing and developing training modules for allied health professionals- **Non prescribers' module.**

- **Strategic priority 4- Optimise the use of antimicrobial agents in human health**

The intervention activities mentioned for achieving the objective are-
Improve knowledge and skills of prescribers, dispensers & medical trainees

This is to be achieved by-

- Developing structured (and mandatory) training programmes on optimal antimicrobial use
- Collaborate with regulatory bodies to mandate periodic training to optimise antibiotic use through pre-service and in-service trainings

The aim of the Prescribers module is to facilitate institutions and professionals in developing an understanding of AMR and its importance in clinical practice and medical education. This training module will assist in imparting required knowledge and skill of the prescribers and will assist in rational prescription of antimicrobials and implementation of antimicrobial stewardship in teaching hospitals.

Two other modules are in process of development-

- The training module and toolkit for undergraduate students
- The training module and toolkit for Non-prescribers i.e. for allied health professionals

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Clinical Approach for Prescribing Antimicrobials

2

Learning Objectives

At the end of the session, a prescriber should be able to:

- identify common presentations of infective syndromes
- know the importance of taking thorough history, clinical examination and selection of appropriate investigations for diagnosis of infective disease.

2.1 Introduction

The use of antimicrobials has grown manifold in the recent years. Easy access of antimicrobials and the haste to start them in any suspected infective aetiology is primarily responsible of their misuse, and in turn lead to increased anti-microbial resistance (AMR). Infective disorders can be bacterial, viral, fungal or parasitic. Identification of the clinical problem and making a differential diagnosis at the bed side will help in deciding of whether to start or not to start any antimicrobial.

The history should assess the risk of infection based on the symptoms and signs and the common patterns of presentation of different diseases such as upper respiratory tract infections (URTI), lower respiratory tract infection (LRTI), urinary tract infection (UTI), meningitis, diarrhoea, skin and soft tissue infections etc.

2.2. One way of clinical assessment is to follow a "Syndromic Approach". **(Fig 2)** A patient suspected of infective disorder may be classified into following syndromes:

- **Acute febrile illness with Rash**:

  An acute febrile illness with a rash can have various causes, ranging from infectious to non-infectious etiologies. Some common conditions that present with fever and rash include:

1. Viral Infections:
   - Dengue Fever: A mosquito-borne viral infection characterized by sudden onset of high-grade fever, headache, backache, joint pain, muscle pain and rash.
   - Chickenpox (Varicella): Fever, malaise and a rash that starts as red spots and progresses to vesicles.
   - Measles: Characterized by a high fever, cough, running nose, red eyes (conjunctivitis) and a rash that starts as erythematous macule behind the ear, on the neck and hairline and spreads to the trunk and the extremities by the 2nd day.
   - Rubella (German measles): Presents with a low-grade fever, enlarged lymph nodes and a rash that starts on the face and spreads to the trunk and extremities.
2. Bacterial Infections:
   - Scarlet Fever: Caused by streptococcal bacteria, it presents with fever, sore throat, and a characteristic sandpaper-like rash.

- Rocky Mountain Spotted Fever: Caused by rickettsial infection and transmitted by ticks, it presents with fever, headache, and a rash that starts on the wrists, ankles, and spreads centrally.
- Meningococcemia: Infection with *Neisseria meningitidis* can cause fever, headache, and a petechial rash.

3. Other Infections:
   - Lyme Disease: Caused by *Borrelia burgdorferi* transmitted by ticks, it presents with fever, headache, and a characteristic bull's eye rash (erythema migrans).
   - Rickettsial Diseases: Various infections such as Typhus and Q fever can present with fever and rash.
4. Non-Infectious Causes:
   - Drug Reactions: Some medications can cause febrile illnesses with rashes, such as Stevens-Johnson syndrome or Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS).
   - Autoimmune Diseases: Conditions like lupus erythematosus or Kawasaki disease may present with fever and rash.
   - Toxic Shock Syndrome: Associated with certain bacterial infections or tampon use, it presents with fever, rash, and other systemic symptoms.

- **Acute febrile illness with Jaundice:**

1. **Viral Hepatitis**: Viral infections, particularly Hepatitis A, B, C and E viruses, can cause acute febrile illness with jaundice. Symptoms may include fever, fatigue, abdominal pain, nausea, vomiting, dark urine, and yellowing of the skin and eyes (jaundice).
2. **Malaria**: Severe cases of malaria, caused by *Plasmodium* parasites and transmitted by mosquitoes. If the case turns into a complicated malaria, the patient may present with jaundice because of the haemolysis.
3. **Leptospirosis**: This bacterial infection, typically acquired through exposure to contaminated water or soil, can cause fever, muscle aches, headache, and jaundice.
4. **Typhoid Fever**: Caused by *Salmonella* Typhi bacteria, typhoid fever can present with high fever, abdominal pain, splenomegaly, headache, and jaundice in severe cases.
5. **Acute Biliary Tract Infections**: Cholangitis and cholecystitis can lead to fever, abdominal pain, and jaundice. Every patient of jaundice does not require antimicrobials. Their blood sample should be sent to laboratory for identifying type of hepatotropic virus and symptomatic management should be initiated. Conditions like leptospirosis and acute biliary tract infections are emergencies which require empirical antibiotics as per guidelines.

- **Acute febrile illness with Neurological involvement:**

Some possible causes of acute febrile illness with neurological involvement are:

1. **Meningitis**: Inflammation of the protective membranes covering the brain and spinal cord (meninges) can be caused by bacterial, viral, parasitic or fungal infections. Symptoms include fever, severe headache, neck stiffness, altered mental status, and photophobia.
2. **Encephalitis**: Inflammation of the brain, often caused by rickettsial infections like scrub typhus and viral infections such as Herpes Simplex virus, Japanese Encephalitis virus, West Nile virus. Symptoms may include fever, headache, confusion, seizures, and focal neurological deficits.
3. **Cerebral Malaria**: A severe form of malaria caused by *Plasmodium* parasites, which can lead to neurological symptoms such as altered consciousness, seizures, and coma, in addition to fever and other systemic manifestations.
4. **Acute Flaccid Paralysis**: Certain viral infections, such as poliovirus or enteroviruses, can cause acute flaccid paralysis, characterized by sudden weakness or loss of muscle tone. Fever may or may not be present, depending on the specific virus.
5. **Guillain-Barré Syndrome (GBS)**: An autoimmune disorder where the immune system attacks the peripheral nerves, leading to muscle weakness and sometimes paralysis. GBS can be triggered by viral or bacterial infections, and fever may accompany the neurological symptoms.

   Bacterial meningitis is a life threatening condition. CSF examination should be done if there are no contraindications, and the sample should be sent to laboratory for analysis. Empirical antibiotics are initiated and later modified as per available results from laboratory. Cerebral malaria requires rapid identification of malarial parasite in the blood and initiation of antimalarials.

- **Acute febrile illness with Respiratory syndrome:**

  Most of the respiratory illnesses do not require antimicrobials. Viral infections are self-limited and treated symptomatically. However, if patient of respiratory symptoms presents with expectoration and signs of septicaemia, pneumonia should be suspected. Sputum sample should be sent to laboratory and empirical antibiotic may be initiated.

Some of the causes of acute febrile illness with respiratory involvement are:

1. **Influenza (Flu)**: A viral infection caused by influenza viruses, which can lead to fever, cough, sore throat, nasal congestion, body aches, and fatigue. In severe cases, pneumonia may develop.
2. **Pneumonia**: Inflammation of the alveoli in one or both lungs, typically caused by bacterial, viral, or fungal infections. Symptoms include fever, cough, shortness of breath, chest pain, and sputum production.
3. **Acute Respiratory Infections (ARIs)**: Various viral infections, such as respiratory syncytial virus (RSV), adenovirus, or parainfluenza virus, can cause ARIs with fever, cough, and difficulty in breathing.
4. **COVID-19**: The disease caused by the novel coronavirus (SARS-CoV-2) can present with fever, cough, shortness of breath, fatigue, muscle aches, and loss of taste or smell.

In severe cases, it can lead to pneumonia and acute respiratory distress syndrome (ARDS).

5. **Tuberculosis (TB)**: An infectious disease caused by *Mycobacterium tuberculosis* bacteria, which primarily affects the lungs. Symptoms may include fever, cough (haemoptysis sometimes), chest pain, weight loss, and fatigue.

- **Acute febrile illness with abdominal involvement:** Gastroenteritis, acute appendicitis, cholecystitis, diverticulitis, acute viral hepatitis and liver abscess are the conditions involved.
- **Acute febrile illness with Renal involvement**:

1. **Urinary tract infections:** Patient present with symptoms like increased frequency of micturition, burning micturition and fever. Morning mid-stream sample as discussed later in the module should be collected and sent to laboratory for microscopic and culture examination. Antimicrobials may be initiated empirically in situations like pregnancy, diabetes etc and can then be modified as per available reports.

   Pyelonephritis: This is a bacterial infection of the kidneys, often causing fever, flank pain, and urinary symptoms. Antibiotics have to be started in suspected cases after sending complete urine examination and urine culture. If there is a suspicion of pyelonephritis blood cultures also need to be sent.
2. **Scrub typhus** can rarely present as fever, pneumonia, hepatitis and acute renal failure.
3. **Glomerulonephritis**: This refers to inflammation of the glomeruli, can be caused by infections, autoimmune diseases, or other systemic conditions.
4. **Haemolytic Uremic Syndrome (HUS):** This is a rare but serious condition characterized by the destruction of red blood cells, acute kidney injury, and low platelet count. It is often caused by certain strains of bacteria, such as *E. coli*, and can occur following gastrointestinal infections or urinary tract infections.
5. **Systemic Lupus Erythematosus (SLE):** This is an autoimmune disease that can affect multiple organs, including the kidneys and can lead to acute kidney failure, nephrotic syndrome and chronic renal failure (CRF).

- **Acute febrile illness with cardiovascular involvement:**

  Myocarditis, infective endocarditis, pericarditis, Kawasaki disease, viral haemorrhagic fevers such as dengue fever, yellow fever, Ebola fever present with cardiovascular involvement including vascular leakage, haemorrhage and shock.

2.3 Accurate history and thorough clinical examination

- The clinician should always take a detailed history of presenting infection, history of any surgical, medical disorders, co-morbidities like diabetes as these may predispose an individual to infections. History of previous hospital admission, recurrent infections in the past, surgical intervention or any organ transplant should be taken. Previous use of antibiotics in such situations may predispose for AMR in current illness.

- A detailed physical examination is an important part of the evaluation of a patient with fever to arrive at a diagnosis. Finding an eschar on general physical examination pinpoints the diagnosis of scrub typhus. Finding a murmur on examination of cardiovascular system examination can point towards an infective endocarditis
- Urinary tract infections (UTI) and skin infections like foot ulcers develop in diabetic patients. The collection of mid-stream urine samples in suspected UTI cases should be done. Prescribers may refer to the proper collection technique of urine samples in male and females as described later in this module.
- Recording cardinal symptoms of major systems like fever, cough, sputum, breathlessness, haemoptysis, chest pain may suggest an infective respiratory illness like pneumonia. The decision to treat with antibiotics should be made by the presence of severity and laboratory report of sputum and culture examination.
- Jaundice and abdominal pain may be present in medical conditions like viral hepatitis, alcoholic hepatitis, leptospirosis, malaria, dengue etc. or in surgical conditions like choledocholithiasis or cholangitis. Prescribers should take a detailed history of any recent travel, drug abuse, blood transfusion, recent surgeries etc. to narrow down the differential diagnosis.
- History of unconsciousness, headache, and altered behaviour should raise the suspicion of meningitis or meningoencephalitis and if accompanied by signs of meningeal irritation, CSF should be done. As CSF is a precious sample, prescribers should be aware of collection technique and transportation of this sample to the laboratory.
- Sometimes a patient of valvular heart disease may present with fever raising the suspicion of infective endocarditis. Blood culture is the diagnostic test of choice for identifying the causative organism in such cases. Therefore, proper technique of blood culture sampling and proper communication with the microbiology laboratory is the key to successful diagnosis and management in such cases.
- The communication between the clinicians and laboratory is vital. The positive culture reports must be conveyed rapidly to prescribers so that the therapeutic interventions can be made in desired time frame. The decision of starting antibiotics should be governed by the antibiograms.
- This will not only be a cost-effective approach of treating infections but also reduce AMR.

2.4 Prescription of antimicrobials should be based on the following steps:

Step 1: Making a clinical diagnosis based on accurate history taking and thorough clinical examination helps in selecting the right test for the right patient. A clinical diagnosis also helps in predicting most likely organism causing a clinical syndrome. The sample must be collected before the start of antimicrobials.

Step 2: The empiric antibiotic therapy must be limited to seriously ill patients. This choice should be based upon institutional/local antibiograms.

Step 3: Choose the appropriate antibiotic based on clinical evaluation and most likely pathogen keeping antibiogram in mind.

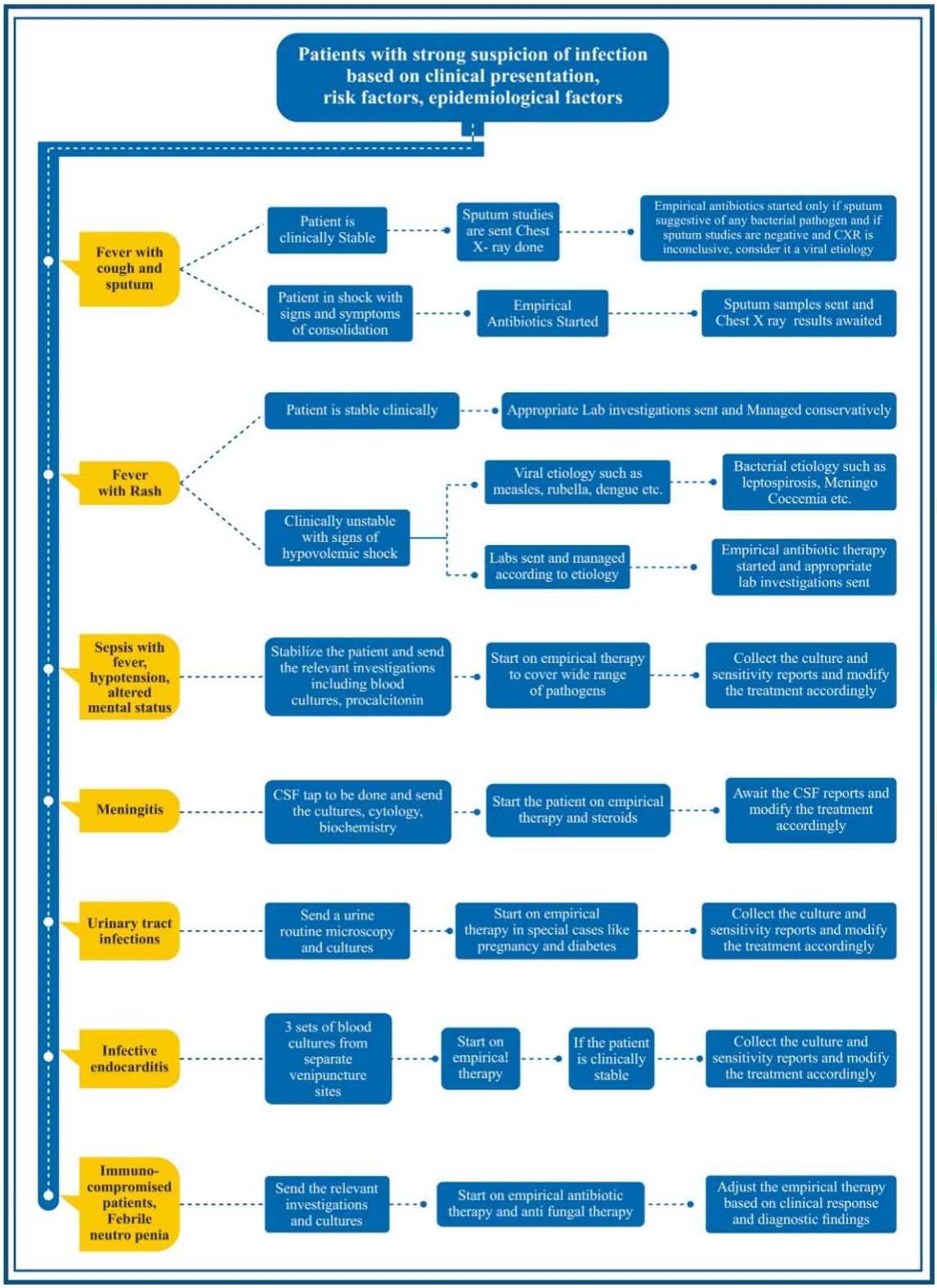

Fig 2: Syndromic approach to Acute Febrile Illness

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Microbiological Diagnostic Stewardship

3

Learning Objectives

On completion of this chapter, the prescriber should be able to:

- define diagnostic stewardship
- understand the difference between infection and colonization
- describe the sample collection techniques, precautions, transport and rejection criteria of common samples.

3.1 Introduction

Diagnostic stewardship refers to **"co-ordinated guidance and interventions to improve appropriate use of microbiological diagnostics to guide therapeutic decisions. It should promote appropriate, timely diagnostic testing, including specimen collection, and pathogen identification and accurate, timely reporting of results to guide patient treatment."**

3.2 Correct sample for correct report

- The microbiology laboratories must be effectively utilized by the clinicians to assist them to prescribe appropriate antimicrobials.
- The 4 T of diagnostic stewardship:
  1. choosing the right **Test** from
  2. the right **Type** of sample, collected at
  3. the right **Time**, in order to
  4. guide **Treatment** decisions.
- Appropriate selection of samples, their proper collection and transport helps to improve the diagnostic performance of a microbiology laboratory.
- The turn-around time for laboratory investigations must be known to all clinicians.
- The ability to distinguish between viral and bacterial infection is also useful, since patients with viral infections may be able to be managed without antimicrobials.
- Many pathogenic microorganisms may be found as part of the normal commensal flora. Isolation of these organisms may not necessarily indicate infection. Likewise, many body sites have a normal commensal flora and samples sent to the laboratory in the absence of signs or symptoms of infection may be difficult to interpret. Therefore, the clinician must understand the limitations of testing and result interpretation and be able to put these into clinical context rather than simply take a result at face value.

- A common mistake is to send a sample for a wide range of diagnostic tests when the likelihood that the patient has the conditions concerned is low. This often means that a positive test result is more likely to be a false-positive result than a genuine result. So, the patient may be given an incorrect diagnosis and be treated for something that they do not have. Equally important, they are not treated for whatever it is that they do have.
- A blood culture can easily be contaminated with skin organisms at the time that the sample is being taken. Patients with contaminated blood cultures are often commenced on unnecessary antimicrobial therapy while the issue is being investigated. They may also have other investigations to investigate an infection that they haven't got.

3.3 General precautions while collecting samples

- The sample for bacterial culture must be collected prior to antimicrobial therapy whenever possible.
- Appropriate specimen from suspected site of infection must be collected in correct container according to case definition.
- The sample must be collected by trained staff after precise instructions to the patient.
- It must be transported within 1-2 hours after collection, in the correct package.
- Blood and CSF should never be refrigerated, can be kept at room temperature (37ºC) at the collection site and transported at room temperature.
- All samples must be accompanied by a request form with complete clinical, demographic and epidemiological information.

3.4 Colonization and infection

- Most organisms which colonize are harmless commensals and should not be treated.
- An organism isolated from a sample taken from a normally sterile site like the CSF, blood, pleural fluid etc. is likely to be a true invader and the causative pathogen.
- An organism isolated from a non-sterile specimen like sputum or a wound swab may be a colonizer.
- If the organism is persistently isolated despite 'effective' systemically administered therapy, careful clinical decision must be taken keeping in mind the organism may be a multidrug resistant pathogen or simply a colonizer.

3.5 Sample collection techniques

1. Blood

- Preferably collect paired blood sample for culture from two different sites (e.g. right and left antecubital fossa) to differentiate between probable pathogens and possible contaminants and to increase the rate of isolation. The dilution ratio should be 1 ml of blood to 10 ml of culture media.
- Wear gloves, thoroughly disinfect the venepuncture site.

- Cleanse an area about 50 mm in diameter with 70% ethanol and allow to air-dry.
- Apply 2% tincture of iodine or chlorhexidine/ alcohol-based disinfectant in a circular action, swab the area beginning at the point where the needle will enter the vein.
- Allow the disinfectant to dry on the skin for at least 1 minute.
- Wipe the top of the bottle cap using an ethanol swab and allow to dry before injecting the sample aseptically into the bottle.
- Inoculated blood culture bottles should be transported to the laboratory immediately or held at room temperature until they reach the laboratory.

2. CSF

- Sequentially collect CSF into a minimum of three sterile calibrated tubes.

Lumbar puncture

- Disinfect the puncture site with antiseptic solution and alcohol in a manner identical to phlebotomy skin preparation for blood culture to prevent specimen contamination and introduction of infection.
- Insert a needle with stylet at the L3-L4, L4-L5, or L5-S1 interspace. When the subarachnoid space is reached, remove the stylet; spinal fluid will appear in the needle hub.
- Measure the hydrostatic pressure with a manometer.
- Sequentially collect the CSF into three calibrated sterile tubes labelled.
- Physicians should be instructed to sequentially collect 0.5-2.0 ml of CSF into three sterile calibrated tubes (in each tube) if only routine chemistry (total protein and glucose), bacteriology (culture & sensitivity), and haematology (cell count) are required.

3. Sterile body fluids

- Normally sterile body fluids such as pleural, pericardial, peritoneal, synovial, etc. should be collected with needle and syringe using sterile technique.
- The aspirated fluid (1-5ml) should be transferred into aerobic and anaerobic blood culture bottles preferably, retaining some (0.5 ml) in syringe for Gram stain and direct plating.
- If culture bottles are not available at site the aspirated fluid should be transferred to a sterile screw-capped tube or a paediatric isolator tube.
- The sample should not be submitted in syringe with needle attached. The syringe should be cap secured to prevent leakage.
- Swab specimens are inferior and should NEVER be used if fluid specimens can be obtained.

4. Urine

- Preferably, early morning first midstream urine (2-5ml) to be collected in sterile, wide mouth, leak proof container.

- In catheterized patients, clamp the catheter, clean the catheter wall vigorously with 70% ethanol and aspirate 5 to 10 ml of urine via a sterile needle and syringe above the clamp. Never collect urine sample from the urine collection bag or by disconnecting the catheter from the tube of the urine collection bag.
- In non-catheterized patients, the following instructions should be given:

✓ Female: Wash the hands, cleanse the area around the urethral opening with soap and water, and collect the midstream urine in a sterile container with the labia held apart.

✓ Male: Wash the hands, retract the foreskin, cleanse the glans with soap and water, collect midstream urine in the sterile container.

- Urine samples must be sent to the laboratory as soon as possible (preferably immediately). In case of delay of more than 1 hour, the sample must be refrigerated.

5. Sputum

- Use a clean/sterile, wide mouth leak-proof container, and collect the sample preferably during early morning after rinsing mouth with water but before brushing, fluid or food intake.
- Patient is instructed to cough deeply after taking a deep breath.
- Specimen must be sputum, and not saliva.
- Samples must be sent to the laboratory as soon as possible preferably within (2 hours of collection). In case of delay, the sample should be refrigerated (except in case if *Streptococcus pneumoniae* and/or *Haemophilus influenzae* infection is suspected).
- In case of external soiling of the sample container with sample, a phenol-containing disinfectant should be used to wipe the outside of the container.

6. Endotracheal aspirate (ETA)

- Endotracheal aspiration is done with a sterile technique using a 22-inch, 12F suction catheter.
- The catheter is introduced through the endotracheal tube for at least 30 cm. Gentle aspiration is then performed without instilling saline solution.
- The first aspirate is discarded, the second aspirate is collected after tracheal instillation of 5 ml saline in a mucus collection tube.
- If very little secretion is produced by the patient, chest vibration or percussion for 10 min is used to increase the retrieved volume (> 1 mL).
- Send the specimen to the laboratory as soon as possible.

7. Bronchoalveolar lavage (BAL)

In this procedure 100-300 ml volume of saline is infused to a lung segment through the bronchoscope to obtain cells and protein of the pulmonary interstitium and alveolar spaces and a portion of it to be sent to the laboratory as soon as possible.

8. Throat/nasopharyngeal swabs

- The procedure is explained to the patient, including that they may gag briefly.
- After wearing appropriate PPE the patient should be positioned such that the light source illuminates the posterior oropharynx.
- The patient is asked to open the mouth and relax the tongue by saying "aaaah" and the tongue is pressed down using a tongue depressor.
- Both tonsils and the posterior pharynx are swabbed.
- The swab is then placed in the culture medium, or a suitable transport medium, or sterile test tube.
- For collection of nasopharyngeal swabs, the patient must be seated comfortably with the back of their head against the headrest. The swab is inserted in the nose horizontally, along an imaginary line between the nostril and the ear.
- The swab should be placed in viral transport medium (VTM) if viral diagnostics is required.

9. Stool

- Freshly voided sample should be collected in a clean/sterile wide mouth leak-proof container.
- If the above is not possible, then the patient can be advised to transfer stool from a clean bedpan / nappy pad which is not mixed with urine, disinfectant etc. including mucus or blood part.
- If the patient (infant/small children) is passing loose stool then sterile plastic catheter (disposable) no. 26 is to be used. Transport to the laboratory within 2 hrs of collection.
- Collect at least 5 ml of sample in case of liquid stool, approximately 1 g (walnut-sized) sample in case of semi-formed or formed stool.
- In case of delay, contact to microbiologist for preferable transport media.

10. Pus/ tissue biopsy aspirate

- **In case of open wounds**, debride to clear overlying debris with scalpel and swabs or sponges, and thoroughly rinse with sterile saline prior to collection of samples.
- Collect biopsy or curette sample from base or advancing margin of the lesion. The specimen must never be sent in formalin for culture.
- **In case of closed wounds**, disinfect the area as for collection of blood sample before aspiration.
- Pus from an abscess is best collected at the time the abscess is incised and drained, or after it has ruptured naturally.
- Collect the sample (at least 1 ml) by using a syringe and needle and put in a sterile container or blood collection tube without anticoagulant (e.g., vacutainer or similar type).

- A portion of the samples should also be placed in a sterile tube containing anaerobic medium like Robertson's cooked meat media (RCM) if an anaerobic culture is required.
- Collect swabs only when tissue or aspirate cannot be obtained as swab is not an appropriate/ preferred sample for culture.
- Send the specimen to the laboratory as soon as possible.

11. Genital swabs

- For vaginal swabs the excess mucus is cleaned with cleaning swab and discarded.
- The swab is inserted into the cervical canal and rotated for 15-30 seconds.
- The swab should be immediately broken off and placed into the transport tube.
- For endocervical swabs, the sample should be collected with help of speculum.

Table 1 summarizes the sample collection techniques described above.

3.6 Sample rejection criteria

- Samples collected in incorrect containers or in broken, poorly sealed and leaking containers.
- Unlabelled specimens or mismatch between sample requisition form and container.
- Unacceptable delay between specimen collection and arrival at laboratory.
- Sample stored incorrectly before or during transport.
- Inadequate quantity of specimen.
- 24 hours urine collection.
- Foley's catheter tips and endotracheal tube tips.
- Urine from the bag of a catheterized patient.

3.7 Follow up cultures

- 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.

3.8 Rapid tests

- These tests rapidly confirm the presence of a bacterial pathogen or help to rule out a bacterial infection and hence used for selection of appropriate therapy.
- PCR identification of respiratory viruses in children with lower respiratory tract infection help to exclude viral infection.
- Inflammatory markers such as Procalcitonin, C-Reactive Protein etc. guide prescribers to institute rational therapy especially in sepsis cases. They can be useful to differentiate between a bacterial and a viral infection and therefore is a potential guide to initiate antimicrobial therapy.

Table 1: Summary of sample collection and transport

Sample	Collection	Transport	Remarks
Blood	1ml blood per 10ml media for conventional culture; and as per instruction in case of automated culture	Immediately or at room temperature	
CSF	0.5-2 ml in sterile container	Immediately or at room temperature	Never refrigerate
Sterile body fluids (Pleural, Pericardial, peritoneal etc.)	1-5 ml sterile container	Immediately or refrigerate if delay up to 2 hours	Do not transport in capped syringe
Urine	2-5ml	Immediately or refrigerate if delay of more than 1 hour	Give proper instructions for collection and transport to patient
Sputum	Sample coughed up into container	Immediately or at room temperature	
Throat/ oropharyngeal swabs	two swabs (culture and microscopy)	Immediately before drying, in VTM for viral diagnostics	Wear appropriate PPE
Stool	1g (formed stool) to 5ml (liquid stool)	Immediately or at room temperature	Sample to be sent to the laboratory within 15minutes for trophozoites
Pus/ Tissue biopsy/ aspirates	Sterile wide mouth container	Immediately or refrigerate if delay up to 4 hours	Do not add formalin or saline
Genital swabs	Dacron or rayon swabs	Immediately	Add to VTM if viral diagnostics is required.

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Interpretation of Antimicrobial Sensitivity Results

4

Learning Objectives

On completion of this chapter, the prescriber should be able to:

- understand the importance of quality assured antimicrobial susceptibility testing (AST)
- interpret the antimicrobial susceptibility testing report
- interpret the surrogate and cascade reporting.

4.1 Introduction

- The microbiology laboratory must be accessible for 24 hours.
- The communication between the clinicians and laboratory is vital.
- The reports must be conveyed promptly to the prescribers so that the therapeutic interventions can be made in desired time frame.
- The results of AST are used to:
  - ✓ choose the most appropriate empirical antimicrobial agent.
  - ✓ establish antimicrobial prescription policies at institutional/state/national level.
  - ✓ predict upcoming resistance.
  - ✓ assess the efficacy of newly developed antimicrobial agents.

4.2 Antimicrobial Susceptibility Testing

- Antimicrobial susceptibility testing is done by manual and automated methods.
- Automated methods are available commercially that provide extrapolated Minimum Inhibitory Concentration (MIC) results within 12-18 hours.
- Worldwide there are two popular guidelines to ensure quality testing in AST: Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS) and European Committee on Antimicrobial Susceptibility Testing (EUCAST).
- The choice of antimicrobials for AST must be made as per guidelines and in consultation with clinicians keeping the hospital formulary in mind.

4.3 Interpretation of AST result

- Interpretive criteria of susceptibility are based on standard dosing in a patient with normal renal function tests and in absence of co-morbidities. The results of AST are reported as:

  i. **Susceptible:** The bacteria are inhibited by the usually achievable concentrations of antimicrobial agent when the dosage recommended to treat the site of infection is used.

  ii. **Intermediate:** The bacteria for which the response rates to usually attainable blood and tissue levels of antimicrobial agent are lower compared to susceptible isolates. It

is a buffer zone between the susceptible and resistant categories. It also indicates that the clinical response will be achieved in cases where antimicrobials are concentrated at the site of infection such as urine.

iii. **Resistant:** The bacteria which are not inhibited by the usually achievable concentrations of the agent with normal dosage regimens and that the clinical efficacy of the agent against the isolate may not be sufficient.

iv. **Susceptible-dose dependent (SDD):** The susceptibility of the bacteria depends on the dosage regimen that is used in the patient.

v. **Non-susceptible (NS):** Only a susceptible breakpoint is designated because of the absence or rare occurrence of resistant strains. Also, it does not necessarily mean that the isolate has a resistance mechanism.

- **Indicator/Surrogate drugs**: An indicator drug is used to detect the presence of the mechanism that gives resistance not only to the indicator, but also to related agents (**Table 2**).

Table 2: Indicator/surrogate/equivalent antimicrobials used in AST reports

Bacteria	Antimicrobial tested	Inference (if indicator found resistant)
***Staphylococcus* spp.**	Cefoxitin as surrogate for predicting MRSA	Cefoxitin resistant is MRSA: Resistant to all beta-lactam agents except ceftobiprole and ceftaroline
	Ciprofloxacin or ofloxacin	Acquisition of at least one target mutation that leads to resistance to all fluoroquinolones. This may lead to development of resistance during therapy with other quinolones
	Erythromycin	Can be used to predict the activity of azithromycin or clarithromycin also
***Enterococcus* spp.**	Ampicillin	Can be used to predict the activity of amoxicillin, amoxicillin-clavulanate, ampicillin-sulbactam, and piperacillin-tazobactam among non–β-lactamase producing enterococci.
***Enterococcus* spp.**	Gentamicin (high level)	Determines loss of synergism of aminoglycosides with beta-lactam agents and glycopeptides irrespective of MIC value
Enterobacterales	Ciprofloxacin	Resistant to all fluoroquinolones
	Ceftriaxone or cefotaxime	3rd generation cephalosporin
Enterobacterales, *P.aeruginosa*, *Acinetobacter baumannii* complex	Colistin or polymyxin b	Any one agent can be used
Klebsiella* spp./ *E. coli	Ceftazidime	Resistant to all cephalosporin except cephamycins (cefoxitin, cefotetan)

Gram-negative isolates from uncomplicated UTIs	Cefazolin	Predicts results for all oral cephalosporins such as cefaclor, cefdinir, cefpodoxime, cefprozil, cefuroxime, cephalexin, and loracarbef

- **Equivalent Agents**: Results from one antimicrobial can be used to predict results for the other antimicrobials. For example, sensitivity to erythromycin can be used to predict sensitivity to clarithromycin or azithromycin.

4.4 **Selective Testing:** AST for particular drug- microbe combinations are not performed due to the following reasons (**Table 3**):

Table 3: Reasons for selective testing and reporting

Reasons	Examples
Bacteria suspected of being contaminants or normal flora.	If one of the two blood cultures reveals the growth of *Staphylococcus epidermidis*, AST is not reported in ordinary circumstances as the isolate is usually a suspected contaminant/ commensal flora.
Susceptibility or resistance can be predicted based on the organism identification alone (i.e., no resistance yet identified or intrinsic resistance*).	Ceftriaxone AST is not performed for *Pseudomonas aeruginosa* because *P. aeruginosa* is intrinsically resistant to ceftriaxone. Group A streptococci is not tested against penicillin as resistance has not been reported.
A particular drug-microbe combination may not have interpretative breakpoints	CLSI or FDA breakpoints for tigecycline in case of *Acinetobacter baumannii* are not available
A particular drug-microbe combination may be inappropriate for a given site of infection.	Daptomycin AST results are not reported on isolates from a respiratory source as it is inhibited by surfactant.
A drug may be inappropriate for a particular patient population.	AST results for certain drug classes such as fluoroquinolones or tetracyclines may not be reported for children.

4.5 **Cascade reporting (CR)**: In this, AST results of secondary (e.g., broader-spectrum, costlier) agents may only be reported if an organism is resistant to primary agents within a particular drug class. This helps to guide clinicians toward using narrower-spectrum agents. Restricted antimicrobials/second-line antimicrobials should be reported only in cases of resistance to first-line/unrestricted antimicrobials.

Example: Carbapenem AST results are not reported for *Escherichia coli* if the isolate is susceptible to ceftriaxone.

4.6 Interpretation of MIC results

- MIC is the lowest concentration of antimicrobial agent that prevents the in- vitro growth of bacteria.
- The absolute value of the MICs reported on susceptibility testing must not be evaluated vertically between the different drugs tested. For example, if there is an antimicrobial A with a MIC of 0.5 mg/L and the breakpoint 2 mg/L, and an antimicrobial B with a MIC of 2 mg/L but breakpoint of 16 mg/L, the drug with a MIC more favourable is the antimicrobial B. The ratio of clinical breakpoint MIC to MIC of organism is named breakpoint to MIC quotient (BMQ). Higher the BMQ, better the clinical response.

4.7 Organism specific AST results

- **Enterococci**

✓ Cephalosporins, clindamycin, and trimethoprim-sulfamethoxazole may appear active in- vitro but are not effective clinically and should not be reported as susceptible or prescribed even when reported as susceptible.

✓ Combination therapy with ampicillin, penicillin, or vancomycin (for susceptible strains) plus an aminoglycoside is usually indicated for serious enterococcal infections. This synergy is lost in presence of penicillin resistance or high-level resistance to gentamicin (HLGR).

- **Staphylococci**

✓ Penicillin-susceptible staphylococci are also susceptible to other β-lactam agents with established clinical efficacy for staphylococcal infections.

✓ Methicillin (oxacillin)-resistant staphylococci are resistant to all currently available β-lactam antimicrobial agents, with the exception of ceftaroline.

✓ Inducible clindamycin resistance if present then antimicrobial therapy with clindamycin may fail clinically.

- ***Salmonella* and *Shigella* species**

✓ Aminoglycosides, first- and second-generation cephalosporins and cephamycins may appear active in- vitro but are not effective clinically and should not be reported as susceptible or prescribed even when reported as susceptible.

✓ For extraintestinal isolates of *Salmonella* spp., a third-generation cephalosporin should additionally be tested and reported, and if requested, chloramphenicol and azithromycin may be tested and reported.

✓ Susceptibility testing is indicated for typhoidal Salmonella (*S. enterica* ser. Typhi and *Salmonella enterica* ser. Paratyphi (A–C) isolated from extraintestinal and intestinal sources.

✓ Routine susceptibility testing is not indicated for non-typhoidal *Salmonella* spp. isolated from intestinal sources. However, susceptibility testing is indicated for all *Shigella* isolates.

- ✓ Only ampicillin, a fluoroquinolone, and trimethoprim-sulfamethoxazole should be reported routinely in case of stool isolates of *Salmonella* and *Shigella* spp.

- For CSF isolates, the following must not be prescribed/ reported:

- ✓ Only orally administered antimicrobials
- ✓ First- and second-generation cephalosporins and cephamycins
- ✓ Doripenem, ertapenem, and imipenem
- ✓ Clindamycin
- ✓ Macrolides
- ✓ Tetracyclines
- ✓ Fluoroquinolones

4.8 Sample specific AST results

AST results are provided only if clinical assessment suggests infection in the following situations:

- ***Urine***: The urine of patients with indwelling catheters frequently becomes colonised. Unless the patient becomes systemically unwell, treatment is not indicated.
- ***Sputum***: Antimicrobial therapy may be indicated if clinical or radiological evidence of lower respiratory tract infection is present. Otherwise, this probably represents upper airway colonisation, for which antimicrobial therapy is not required.
- ***Pus Swab***: Antimicrobial therapy may be indicated in case of cellulitis or deep-seated infection only.

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Antimicrobial Resistance: Principle and Implications

5

Learning Objectives

On completion of this chapter, the prescriber should be able to:

- define and explain the differences between antimicrobials and antibiotics
- outline the drivers for resistance
- outline the global epidemiology of key antimicrobial resistant pathogens and antimicrobial consumption
- explain the clinical and economic impact of drug resistant infections and health care acquired infections.

5.1 Introduction

- 'Antimicrobials' is a broad term that is used for all agents that act against different types of microorganisms namely bacteria (antibacterial), viruses (antiviral), fungi (antifungal) and parasites (antiparasitic).
- Antibiotic refer to compounds that are produced by microorganisms and act against bacteria.
- Antimicrobials are unique, and pose special challenges due to following:
  - ✓ Limited shelf life: The efficacy of antimicrobials wanes over time.
  - ✓ Multispecialty usage: They are used for prophylaxis and treatment of various conditions in a variety of situations.
  - ✓ Inappropriate use: May harm other people who are even not exposed to the antimicrobial.
  - ✓ Limited drug development: Past three decades have not seen significant development and licensing of antimicrobials.
  - ✓ Change in natural bacterial flora: Overuse of antimicrobials tend to select bacteria with resistance to proliferate in environment and body.

5.2 Overview of Antimicrobial resistance

- Antimicrobial resistance (AMR) occurs when microorganisms such as bacteria, viruses, fungi, and parasites develop changes and fail to respond to antimicrobials.
- This makes standard treatments ineffective, prolonging infections that can increase the risk of spread to others. The resistant microbes are able to grow/multiply in the presence of drug that would normally kill them or limit their growth.
- AMR is a now recognized as a grave public health problem. As per estimations, AMR will be responsible for the death of 10 million people by 2050 and will cost as much as US$ 100 trillion.

- Multiple agencies including WHO agree that spread of AMR is an urgent issue that requires a global, coordinated action plan to address. A report in lancet estimates that the magnitude of bacterial AMR is almost equivalent to major diseases such as HIV and malaria, and potentially much larger.

5.3 Mechanism of action of antimicrobials

Antimicrobials act on bacteria in multiple ways. They can kill the cell (bactericidal) or retard its multiplication (bacteriostatic) (**Table 4**). They can act by

- Inhibition of cell wall or cell membrane synthesis in microbes.
- Disruption of essential processes such as protein synthesis of microbes.
- Disruption of nucleic acid synthesis in microbes.

Table 4: Bacteriostatic and bactericidal antimicrobials

Bactericidal	Bacteriostatic
Beta lactams, glycopeptides, cyclic lipopeptides, aminoglycosides, fluoroquinolones	Macrolides, clindamycin, tigecyclines, tetracyclines, linezolid

5.4 Mechanism of antimicrobial resistance

Bacteria may develop resistance to an antimicrobial by several mechanisms and resist getting killed or inhibited by the antimicrobial. Some bacteria inherently do not respond to certain drugs (intrinsic resistance) while others may stop responding to a drug to which it is originally sensitive (acquired resistance). Some of the common intrinsic resistance in common bacteria is given in **Table 5**:

Table 5: Intrinsic resistance in some commonly isolated bacteria

Bacteria	Drug
Gram positive bacteria	Aztreonam
All Gram negative bacteria	Glycopeptides, Lipopeptides
***Klebsiella* species**	Ampicillin, Amoxicillin-clavulanate, Ticarcillin, Cefazolin
***Citrobacter* species**	Ampicillin, 1st & 2nd generation Cephalosporins, Cephamycins
***Proteus* species**	Colistin, Cefazolin, Tetracycline, Nitrofurantoin
Pseudomonas aeruginosa	Ampicillin, Amoxicillin, Amoxicillin-clavulanate, Trimethoprim-suphamethoxazole, Sulfonamides,

	1st and 2nd generation Cephalosporins, Cefotaxime, Ceftriaxone, Ertapenem, Chloramphenicol, Tetracycline
***Acinetobacter* species**	Ampicillin, Amoxicillin-clavulanate, Aztreonam, Chloramphenicol, Fosfomycin, Ertapenem,
Enterococcus	Aminoglycosides, Cephalosporins, Clindamycin, many β-lactams, Aztreonam, Polymyxin B/colistin, and Nalidixic acid

Acquired resistance: Bacteria may stop responding to a drug to which it is originally sensitive) by in any of the following actions:

- Production of enzymes that destroy the antibacterial drug (e.g., beta-lactamases in penicillin and cephalosporins)
- Expression of efflux systems that prevent the drug from reaching its intracellular target (e.g., efflux pump mechanism [fluoroquinolone resistance])
- Reduction of permeability of drug through mutation of porin proteins (as seen with aminoglycosides)
- Modification of the drug's target site (e.g., penicillin-binding protein)
- Production of an alternative metabolic pathway that evades the action of the drug (e.g., folate metabolism)

5.5 Drivers of Antimicrobial Resistance

In the latter half of the 21st century, bacteria have developed resistance against every class of antimicrobial drug. The development of AMR is multifactorial. The risk factors most commonly found to be associated with development of antimicrobial resistance are:

1. Excessive and irrational prescriptions of antimicrobials in community and hospitals
2. Increase in invasive procedures, transplants surgeries and immunosuppressive therapy.
3. Increase use of prosthetic devices amenable to super-infection and resistant bacteria.
4. Lack of effective preventive infection control measures such as hand hygiene, isolation procedures of patients with multi drug resistant organisms.
5. Lack of effective antimicrobial stewardship programs restricting antimicrobial usage in community and hospitals.
6. Use of antimicrobial in agriculture sector, animal husbandries and fisheries.
7. Improper disposal of antimicrobials and antimicrobial residues which leads to finding their way in community and entering food chain through food, animals and water.

5.6 Key Antimicrobial Resistant Pathogens:

The World Health Organization (WHO) has identified a list of priority pathogens that pose a critical threat to human health due to their resistance to antimicrobials. These pathogens as per the recent 2024 list include:

- **Carbapenem resistant Enterobacterales (CRE)** These include *Klebsiella* spp. and *Escherichia coli* that are resistant to carbapenems and are placed atop in the critical list of priority pathogens.
- **Third generation cephalosporin-resistant Enterobacterales (3GCREB)** - Gram-negative bacteria resistant to third-generation cephalosporins, a broad class of antibiotics used to treat many different types of infections.
- **Carbapenem resistant Acinetobacter baumannii (CRAB)** The emergence of CRAB poses a formidable challenge due to limited treatment options particularly in ICU settings.
- **Methicillin-resistant *Staphylococcus aureus* (MRSA)** – *S, aureus* resistant to many common antibiotics, making it difficult to treat skin infections, pneumonia, and bloodstream infections.
- **Vancomycin-resistant *Enterococcus* (VRE)** - one of the last-resort antibiotics used to treat serious infections.
- **Fluoroquinolone-resistant bacteria** - This includes strains of *E. coli*, *Salmonella* and *Campylobacter* that are resistant to fluoroquinolones, commonly used to treat urinary tract infections, diarrhea, and respiratory infections

5.7 Global Epidemiology of AMR:

AMR is a global problem, but its impact varies from country to country. Low- and middle-income countries are often disproportionately affected due to factors like limited access to clean water and sanitation, overcrowding, and poor infection control practices in healthcare settings. The breakdown of the global epidemiology of AMR is as follows:

- **High burden:** Low- and middle-income countries in Southeast Asia, Africa, and Latin America.
- **Emerging burden:** Eastern Europe and Central Asia.
- **Established burden:** High-income countries in Europe and North America.

5.8 Antimicrobial Consumption: The overuse and misuse of antimicrobials are major drivers of AMR. This includes:

- Using antibiotics for viral infections, which are ineffective.
- Taking antibiotics for an incomplete course of treatment.
- Using antibiotics for non-medical purposes, such as promoting growth in livestock.

5.9 Impact of AMR: The consequences of AMR include:

- Increased morbidity and mortality from infections.
- Longer hospital stays and higher healthcare costs.
- Limited treatment options for common infections.
- The emergence of untreatable "superbugs."

For Combating AMR a multi-pronged approach has been included in NAP-AMR that includes-

- **Surveillance:** Monitoring AMR trends to identify emerging threats.
- **Stewardship:** Promoting the responsible use of antimicrobials in humans and animals.
- **Infection prevention and control:** Implementing measures to prevent infections in healthcare settings.
- **Research and development:** Developing new antibiotics, diagnostics, and vaccines.

5.10 Clinical Impact: both drug resistant infections (DRIs) and hospital acquired infections (HAIs) pose significant challenges for patient care. The clinical impact are-

- **Drug resistant infections**
  - **Increased mortality:** DRIs are associated with higher death rates, because effective treatment options become limited, and alternative drugs may have lower efficacy or more severe side effects.
  - **Treatment delays:** due to delay in diagnosis worsen the course of the infection.
  - **Limited treatment options:** for DRIs, effective antibiotics may be scarce or unavailable or having serious side effects.
  - **Increased length of hospital stay**
- **Hospital acquired infections**
  - **Increased mortality** compared to community-acquired infections due to compromised immune status of the patient making them more susceptible to severe complications.
  - **Antibiotic resistance:** the frequent use of antibiotics in hospitals selects for resistant strains, making it harder to treat future infections.
  - **Increased complications** like pneumonia, sepsis, and organ failure.
  - **Psychological impact in form of** anxiety, stress, and depression in patients, impacting their overall well-being.

5.11 Economic impact: combined effect of DRIs and HAIs are-

- **Increased costs:** due to longer hospital stays, the use of more costly antibiotics, and the need for additional treatments for complications.
- **Reduced productivity:** due to longer recovery times, leading to lost workdays and decreased productivity.
- **Strain on healthcare systems:** due to increased demand for resources to treat DRIs and HAIs limited resources available for other patients.
- **Global economic impact:** The World Bank estimates that AMR alone could push an additional 10 million people into poverty by 2030.

5.12 To mitigate impact of AMR

To reduce the clinical and economic burden of DRIs and HAIs, several strategies are crucial:

- **Antimicrobial stewardship**
- **Infection prevention and control**
- **Surveillance**
- **Research and development** of new antibiotics, diagnostics, and vaccines to combat DRIs and HAIs.

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Antimicrobial Policy

6

Learning Objectives

On completion of this chapter, the prescriber should be able to:

- describe the attributes and features of antimicrobial policy
- understand the key elements of developing hospital antimicrobial policy
- assist in developing antimicrobial policy.

6.1 Introduction

- Hospital antimicrobial policy helps to minimize the morbidity and mortality due to antimicrobial-resistant infection; and helps to preserve the effectiveness of antimicrobial agents in the treatment and prevention of communicable diseases.
- The policy must define prophylaxis, empirical and definitive therapy and must incorporate specific recommendations for the treatment of different high-risk/special groups such as immunocompromised hosts; hospital-associated infections and community-associated infections.
- The hospital antimicrobial policy should be based upon the following factors:
  - ✓ prevalent local antibiogram
  - ✓ spectrum of antimicrobial activity
  - ✓ pharmacokinetics/ pharmacodynamics of antimicrobials
  - ✓ adverse effects and potential to select resistance of antimicrobials
  - ✓ cost of the therapy
  - ✓ special needs of individual patient groups like immunosuppressed, pregnant women, etc.

6.2 Development of antimicrobial policy

Key elements of developing hospital antimicrobial policy are given in **Fig 3**.

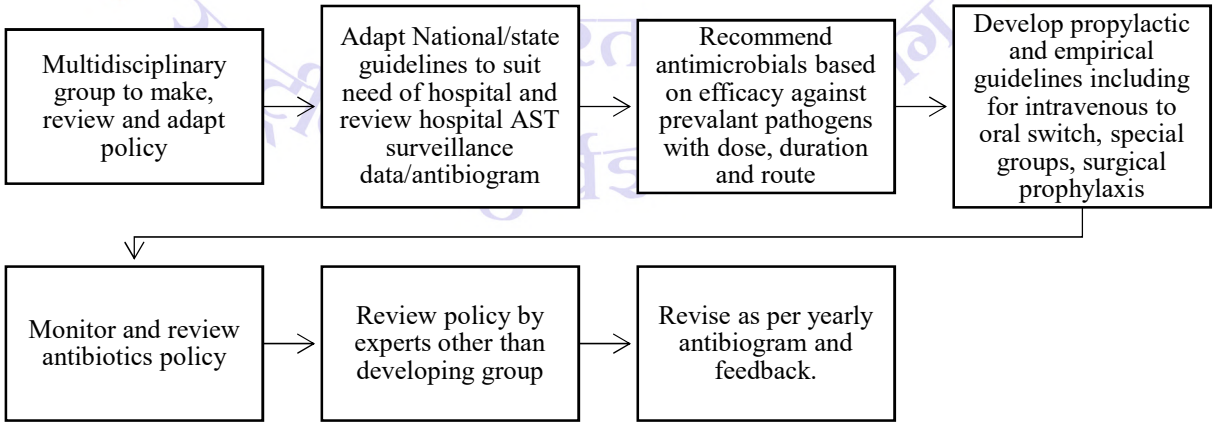

Fig 3: Key elements of developing hospital antimicrobial policy

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Antimicrobial Stewardship in Humans

7

Learning Objectives

On completion of this chapter, the prescriber should be able to:

- define antimicrobial stewardship
- outline the goals, strategies and interventions of antimicrobial stewardship
- describe the core and supplemental interventions
- outline the pharmacokinetics and pharmacodynamics approach to antimicrobial prescription
- describe and interpret antibiogram
- understand the utility of antibiogram in formulating empirical therapy.

7.1 Introduction

- **Antimicrobial stewardship** has been defined as ***"coordinated interventions designed to improve and measure the appropriate use of antimicrobial agents by promoting the selection of the optimal antimicrobial drug regimen including dosing, duration of therapy, and route of administration".***

7.2 Goals of Antimicrobial stewardship

The goals can be briefly described as:

- Ensure the best clinical outcome, for treatment or prevention of infection
- Minimize unintended consequences of antimicrobial use such as adverse drug reactions, emergence of clones of antimicrobial resistance
- Minimize healthcare costs without compromising quality of care
- Accurate diagnostics and diagnostic pathways

Antimicrobial stewardship program (AMSP) have a direct responsibility to ensure prudent antimicrobial prescribing. It focuses on "4Ds" of prescribing antimicrobials (**Fig 4**).

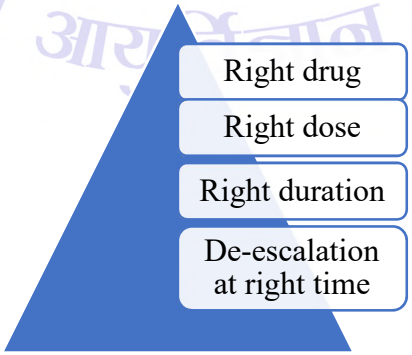

Fig 4: 4Ds of prescribing antimicrobials

7.3 AMSP interventions

Interventions can be introduced in phased manner or in whole hospital depending upon the facilities and motivation. Broadly the interventions that can be introduced are given below (**Table 6**).

Table 6: Core and supplemental interventions in antimicrobial stewardship

Core interventions	Supplemental interventions
Prospective audit	Dose optimization and combination therapies
Antimicrobial timeouts	Streamlining or de-escalation of therapy
Antimicrobial consumption analysis	Parenteral to oral conversion
Formulary restriction	Laboratory surveillance and feedback
Guidelines and clinical pathways	Information, education and communication

Core Interventions

Prospective audit

Regular bedside review of the patients to be done to analyse the prescriptions related to antimicrobial prescribing. After reviewing, feedback should be provided to the prescriber advising change if required on the optimal antimicrobial therapy.

Antimicrobial "Time outs"

Antimicrobials are often started empirically in hospitalized patients while diagnostic information is being obtained. All prescribers should review antimicrobials prescription after 48 hours to assess all 4Ds of antimicrobial stewardship.

Antimicrobial consumption analysis

Quantitative analysis of antimicrobial consumption: It should be collected from pharmacy purchase stores which will give proxy data of overall consumption of antimicrobials by the population (antimicrobial consumption surveillance).

- Qualitative analysis of appropriateness of prescription: Information regarding which patients are being given what antibiotics, their indications, dose and duration is collected using point prevalence surveys. It gives antimicrobial use surveillance.

Formulary Restriction

- Antimicrobials included on the hospital formulary should be divided into three groups:

1. Unrestricted: may be prescribed by any clinician
2. Consultant only: may only be prescribed by a consultant
3. Restricted: may only be prescribed following prior discussion with, and approval by, the antimicrobial stewardship team

- This list should be reviewed periodically preferably every year on the basis of antimicrobial usage data and rates of antimicrobial resistance.

Guidelines and clinical pathways

- Every hospital must develop antimicrobial prescription guidelines based on principles of rational antimicrobial prescription.
- In absence of local guidelines, National Antimicrobial prescription guidelines may be adopted.

Supplemental Interventions

Dose optimization and combination therapies

- Antimicrobial must be given at the optimal dose, frequency and duration, based on individual patient characteristics such as age, weight, renal function, likely causative organism, site of infection, and pharmacokinetic and pharmacodynamic characteristics of the antimicrobial agent(s).
- A few combinations are considered synergistic, such as:
  - ✓ Aminoglycoside and beta–lactam antimicrobial.
  - ✓ Beta –lactam antimicrobial and beta–lactamase inhibitor.
  - ✓ Beta –lactam antimicrobial and glycopeptide (vancomycin/teicoplanin)
  - ✓ Sulphamethoxazole and Trimethoprim

  Antimicrobial drug therapy cannot be considered in isolation, it may be ineffective in cases where pus is not drained, septic shock is not treated and hypoxia/ anaemia are not corrected.

Streamlining or de-escalation of therapy

All empiric antimicrobial therapy should be reviewed on a daily basis by the clinician responsible for the patient's care. Special attention must be paid to factors such as:

- Antimicrobial combinations with overlapping spectrum of activity. For example: Drugs like meropenem, clindamycin and piperacillin tazobactam provide cover against anaerobic bacteria and hence additional anaerobic antimicrobial such as metronidazole should not be given.
- Prolonged use of broad spectrum antimicrobials
- Unauthorised use of restricted agents
- Antimicrobial use not in accordance with hospital antimicrobial policy.
- Clear criteria for prescribing intravenous antimicrobials.

Parenteral to oral conversion

- Always review intravenous prescription after 48 hours (at least) and switch to oral if possible.

- Early switch from intravenous (IV) agents to the equivalent oral preparation offers several benefits:
  - ✓ Decreased total cost of therapy,
  - ✓ Decreased potential for line associated infections,
  - ✓ Potential for decreased length of stay and patient preference,
  - ✓ Increased patient comfort and mobility,
  - ✓ Savings in nursing time spent preparing and administering intravenous doses.

Laboratory surveillance and feedback

The Microbiology laboratory must share antimicrobial susceptibility data as an antibiogram with the prescribers. Also, feedback on follow up cultures must be promptly provided to allow timely review of antimicrobial prescriptions.

Utility of antibiograms

- Empiric antimicrobial therapy is started to provide initial control of a presumed infection of unknown cause. Hence, local cumulative antibiograms are required to select appropriate empiric antimicrobials for patients with common infections.
- It also provides a broad overview of local antimicrobial resistance over time (e.g. the proportion of *S. aureus* isolates that are methicillin-resistant).
- Can provide an overview of the emergence of antimicrobial resistance in particular settings over time.
- It can assist in managing infections due to multidrug-resistant organisms.

Information, Education and Communication (IEC)

- **Prescriber IEC**: Educational aids to guide prescribers at the point of prescribing such as clinical algorithms for the diagnosis of infection, or methods to standardise documentation of treatment decisions must be displayed at important locations in hospitals by the hospital administration in consultation with the AMSP committee.
- **Patient IEC**: Patients, their families and general public should be educated through awareness program, regarding appropriate use of antimicrobials such as:
  - ✓ When antimicrobials are not needed, like in cases of upper respiratory tract infections which are mostly of viral etiology and do not require antimicrobials.
  - ✓ Inappropriate use may cause antimicrobial associated diarrhoea, allergic reaction, colonization with drug resistant bacteria, and autoimmune diseases, likely through disturbing the microbiome etc.
  - ✓ They should be made aware of the importance of adherence to antimicrobial treatment.

7.4 Pharmacokinetic (PK) and pharmacodynamic (PD) approach to optimize antimicrobial prescription: right antimicrobial selection for an infection PK and PD both

to be considered (PK -how the drug behaves in the body and PD (how it interacts with the target pathogen)-

- **Matching the antibiotic to the site of infection:** like tissue penetration ensures the antibiotic reaches the target location in sufficient concentrations.
- **Dosage Optimization:** the appropriate dose and dosing frequency to maintain effective antibiotic levels throughout the treatment course.
- **Patient-Specific Adjustments:** Factors like age, weight, kidney function, and liver function can affect PK parameters. PK/PD allows for adjustments to ensure optimal drug exposure for each patient.

7.5 Interpretation of antibiogram results: should be interpreted in conjunction with other factors like-

- the patient's clinical condition,
- local resistance patterns, and
- potential for adverse effects.

7.6 Principles of rational prescription

The general principles guiding antimicrobial prescription must be followed for all patients. Some of these principles are given below:

- Do NOT use antimicrobials
  - ✓ To treat colonization or contamination unless there is clear indication such as immunosuppression or post splenectomy.
  - ✓ As general prophylaxis or "Feel good" factor.
  - ✓ To treat infections which have high suspicion of viral causes such as influenza
- Use antimicrobials only
  - ✓ In cases of high degree of suspicion of infection.
  - ✓ After a treatable infection has been recognized
  - ✓ For prevention of infection where evidence has demonstrated that the potential benefits outweigh the risks.
- Empirical therapy must be based on local/national prescribing guidelines.
- Use targeted therapy instead of broad-spectrum antimicrobials unless there is a clear clinical reason (for example, mixed infections or life-threatening sepsis).
- Review broad spectrum antimicrobials as early as possible and promptly switch to narrow spectrum agents when sensitivity results become available.
- Choose antimicrobials as determined by the sensitivity of identified causative organism.
- The indication for which the patient is being prescribed the antimicrobials should be documented in the drug chart and case notes by the prescriber.
- Always have a stop/review date on antimicrobial order form/ patient chart. No antimicrobial should be written for indefinite time.

- Pre-surgical prophylaxis guidelines must be followed.

7.7 Strategic approach for development and intervention of AMSP

The strategic approach must be as per the availability of resources in the local settings:

- **Committee preparation:** An AMS committee is required to provide leadership and overall coordination of the AMS programme. Committee must include Administrative leader, Clinicians from each clinical department, Clinical pharmacist, Microbiologist, Nursing officer etc. as per standard guidelines.
- **Prescribers' education:** The policy-makers and health care administrators to provide opportunities for physicians to address information gaps through clinical education and continuing professional development.
- **Development of Institution-specific guidelines and interventions**: Institution-specific guidelines or algorithms can be adapted from national or international evidence-based guidelines to reflect local epidemiology, access to diagnostic testing and drug availability.

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Infection Control

8

Learning Objectives

On completion of this chapter, the prescriber should be able to:

- define and describe the elements of standard precautions
- define and describe transmission-based precautions.
- define biomedical waste management
- describe various segregation methods and their disposal as per BMW rules.
- define device associated infections
- define and describe preventive care bundles for device associated infections

Introduction

Microbes are a part of everyday life and are found in our environment (air, soil, water), and in/ on our bodies. Many microbes live in and on our bodies without causing harm but a small portion of them are known to cause infection. Many microbes live without causing harm but a small portion of them is known to cause infection. For any infection to occur, a sequence of events occur that transmit an infectious microorganism to a susceptible host. Three things are necessary for an infection to occur:

- **Source:** Places where infectious agents live (e.g., sinks, surfaces, human skin, water, food)
- **Susceptible Person** with a way for microbes to enter the body
- **Transmission:** how the microbes are moved to the susceptible person

Interactions are more common in hospital environment and provide microorganisms an opportunity to cause infection in susceptible host. Healthcare-associated infections (HAIs/ HCAIs) are influenced by the interaction between host, pathogen and environmental factors. This chain of transmission is favoured by health care workers.

In order to prevent HAIs, this chain of transmission needs to be broken by appropriate infection control Practices

Infection control prevents or stops the spread of infections in healthcare settings. There are two tiers of recommended precautions to prevent the spread of infections in healthcare settings: Standard precautions and transmission-based precautions.

8.1 Standard Precautions

Standard precautions (previously known as universal precautions) are the minimum infection prevention practices that apply to all patient care, regardless of the suspected or confirmed infection status of the patient, in any setting where healthcare is delivered. Standard precautions consider every person (patient or staff) as potentially infectious and susceptible to infection. It aims to prevent transmission of infections from:

- Patient to healthcare worker
- Healthcare worker to patient
- Patient to patient (cross-transmission)
- Hospital environment to patient
- Hospital waste to community (spread)

The basis of standard precautions is that it presumes all specimens are potentially infectious. Standard precautions apply to blood, semen, vaginal secretions, synovial fluid, cerebrospinal fluid, pleural fluid, peritoneal fluid, pericardial fluid and amniotic fluid. They do not apply to feces, nasal secretions, sputum, sweat, tears, urine, vomitus and saliva. Given below in **Table 7** are the elements of standard precautions:

Table 7: Elements of standard precautions

i. Hand hygiene ii. Personal protection equipment/ PPE (gown, mask, face protection, gloves, goggles etc.) iii. Safe injection practices iv. Sharp management v. Spill management	vi. Patient care equipment/ devices management vii. Environmental control viii. Respiratory hygiene/cough etiquettes ix. Proper disposal of biomedical waste

(Source:www.cdc.gov/HAI/settings/outpatient/outpatient-care-gl-standared-precautions.html, Version 2.3 - September 2016)

i) Hand hygiene

- Hand hygiene is the single most important strategy in preventing HAIs. Clean hands prevent infections and this applies in any setting, at home, at school or at work.
- In healthcare settings, handwashing is the simple and most effective way to prevent potentially fatal infections spreading from patient to patient and from patient to healthcare worker and vice versa. However, this is often overlooked by most healthcare personnel.
- Hence, it is essential to emphasise its importance and educate the personnel about the correct technique of handwashing.
- Key points where hand hygiene should be performed are known as the five moments of hand hygiene as given below:

- ✓ Before touching a patient, even if gloves are to be worn,
- ✓ Before coming out of the patient's care area after touching the patient or the patient's immediate environment,
- ✓ After contact with blood, body fluids or excretions or wound dressings,
- ✓ Prior to performing any aseptic task (e.g., placing an intravenous line or preparing an injection),
- ✓ If hands are likely to move from a contaminated body site to a clean body site during patient care; and after removal of gloves

The 5 moments of hand hygiene are given in **Fig 5**

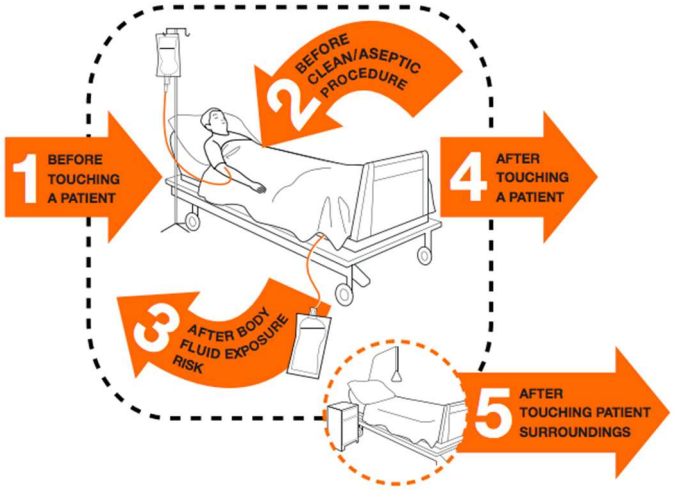


Fig 5: The WHO 5 moments of hand hygiene

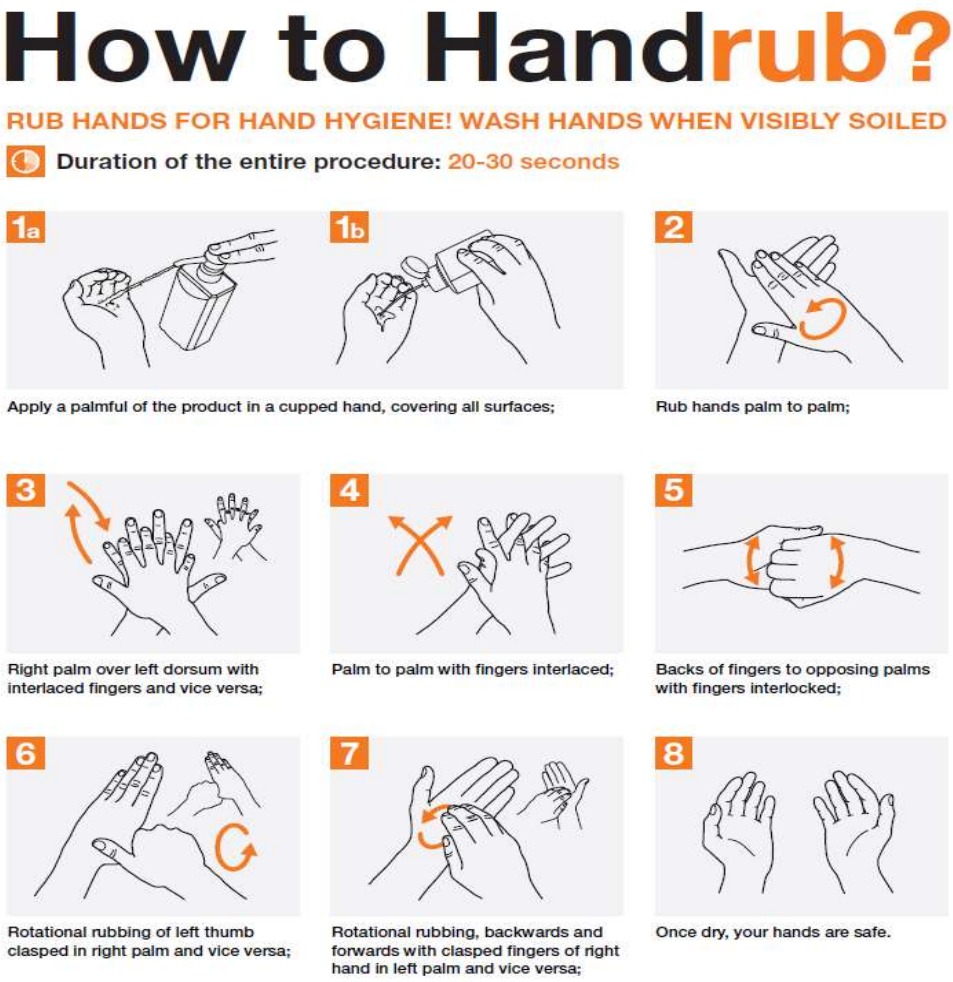
(Source: https://openwho.org/courses/IPC-HH-en)

- **Good hand hygiene practices**, which include the use of alcohol-based hand rubs and washing with soap and water, are critical to reducing the risk of spreading infections in ambulatory care settings.
- The process takes around 40–60 seconds in its entirety. Steps of hand washing are given in **Fig 6**.
- Hands must be fully dried, as moisture can breed microorganisms. A cloth towel should not be used as the organisms can remain and be transmitted. If possible, paper towel should be used to turn off the tap and dry hands. Unwashed hands of a nurse or any healthcare worker are loaded with bacteria.

(Source:https://www.who.int/teams/integrated-health-services/infection-prevention-control/hand-hygiene/training-tools)

Fig 6 : Steps of handwashing

If soap and water are not available, then alcohol- based hand sanitiser (hand rub) can to use to clean hands. They significantly reduce the number of organisms on skin and are fast- acting. However, if hands are visibly dirty, then washing with soap and water is the only method that should be used. Using a hand rub generally reduces the time to around 15–20 seconds (**Fig 7**). However, for surgical scrub (prior to performing surgery), the process takes five minutes. When using an alcohol-based hand sanitiser: Apply product to the palm of one hand, rub hands together and then rub the product over all surfaces of hands and fingers until hands are dry.



(Source: Guideline on Hand Hygiene in Health Care in the Context of Filovirus Disease Outbreak Response, WHO, 2014)

Fig 7 : Steps of hand rub

ii) Personal protective equipment (PPE)

As per OSHA (Occupational Safety and Health Act) PPE is defined as *"Specialized clothing or equipment worn by an employee for protection against infectious materials"*. It refers to wearable equipment intended to improve healthcare workers safety from exposure to or contact with infectious agents. It includes gloves, lab coats, gowns, goggles, and masks.

The purpose of PPE is to prevent blood and body fluids from reaching the worker's skin or mucous membranes. A full PPE is required while providing care to patients who have highly infectious diseases like COVID-19, Ebola and Nipah virus infections, which require isolation and barrier nursing in containment areas of the hospital.

The group of items used in PPE can be used separately or in combination, acting as a barrier to prevent contact between health workers and a patient/object/environment.

Recommendations on use of PPE is based on the expert opinions regarding disease transmissions, known portals of entry, perception of risk and severity of transmission. All PPE should be made of standard impervious material.

Components of PPE

- **Gowns and aprons**: Gown is meant to cover the body from the neck to the knees and the arms down to the wrists with an opening and closing mechanism, usually at the back. These protect health care worker's clothes/scrubs from getting contaminated while performing procedures that might create spatters of blood or body fluids.

  The gowns can be disposable or non-disposable. Apron is made of waterproof material and is worn over gown as barrier. The same gown should not be worn for the care of more than one patient.

- **Safety eyewear such as glasses, wraparounds, goggles**: The purpose of safety eyewear is to prevent aerosols, spatters and droplets from coming in contact with conjunctival mucus membrane. Personal glasses are not a substitute for goggles. The safety eyewear should fit snuggly over and around eyes. To wear, the goggles must be positioned over eyes and secured to the head using the ear pieces or headband.

- **Face protectors and face shields**: These should cover forehead, extend below chin and wrap around side of face. To wear face shield, position it over face and secure on brow with headband. It should be then adjusted to fit comfortably covers the entire face and wearer does not require additional eye protection or a mask to guard against droplet-transmissible agents. Mouth, nose and eye protection should be in place during procedures likely to generate splashes or sprays of blood or other body fluids.

- **Masks**: Just like conjunctiva, mucous membranes of the nose and mouth are portals of entry for infectious agents. So, it is essential to protect them. The barriers can be in the form of mask or respirators. Masks are made up of impervious material and can be pleated or preformed. Efficiency of masks reduces with moisture and should be changed frequently. Masks can be surgical or N-95 NIOSH or CDC certified.

- **Boots, jumpsuits, overall and hoods**: These do not provide any added protection but only prevent soiling of clothes or street shoes.

- **Gloves:** These are intended to prevent contact of hands with contaminated sources such as the skin of patients colonized or infected with multidrug resistant microorganisms. A surgical mask should be worn when placing a catheter or injecting material into the spinal canal or subdural space. There are two methods of wearing sterile gloves:

- **Closed gloving**: In this method the hands are covered by the gown sleeves. The hands remain inside the cuff and the gloves are worn one hand after another.
- **Open gloving**: The gloves are worn by touching the inner surface of the gloves for one hand followed by outer sterile surface for the other hand.

  The gloves should be placed on top of the cuff of the gown while using long-sleeve gowns. With reference to gloves, the following precautions are recommended:

- Gloves should be worn when there is a possibility of contact with blood, body fluids, mucous membranes, non-intact skin or contaminated equipment.
- Gloves should always be changed between patients or if they develop breaks or tears.
- Gloves should not be washed for the purpose of reuse.

- Under no circumstance should glove use replace hand hygiene.
- Hand hygiene should be performed immediately after removing the gloves.

Donning of PPE

Before donning PPE make sure that hair is tied and all jewellery is removed. The worker must ensure that the PPE is of correct size before breaking open the seal.

The PPE must be worn in the following order as shown in **Fig 8**.

Fig 8: Donning of PPE (source: https://www.cdc.gov>hai>pdfs>ppe-sequences)

Doffing of PPE

PPE should be removed in an order that minimizes the potential for cross contamination. PPE should be doffed in the following order as shown in **Fig 9.**

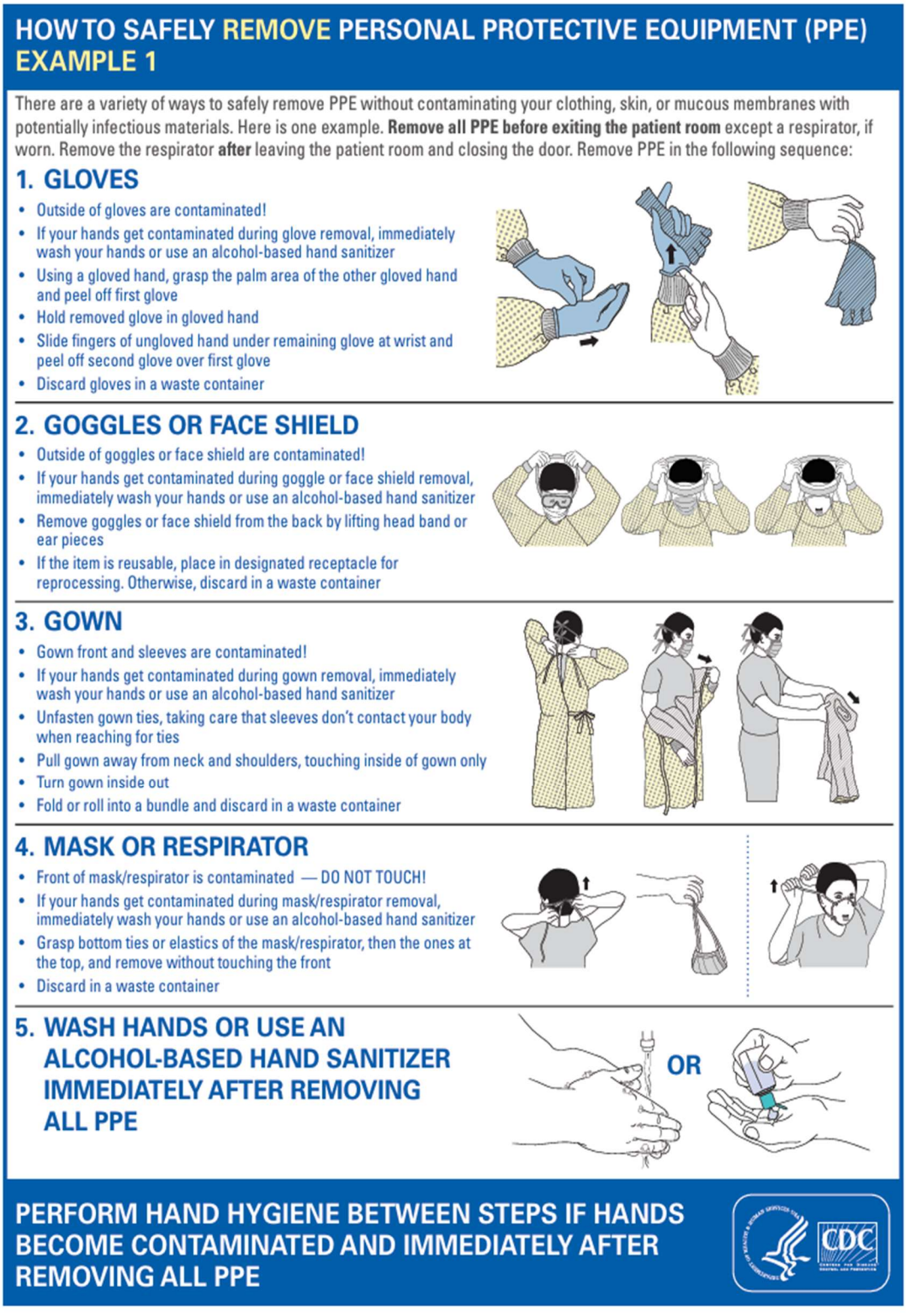


Fig 9: Doffing of PPE (source: https://www.cdc.gov>hai>pdfs>ppe-sequences)

iii) Safe injection practices

Safe injection practices prevent transmission of infectious diseases between patients and between patients and healthcare workers (HCW) during the preparation and administration of parenteral medicines. The following are recommended:

- Aseptic techniques should be used when preparing and administering medicines.
- Access diaphragms of medicine vials should be cleaned with 70% alcohol before inserting a device into the vial.
- Medicine should never be administered from the same syringe to multiple patients.
- A used syringe should not be used to draw medicine from a vial or solution.
- Fluid infusion or administration sets (e.g., intravenous tubing) should not be used for more than one patient.

Multi-dose vials should be dedicated to a single patient whenever possible.

iv) Sharp management

- Sharps like needle and syringes have to be rendered unusable and disinfected immediately on use at source before disposal.
- Containers should be available at point of use or generation point.
- Sharps or needles should not to be purposely bent or broken by hand. The needle is put inside disposal container with the sharp end first. Never push or force in with the hand. Have a clear view of the container opening and the inside of the container during disposal.
- Used needles should not be re-capped on any account. One hand scoop technique can be done if needed.
- If needle and syringe need to be transported from one area to another, then a rigid walled container must be used.
- The sharps container must be removed when half filled. The lids must be securely closed.

Sharp Injury management: In the event of a needlestick injury/ splash of blood or body fluid into the eye, the area should be washed with running tap water or with an eye wash and, the following protocol needs to be followed immediately to prevent transmission of HBV, HCV and HIV.

- The event needs to be reported to the infection control nurse and medical officer incharge/infection control officer. The source patient's status should be verified. (If the status is not known, and with consent of the patient, the person may be tested for HIV, hepatitis B and hepatitis C).
- If the patient is known to be HIV-positive or if the status is unknown, post-exposure prophylaxis (PEP) is initiated (according to NACO, CDC and WHO guidelines).
- Hepatitis B—if the healthcare worker is vaccinated, no treatment is required, but if not vaccinated, HBIg and HB vaccine are initiated as per guidelines.
- Hepatitis C—no treatment is currently recommended.

v) Spill Management

- Body fluid spills can be spills that are visibly contaminated with blood and those which are not. Both types of spills require same treatment.
- Exposure to blood and other body fluids poses a risk of infection to health care persons and patients. Spillages of blood must be dealt with immediately.
- Any splashes of blood or body fluids on the skin must be washed off immediately with soap and water.

Procedure for Spill Management

- Spillage of less than 30 ml is treated as small and more than 30 ml as large spill.
- Infection control nurse must be informed in case of large spill after immediate action has been taken by the concerned department.
- Staff must be trained in proper procedure to manage spills.
- Spill management protocols must also be displayed at prominent locations (sample given in **Fig 10**) in the hospital especially at point of use as a ready reference for the staff for management of spills.

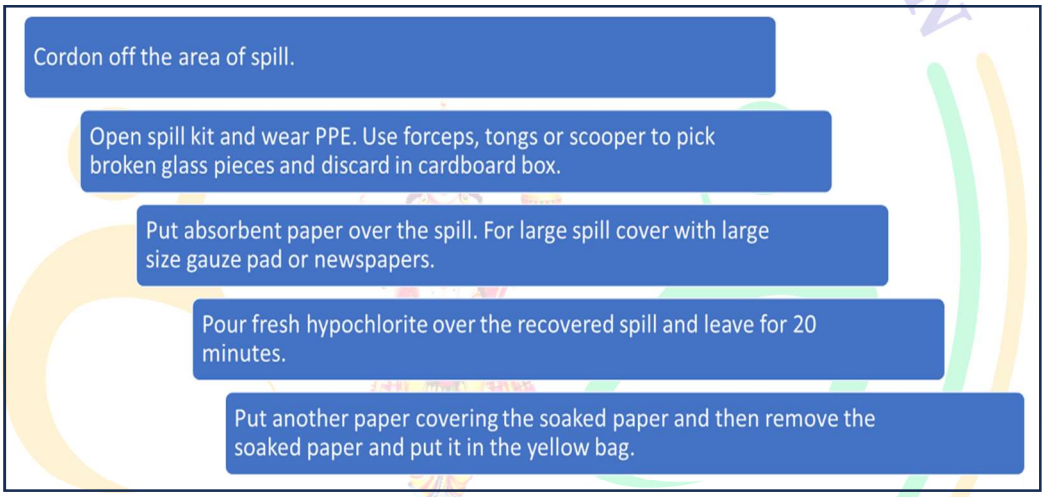


Fig 10: Steps in spill management

Spill kit: A spill kit must be readily available with all departments especially where risk of spill is more, like laboratory, sample collection room, wards etc. Spill kit must have the following contents (**Table 8**):

Table 8: Contents of a spill kit

• Gloves-2 pairs • Apron • Mask • Shoe covers • Absorbent material like newspaper or blotting paper	• Waste disposal bag • Cleaning equipment – bucket, mop, cloth, soap etc. • Freshly prepared 1% sodium hypochlorite solution • Forceps, tongs or scooper

vi) Patient Care Equipment/ Devices management

- Medical equipment may be reusable or meant for single use. Reusable medical equipment (e.g., endoscopes) come with instructions for their cleaning and disinfection or sterilisation, as appropriate. Single-use devices are labelled by the manufacturer for one-time use and come with reprocessing instructions.
- Reusable medical equipment (e.g., blood glucose meters and other point-of-care devices, surgical instruments, endoscopes) is cleaned and reprocessed appropriately before being used on another patient.
- Soiled patient care equipment: Wear gloves if visibly contaminated and practice routine hand hygiene. Follow procedures for routine care, cleaning and disinfection of environment surface, especially frequently touched surfaces in patient care areas.

vii) Environmental Cleaning

- Cleaning refers to the removal of visible soil and organic contamination from a device or environmental surface with appropriate chemical agents. This process removes large number of microorganisms from surfaces and must always be performed before disinfection.
- Handling soiled or contaminated linen: Gloves should be used at all times. The linen must be inspected for any needles, or syringes etc. while stripping. Linen should not to be placed on floor but in a yellow doubled plastic bag sealed by a knot.
- **Terminal disinfection** is the method of thorough cleaning of the patient bed, surroundings, and the patient utilities after the discharge of the patient. Do not admit another patient in the same room for at least 12 hours.

viii) Respiratory Hygiene/Cough Etiquette

- This refers to the standard precautions to be taken by any individual with signs of illness including cough, congestion, rhinorrhoea or increased production of respiratory secretions. Such individuals need to be promptly identified to prevent transmission of respiratory infections.

The elements of Respiratory Hygiene/Cough Etiquette include:

- Education of staff, patients, and visitors in a Health Care Facility (HCF).
- Posted signs (in languages understood by the population served), with instructions to patients and accompanying family members/ friends beginning at the point of initial encounter in a HCF (e.g., triage, reception and waiting areas in emergency departments, outpatient clinics and physician offices).
- Source control measures (covering the mouth/nose with a tissue while coughing with prompt disposal of used tissues or using surgical masks on the coughing person as appropriate).
- Hand hygiene after contact with respiratory secretions.

- Spatial separation (ideally >3 feet), of persons with respiratory infections in common waiting areas when possible.
- Health Care Practitioner (HCPs) are advised to observe Droplet Precautions and perform hand hygiene when caring for such patients.
- HCPs who have a respiratory infection are advised to avoid direct patient contact, especially with high- risk patients. At least a mask should be worn while providing patient care.
- Provide tissues and no-touch receptacles (e.g., foot-pedal operated lid or open, plastic-lined waste basket) for disposal of tissues.

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8.2 Transmission based Precautions

Introduction

CDC recommends two tiers of precautions to prevent transmission of infectious agents. The standard precautions as mentioned earlier apply to all irrespective of their disease status while transmission- based precautions are to be followed in case the patient is known case or is suspected to be infected or colonized with infectious agents.

- As these patients carry a high risk of transmitting the pathogen to the healthcare worker and adjacent patients, further measures are needed in addition to standard precautions to prevent transmission of infection. Usually, these patients must be isolated and the appropriate transmission-based precautions must be used. Following transmission-based precautions are followed in addition to standard precautions (**Table 9**):
  - Airborne precautions
  - Droplet precautions
  - Contact precautions

- **Airborne precautions:** These are to be followed for droplet nuclei <5µm, e.g., tuberculosis, chicken pox, measles and influenza. This requires:
  - Isolation of patients in individual room with adequate ventilation: This includes, where possible, negative pressure; door closed; at least twelve air exchanges per hour; exhaust to outside placed away from intake ducts
  - Staff wearing high-efficiency masks in room

- **Droplet precautions:** These are to be followed for droplet nuclei >5 µm, e.g., meningococcal meningitis, diphtheria, respiratory syncytial virus. The following procedures are required:
  - Individual room for the patient, if available
  - Surgical mask for healthcare workers
  - Restricted circulation for the patient; patient wears a surgical mask if leaving the room
  - Teach the patient to follow respiratory hygiene/cough etiquette.

- **Contact precautions:** Direct contact occurs when performing patient- care activities that require touching the patient's skin. Indirect contact occurs when touching potentially contaminated environmental surfaces or equipment in the patients' environment Individual room for the patient if available; grouping patients if possible
  - Staff wear gloves on entering the room; a gown for patient contact or contact with contaminated surfaces or material
  - Wash hands before and after contact with the patient, and on leaving the room

- Restrict patient movement outside the room
- Appropriate environmental and equipment cleaning, disinfection, and sterilisation

Contact Precautions are to be followed for patients infected with organisms capable of transmission through either direct or indirect contact, e.g., patients with enteric infections and diarrhoea which cannot be controlled or skin lesions which cannot be contained, and multidrug- resistant organisms [MDRO].

Table 9: Elements of specific precautions

Specific precautions	Source Control: patient to wear mask	Isolation of patient	Restriction of movement of patients	Appropriate PPE to be used	Disposable or dedicated patient equipment	Prioritize cleaning or disinfection of patient rooms
Contact Precautions	No	No	Limit movement outside room. Follow contact precautions if transfer is needed covering colonized areas of the patient's body.	Gloves and gown	Yes	Daily and no room and material should be allowed to be used by another patient prior to cleaning.
Droplet Precautions	MUST wear mask.	In single room possibly.	Yes	Gloves, apron and mask	Yes	-do-
Airborne Precautions	Fit-tested NIOSH-approved N95 or higher level respirator for healthcare personnel.	In airborne infection isolation room with negative pressure. If not possible then mask patient and place in a private room with the door closed	Yes	Full PPE with fit-tested NIOS approved N95 or higher level respirator for healthcare personnel.	Yes	-do-

Isolation of Patients

- All patients admitted with contagious infections must be isolated. Patients infected with MRSA and multi drug- resistant organisms, which are resistant to three or more classes of antibiotics, need to be isolated and treated by barrier nursing.
- The nursing care is individualised so that the infection does not spread to other patients via the nurse.
- All personal protective equipment is dedicated to single use.
- For the isolated patients, transmission-based precautions must be followed in addition to the standard precautions.

Table 10 shows patients who should be isolated into separate rooms or wards are those with:

Table 10: Patients with clinical presentations/ diseases that require isolation

• Undiagnosed rashes and fevers • Chickenpox • Measles • Severe acute respiratory syndrome (SARS)	• Influenza • Patients known to be colonised with MRSA, VRE, and other multi-drug resistant organisms • Multidrug-resistant tuberculosis (MDR-TB)

Protective isolation or reverse barrier nursing) is practised when the patient requires protection. **Reverse barrier nursing** works by protecting vulnerable patients, such as those with impaired immune systems (immune- compromised), against infection by medical staff.

Multidrug Resistant Organisms

- The increased occurrence of antimicrobial-resistant microorganisms (methicillin-resistant *S. aureus* [MRSA], extended spectrum beta-lactamase [ESBL] or vancomycin-resistant enterococci [VRE]) is a major medical concern.
- The spread of multi resistant strains of *S. aureus* and VRE is usually by transient carriage on the hands of healthcare workers.
- The following precautions are required for the prevention of spread of MDRO:
  - ✓ Minimise ward transfers of staff and patients
  - ✓ Ensure early detection of cases, especially if admitted from another hospital; screening of high-risk patients may be considered
  - ✓ Isolate infected or colonised patients in a single room, isolation unit or cohorting in a larger ward
  - ✓ Re-enforce handwashing with antiseptic by staff after contact with infected or colonised patients
  - ✓ Use of personnel protective equipment (PPE)
  - ✓ Proper waste segregation and disposal system

Consider treating MRSA nasal carriers with mupirocin.

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8.3. Proper Disposal of Biomedical Waste

Introduction

Biomedical or hospital waste refers to any waste generated while providing health care, performing research and undertaking investigations or related procedures on human beings or animals in hospitals, clinics, laboratories or similar establishments (Management and Handling Rules: Government of India, 2016). The objectives of biomedical waste management are to prevent harm resulting from waste, minimise its volume, retrieve reusable materials and ensure safe and economical disposal.

Reduction in volume of waste can be achieved by proper planning and using reusable items wherever safely possible.

Segregation refers to the separation of waste at the point of generation into the various types with respect to their category and mode. Segregated waste must be put into different coloured containers, as prescribed in the rules, for appropriate treatment. These guidelines were modified in 2018. The colour coding is shown in **Table 11**.

Storage refers to the measures taken to ensure that biomedical waste is kept safely at the point of generation before being sent to the biomedical waste treatment facility.

Treatment of waste means all the procedures and processes intended to reduce the bulk of the waste and make it non-infectious and harmless.

Table 11: Colour-coded bags for biomedical waste segregation

Colour of the bag	Type of waste	Waste treatment
Yellow	a) Human anatomical waste b) Animal anatomical waste c) Soiled waste	Incineration or plasma pyrolysis or deep burial
	d) Expired or discarded medicines	Returned to the manufacturer or supplier for incineration at temperature >1,200°C
	e) Chemical waste	Incineration, plasma pyrolysis, deep burial or encapsulation
	f) Chemical liquid waste	Pre-treatment and then disposal
	g) Discarded linen, mattresses, beddings contaminated with blood or body fluids	Non-chlorinated chemical disinfection followed by incineration or plasma pyrolysis
	h) Microbiology, biotechnology and other clinical laboratory waste	Pre-treat to sterilise with non-chlorinated chemicals on-site as per NACO or WHO guidelines and thereafter send for incineration
Red	Contaminated waste (recyclable) like plastic bag, bottles, pipes or containers	Autoclaving or microwaving/ hydroclaving followed by shredding or mutilation

Colour of the bag	Type of waste	Waste treatment
		Treated waste to be sent to registered or autoclaved recyclers or for energy recovery of plastics to diesel or fuel oil or for road-making
White, translucent	Waste sharps including metals: Needles, syringes with fixed needles, needles from needle tip cutter or burner, scalpels, blades	Autoclaving or dry-heat sterilisation; followed by shredding or mutilation or encapsulation in metal container or cement concrete sent for final disposal to iron foundries (having consent to operate from the state pollution control committees) or sanitary landfill or designated concrete waste sharp pit
Blue cardboard box with blue label or blue leak- and puncture-proof container	Glassware: Broken or discarded and contaminated glass including medicine vials and ampoules except those contaminated with cytotoxic wastes; metallic body implants	Disinfection (by soaking the washed glass waste after cleaning with detergent and sodium hypochlorite treatment) or through autoclaving or microwaving or hydroclaving, then sent for recycling

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8.4 Preventive Bundles for Device Associated Infections

Introduction

- Device associated infections: These healthcare–associated infections are infections that can be associated with the devices used in medical procedures, such as catheters or ventilators.
- Care bundles: These are a set of interventions that when applied together result in better prevention of device associated infections than individual elements implemented alone.
- Some recommended preventive bundles are as below. The hospitals may modify these bundles according to their availability of resources and other logistics.

I) Central line insertion and care bundle

- Hand hygiene
- Maximal barrier precautions upon insertion/manipulation
- PI/ alcohol/ chlorhexidine skin antisepsis
- Optimal catheter site selection, with avoidance of the femoral vein for central venous access in adult patients
- Daily review of line necessity with prompt removal of unnecessary lines

II) Preventive bundle for urinary catheter insertion/care

- Catheterize only if absolutely necessary
- Reduce the duration of catheterization
- Closed drainage
- Intermittent catheterization
- External collection devices
- Ensure dependent drainage
- Use of systemic antimicrobials: Only if patient is symptomatic and culture suggests UTI
- Compared with latex catheters, silastic catheter has a decreased incidence of urethritis and possibly urethral strictures. However, because of its lower cost and similar long term outcomes, latex is preferably used for long term catheterization.
- Remove catheters as early as possible

III) Recommended preventive bundle for Ventilator Associated Pneumonia (VAP)

- Avoid unnecessary antibiotics
- Avoid unnecessary stress ulcer prophylaxis
- Sucralfate for stress ulcer prophylaxis
- Oral intubation
- Selective digestive decontamination
- Short-course parenteral antibiotics

- Appropriate hand disinfection
- Appropriate staffing
- Avoid tracheal intubation
- Shorten duration of mechanical ventilation
- Semi recumbent positioning
- Avoid gastric overdistention
- Subglottic suctioning
- Avoid ventilator circuit changes/manipulation
- Drain ventilator circuit condensate
- Prevent accidental extubation

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Prescribers' toolkit for combating AMR

Prescribers' toolkit for combating AMR

9

Table 12: The competencies, learning objectives and the assessment methods

S. No. and Competency addressed	Learning objectives	Domain	Target audience	Teaching learning methods (TLM)	Assessment method
1. Background and objectives	1.1 Understand the present burden of AMR 1.2 Understand the concept of this national program 1.3 Assist in implementing this program	K	Prescribers	Theory session- 30 min	Written: MCQ, SAQ
2.Clinical approach for prescribing antimicrobials	2.1 Identify common presentations of infective syndromes 2.2 Describe and understand the importance of taking thorough history, clinical examination and selection of appropriate investigations for diagnosis of infective disease soft tissue infections etc).	K	Prescribers	Exploratory and interactive theory session with case studies- 60 min	Written: MCQ -Case based discussion Clinical problem solving
3.Microbiolog -ical diagnostic stewardship	3.1 Define diagnostic stewardship 3.2 Understand the difference between infection and colonization 3.3 Describe the sample collection techniques, precautions, transport and rejection criteria of common samples.	K, A, S	Prescribers	Exploratory and interactive theory session with demonstration of collection containers, videos for collection- 60 min	Written: SAQ, MCQ
4. Interpretation of antimicrobial sensitivity results	4.1 Understand the importance of quality assured antimicrobial susceptibility testing (AST) 4.2 Interpret the antimicrobial susceptibility testing report. 4.3 Interpret the surrogate and cascade reporting.	K, S	Prescribers	Exploratory and interactive theory session with samples of AST reports- 60 min	Written: SAQ, MCQ, Case discussion, AST problem solving

5. Antimicrobial resistance: Principle and implications	5.1 Define and explain the differences between antimicrobials and antibiotics 5.2 Outline the drivers for resistance 5.3 Outline the global epidemiology of key antimicrobial resistant pathogens and antimicrobial consumption 5.4 Explain the clinical and economic impact of drug resistant infections and health care acquired infections	K	Prescribers	Exploratory and interactive theory session- 40min	Written: SAQ, MCQ
6. Antimicrobial policy	6.1 Describe the attributes and features of antimicrobial policy 6.2 Describe the key elements of developing hospital antimicrobial policy 6.3 Assist in developing antimicrobial policy	K	Prescribers	Exploratory and interactive theory session with examples from in house antibiotic policy- 30 min	Written: SAQ, MCQ
7. Antimicrobial stewardship in humans	7.1 Define antimicrobial stewardship 7.2 Outline the goals, strategies and interventions of antimicrobial stewardship 7.3 Describe the core and supplemental interventions 7.4 Outline the pharmacokinetics and pharmacodynamics approach to antimicrobial prescription 7.5 Describe and interpret antibiogram 7.6 Understand the utility of antibiogram in formulating empirical therapy	K, S	Prescribers	Exploratory and interactive theory session with examples of in house antibiograms and their interpretation- 60 min	Written: SAQ, MCQ, Case based problem

8. Infection control	8.1 Define standard precautions 8.1.1 Describe the elements of standard precautions 8.1.2 Describe moments and steps of hand hygiene 8.2 Define and describe transmission-based precautions 8.3 Define and describe various segregation methods of biomedical waste and their disposal as per BMW rules. 8.4 Define device associated infections 8.4.1 Define preventive care bundles for device associated infections 8.4.2 Describe care bundles for different types of device associated infections	K	Prescribers	Exploratory and interactive theory session- 15 + 15 + 15 + 15 min = 60 min	Written: SAQ, MCQ

Case scenario 1

A 55 year old man presented with fever for 5 days, cough and sputum. He was a known diabetic and was hospitalised last year for similar complaints. On examination: conscious, drowsy, pulse: 110/ minute, BP: 100/60 mm Hg, RR: 26/ minute, Temp: 100 degree F. Chest examination: Crepitations right infrascapular region.

Q1: Describe the presenting complaints?
Q2: Discuss the Co- morbidities?
Q3: Discuss the relevant past history of any illness and treatment history and its importance?
Q4: Discuss the differential diagnosis?
Q5: Demonstrate the examination of this patient.
Q6: Discuss based on your examination, the site of care and type of care for this patient.

Case scenario 2

A 45-yr old patient, diagnosed case of chronic kidney disease (on maintenance hemodialysis) presents with high grade fever for two weeks. He complaints of swelling over cheek with blood discharge from nose. The doctor requests for fungal infection screen

a. Discuss the differential diagnosis of infection in this case
b. Plan the investigations and management in the case for infections in immunocompromised.

Case scenario 3

1. A two-year old girl presents with fever for five days with cough and fast breathing for two days. At examination she is lethargic, has weak thready pulses with tachycardia (suggestive of shock).
   a. Demonstrate clinical skills to assess for sepsis and shock in this patient
   b. Identify and prescribe the first-hour bundle of care in sepsis in this child and monitoring care
   c. Plan rational investigations in this case
2. A 4 year old toddler with runny nose, sore throat since two days. On examination she has inflammed tonsils with white patch over it.
   a. Discuss the differential diagnosis of infection in this case (keeping both viral & bacterial etiology)
   b. Plan the investigations & management in this case.

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Powerpoint Presentations on NAP-AMR Module for Prescribers

(The presentations are based on modules, prescribers can modify according to their need)

Background and Objectives

1

NMC Module on AMR for prescribers

Learning Objectives

On completion of this chapter, the prescriber should be able to:

- understand the gravity of problem of AMR
- understand the concept of this program
- assist in implementing this program

Background

- Antimicrobials are essential for treating infectious diseases, and also in facilitating life saving procedures like organ transplants, surgeries, treatment of autoimmune diseases and cancer etc.
- Antimicrobials are also used in animals, such as pets, livestock, wildlife, and aquatic animals to combat infectious diseases.
- Of the 2152 studies published by Indian institutions on AMR, a significant majority focused on humans (48.3 %), while a small fraction in animal-related aspects (3.3 %) and the environment (4.2 %)

Background cont..

- The chances of developing AMR is high due to excessive use of antimicrobials. Various studies have reported an increase in antibiotic consumption among humans in India.
- In 2019 alone, worldwide 1.27 million deaths were directly caused by AMR, exceeding the toll of HIV and Malaria combined.
- 2019 data revealed that humans consumed a total of 5071 million Daily Defined Doses (DDD), with "Watch category" drugs accounting for 54.9 % of DDDs, and "Access category" drugs accounting for 27.0 %.

1. Background and Objectives

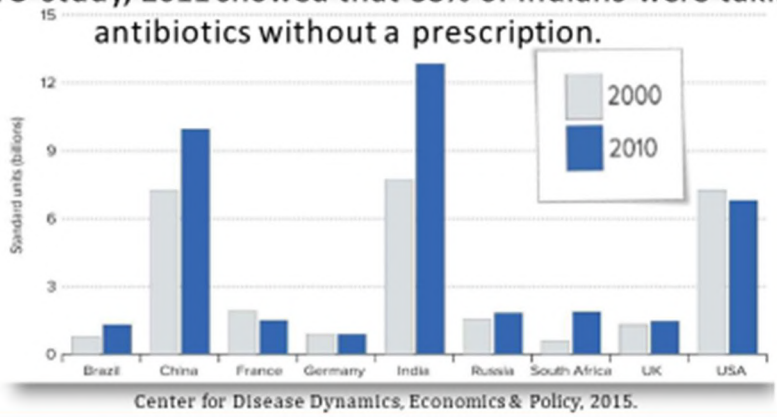
Background Cont..

- Challenging factors that contribute to the AMR burden in India include-
  - a high prevalence of infectious diseases,
  - incompatible IPC practices,
  - easy access to antibiotics without prescriptions,
  - lack of awareness,
  - limited laboratory resources for disease-based diagnosis etc.
- In 2010, India was the largest user of antimicrobials among the BRICS (Brazil, Russia, India, and China) countries.

1. Background and Objectives

TOTAL ANTIBIOTIC CONSUMPTION IN 2000 AND 2010

WHO study, 2011 showed that 53% of Indians were taking antibiotics without a prescription.



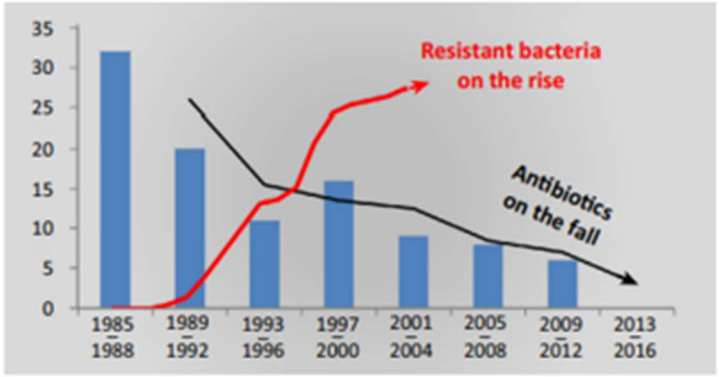
Center for Disease Dynamics, Economics & Policy, 2015.

1. Background and Objectives

Fallout of such antibiotic consumption

- Due to such high consumption of antibiotics, rising antimicrobial resistance is being witnessed across the globe.
- Under pressure to survive the antibiotics, bacteria develop resistance through one or more mechanisms described ahead.
- The issue of AMR is further complicated by the lack or slow development of newer classes of antibiotics.

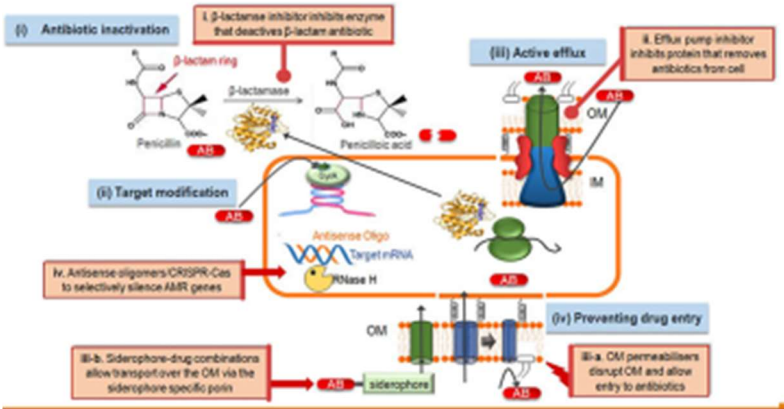
Rise of Antimicrobial Resistance



Adapted from Schäberle TF, Hack IM. Overcoming the current deadlock in antibiotic research. Trends Microbiol. 2014 Apr;22(4):165-7. doi: 10.1016/j.tim.2013.12.007. PMID: 24698433.

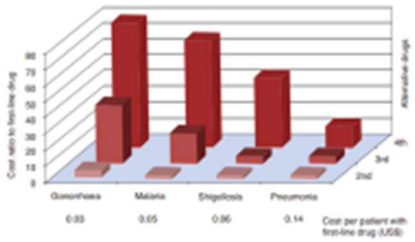
Innovation Gap

Adapted from Hutchings MI, Truman AW, Wilkinson B. Antibiotics: past, present and future. Curr Opin Microbiol. 2019 Oct;51:72-80. doi: 10.1016/j.mib.2019.10.008. Epub 2019 Nov 13. PMID: 31733401.



The Evolving threat of AMR

- Moving towards Post Antibiotic era
- Simple infections like Sore throat, ear infection, urinary tract infection, Tuberculosis and Malaria are becoming incurable.
- Longer treatment /Hospital stay-Financial burden
- Higher chances of treatment failure and death
- As per GRAM project Drug resistant infections were the leading cause of deaths world wide in 2019.



Adapted from:The evolving threat of antimicrobial resistance Options for action, WHO, 2012

GAP-AMR

- In Year 2015, understanding the gravity of the problem of AMR, the World Health Assembly (WHA) has adopted the GAP on AMR including antibiotic resistance in collaboration with WHO, Food & Agricultural Organization (FAO) & World Organization for Animal Health (OIE)
- In February 2016, an International Conference "Combating AMR A Public Health Challenge & Priority" was organised by Government of India & WHO
- In May 2017, the WHO Resolution urges Member States to align NAP on AMR with GAP-AMR

AMR Global Action Plan (GAP)

- Adopted by World Health Assembly in May 2015
- Technical blueprint on what to do
  - Consolidates global scientific consensus & draws upon countries, FAO, OIE, civil society & others
- Reflects stepwise approach recognizing countries have different starting points, priorities

The goal of the plan is to ensure continuity of successful treatment and prevention of infectious diseases with effective and safe medicines that are quality assured, used in responsible way and accessible to all who need them-

1. Background and Objectives

NAP-AMR

- The Core Working Group notified by MoHFW drafted "National Action Plan on AMR" (NAP-AMR)
- The Strategic Objective of NAP-AMR are aligned with the GAP based on National needs & priorities
- In addition to the 5 priorities of GAP- AMR
- India has a **India specific sixth priority** including International, National and Sub-national Collaboration on AMR.

1. Background and Objectives

National Action Plan on AMR (NAP-AMR)

- Developed by Ministry of Health and Family Welfare which needs to be launched across the country so as to bring about an alignment with the Global Action Plan on AMR with a "One Health" approach.
- The NAP-AMR Strategic intervention activity (1.2.1.1; 1.2.1.4 & 4.6.1.1) under NMC, can be accessed at http://www.ncdc.gov.in/writeReadData/linkimages/AMR/File545.pdf
- NAP-AMR released in April 2017;

Cover all five objectives as listed in GAP-AMR and adds an additional objective related to strengthening India's Leadership on AMR

1. Background and Objectives

Alignment of NAP-AMR and GAP-AMR

National action Plan on AMR (NAP-AMR): 6 strategic priorities

The 5 objectives outlined in the GAP-AMR, along with India specific one additional objective

1. Background and Objectives

Strategy 1. Improve awareness and understanding of AMR through effective communication, education and training

Objective 1.2 Improve knowledge and capacity of key stakeholders regarding AMR and related topics.

Strategic intervention and activity

1.2.1 Strengthen and consolidate AMR and related topics as core components of professional education and training.

- **1.2.1.1. Review and revise curricula of professionals in human health**
- **1.2.1.4. Review and develop curriculum and resources for in-service training of different professionals and allied services**

- **Develop a module on AMR to bring together the segmented knowledge being imparted under different subjects (Microbiology, Pharmacology, Medicine, PSM, etc.)**

Key outputs

- Professional curricula revised
- Training module developed on AMR (of in-service and pre-service trainings)

1. Background and Objectives

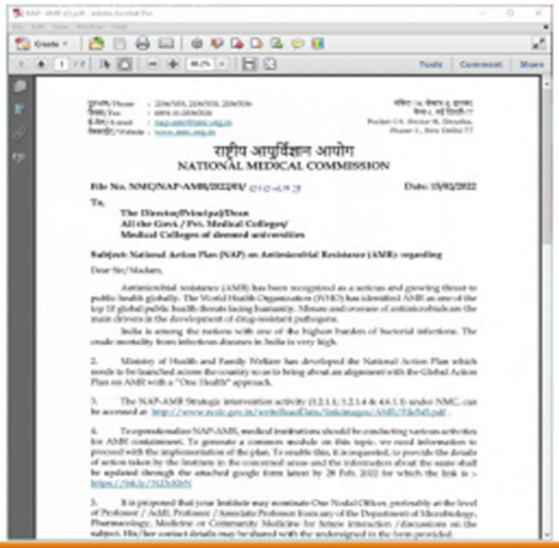
Strategy 4. Optimize the use of antimicrobial agents in health, animals and food.

Objective 4.6 Improve knowledge and skills of prescribers, dispensers and medical trainees.

Strategic intervention and activity-

- 4.6.1. Develop structured (and mandatory) training programmes on optimal antimicrobial use
- 4.6.1.1. Collaborate with regulatory bodies to mandate periodic training to optimise antibiotic use through pre-service and in-service trainings.

1. Background and Objectives

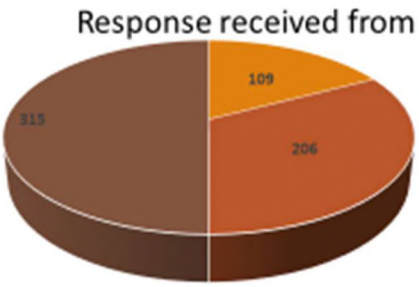


राष्ट्रीय आयुर्विज्ञान आयोग
NATIONAL MEDICAL COMMISSION

Circulated to all Medical colleges & INIs on 15.02.2022 to-

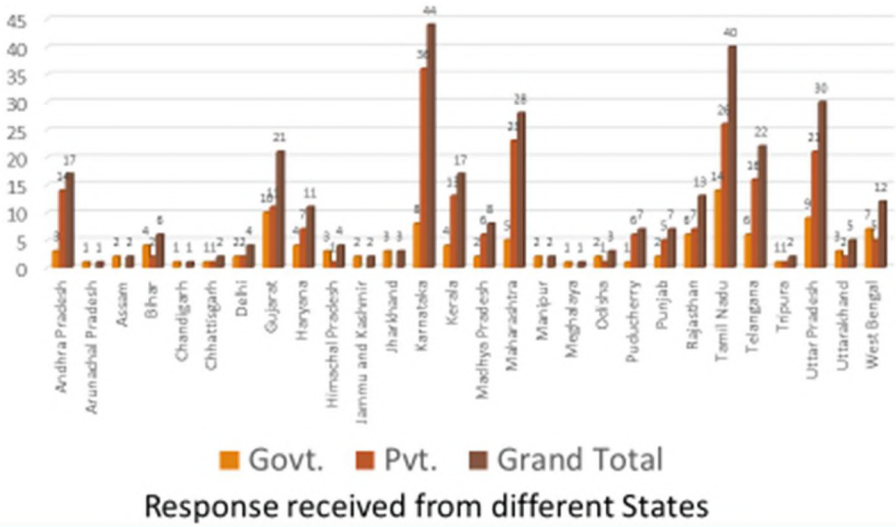
- Collect base line ongoing AMR activities in Medical Colleges & INIs
- Nomination of the Nodal officer from Microbiology/ Pharmacology/ Medicine/ Community Medicine of each Medical Colleges & INIs

1. Background and Objectives



- Circular sent to 606 Medical Colleges
- More than 350 responses received
  - 127 Government Medical Colleges
  - 223 Private Medical Colleges

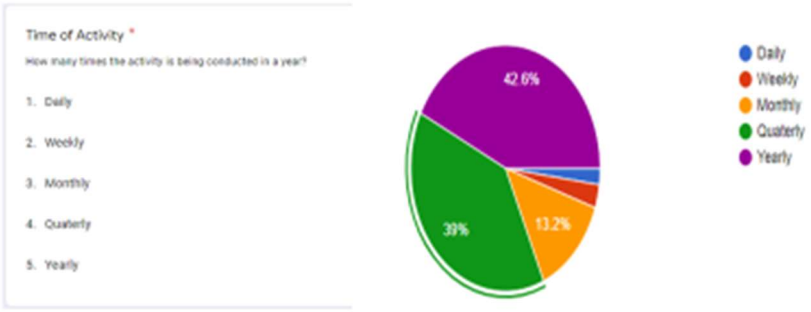
1. Background and Objectives



Response received from different States

1. Background and Objectives

Objective 1. To Improve awareness and understanding of AMR among Undergraduate, Postgraduate students, and Teaching professionals

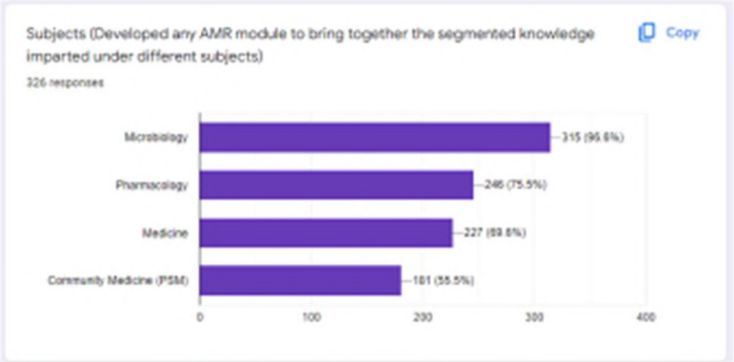


1. Background and Objectives

2. To Improve awareness and understanding of AMR among Allied Health professionals

1. Background and Objectives

3. Developed any AMR module to bring together the segmented knowledge imparted under different subjects



1. Background and Objectives

THANK YOU

1. Background and Objectives

2 Clinical Approach to prescribing antimicrobials

NMC NAP-AMR Module for Prescribers

Learning Objectives

At the end of the session, a prescriber should be able to:

- Identify common presentations of infective syndrome
- Know the importance of taking thorough history, clinical examinations and selection of appropriate investigations for diagnosis of infective disease.

2. Clinical Approach to prescribing antimicrobials

Introduction

The Miracle Maker Sir Alexander Fleming

- Discovered Penicillin in 1928 and Predicted Antimicrobial Resistance.
- The greatest possibility of evil in self-medication is the use of too small doses so that instead of clearing up infection, the microbes are educated to resist penicillin and a host of penicillin-fast organisms is bread out which can be passed to other individuals and from them too other until they reach someone who gets a septicemia or a pneumonia which penicillin cannot save.

Sir Alexander Flemming

2. Clinical Approach to prescribing antimicrobials

Introduction cont...

Decision to Start Antimicrobials is like using "Your most powerful weapon"

✓ Identification of the clinical problem

✓Symptoms and signs and the common patterns of presentation of different diseases. (**Syndromic approach**) (URI, LRTI, UTI, Meningitis, Diarrhoea, Skin and Soft tissue infections etc.

✓Making a differential diagnosis at the bed side

✓Use rapid diagnostic tests

✓Wrong diagnosis/wrong antimicrobial will increase AMR

2. Clinical Approach to prescribing antimicrobials

Introduction cont....

Decision to Start Antimicrobials .....

- ✓ Too small doses can increase AMR
- ✓ Once Antimicrobial started, its immediate withdrawal will increase AMR
- ✓ Clinicians should be aware of side effects and drug interactions
- ✓ Use of broad spectrum antibiotics like fluoroquinolones can cause collateral damage and can impact future treatment options
- ✓ Unnecessary use of fluoroquinolones may be the reason for increased number of pre-XDR TB in India.

2. Clinical Approach to prescribing antimicrobials

Localization of fever

LOCALIZATION	NO LOCALIZATION
• Acute rheumatic fever	• Infective endocarditis
• Hepatitis	• Tuberculosis
• Meningitis	• Enteric fever
• H1N1	• Brucellosis
• Pneumonia	• Malaria
• Urinary tract infection	• Dengue
• Infective endocarditis	• Scrub typhus
• Tuberculosis	• Leptospirosis

2. Clinical Approach to prescribing antimicrobials

It is important to identify *Organ involved and Organism responsible* to treat with appropriate antibiotic for right duration

ORGAN OR SITE OF INFECTION	ORGANISMS CAUSING PNEUMONIA
• **Upper Respiratory Tract Infections:** ➢ Strep throat: full 10 day oral therapy ➢ Rhino viral: none ➢ H1N1: Antiviral • **Meningitis:** 14 day therapy • **Infective Endocarditis:** 6-8 weeks therapy • **Community Acquired Pneumonia:** 2 weeks therapy	• M. tuberculosis: 6 months • Nocardia: 12 months • Melioidosis: 6 months

2. Clinical Approach to prescribing antimicrobials

Empirical use of Antimicrobials may be needed in the presence of Red Flag Signs

- Sepsis/ Septicaemic shock
- Organ dysfunction
- Altered mental state
- Pregnancy
- Immunocompromised
  - ➢ Neutropenic
  - ➢ On steroids
  - ➢ Diabetes
  - ➢ Connective tissue disease
  - ➢ CRF and CLD

2. Clinical Approach to prescribing antimicrobials

History and host factors

- Past hospital admissions
- Comorbidities -DM
- COPD, Tuberculosis, compliance to ATT
- Bronchial asthma
- Drug abuse
- Recent travel
- Blood transfusions
- Recurrent infections
- Surgical interventions
- Immunocompromised state
- Pregnancy
- Extremes of age
- Cancer
- Occupation
- Exposure to pets
- Look at old records

2. Clinical Approach to prescribing antimicrobials

Physical examination and signs of organ dysfunction

An important part of the evaluation of a patient with fever is to arrive at a diagnosis:

- An eschar on general physical examination pinpoints the diagnosis of scrub typhus
- Maculopapular rash can be part of dengue fever
- A murmur on CVS examination can point towards an infective endocarditis
  - Tachycardia
  - Tachypnea
  - Raised JVP
  - Percent Saturation
  - Hypotension
  - Altered sensorium
  - Anuria

Discourage antibiotic prescription over telephone as we can miss vital information

2. Clinical Approach to prescribing antimicrobials

Assessment

- Organ system involvement
- Organism
- Host factors (DM, steroids, immunosuppression, splenectomy, special situations)
- Clinically patient stable or not
- General physical examination- pallor, cyanosis, clubbing, lymph nodes, rash, jaundice, pedal edema, koilonychia, rash, eschar
- Diagnosis at initial evaluation
- Differential diagnosis

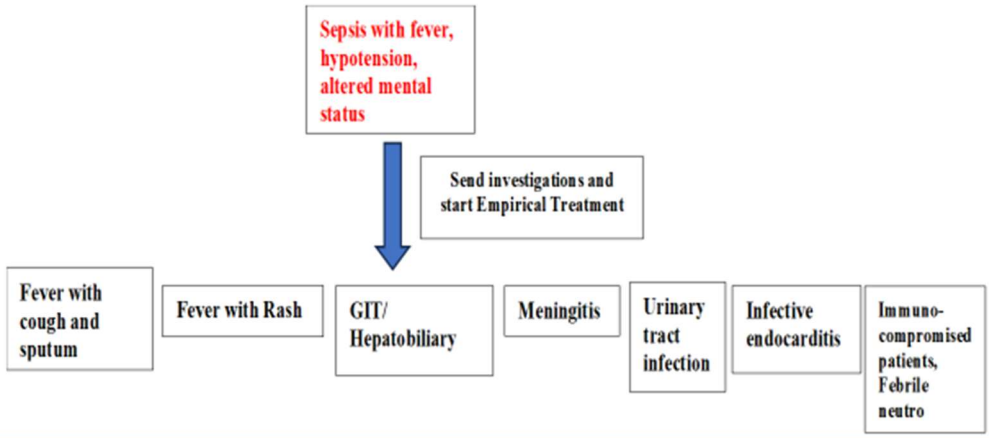
2. Clinical Approach to prescribing antimicrobials

The communication between the clinicians and laboratory is vital.

- ✓ Clinicians should be aware of rapid diagnostic tests and use them appropriately.
- ✓ Blood cultures should be sent before starting IV antibiotics.
- ✓ The positive diagnostic tests and culture reports must be conveyed by phone to clinicians so that the therapeutic interventions can be made in desired time frame.
- ✓ The decision of starting antibiotics empirically should be governed by the local epidemiology and hospital antibiograms.

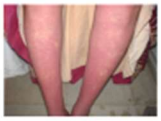
2. Clinical Approach to prescribing antimicrobials

Syndromic Approach to Acute Febrile Illness



2. Clinical Approach to prescribing antimicrobials

i) Fever with rash



Rash of dengue: islands of white in a sea of red

Infectious Causes:

- Dengue Fever: Common viral infection characterized by sudden onset high grade fever, headache, backache, joint pain, muscle pain and rash. We need to establish diagnosis early and avoid antibiotics.
- Chickungunya fever: fever, severe arthralgias and myalgias and rash
- Chickenpox (Varicella): Fever, malaise and a rash that starts as red spots and progresses to vesicles. This is mostly a clinical diagnosis, early antivirals can reduce morbidity.
- Measles and Rubella are not common as they are prevented effectively by vaccines in childhood.

2. Clinical Approach to prescribing antimicrobials

Fever with Rash

Infectious Causes cont….

- **Rickettsial Diseases:**
  Various infections such as Scrub Typhus and Q fever can present with fever and rash.
- **Bacterial Infections**:
  - Meningococcemia: Infection with N. meningitidis can cause fever, headache, and a petechial rash.
  - Lyme Disease: Caused by B. burgdorferi transmitted by ticks, it presents with fever, headache, and a characteristic bull's eye rash (erythema migrans).
  - Toxic Shock Syndrome: Associated with certain bacterial infections or tampon use, it presents with fever, rash, and other systemic symptoms.

Non-Infectious Causes:

- Drug Reactions: Stevens-Johnson syndrome or Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS).
- Autoimmune Diseases: Conditions like lupus erythematosus or Kawasaki disease

2. Clinical Approach to prescribing antimicrobials

Case 1

A 35yr, male TV cable operator from a village in Telangana

History

- Fever
  -2wks, high grade, associated with chills and rigors, intermittent.
- H/o cough with no expectoration.
- No h/o chest pain, or shortness of breath.
- No h/o rash, vomiting or pain abdomen, dysuria.
- No h/o seizures, loss of consciousness.
- Not a diabetic or hypertensive.

Examination

- Well built and well nourished
- Faint maculopapular rash was noted on trunk
- No pallor, cyanosis, clubbing, lymphadenopathy
- Vitals stable, febrile, mild confusion
- Systemic examination normal

2. Clinical Approach to prescribing antimicrobials

Management

- Haemogram showed mild thrombocytopenia
- Urine examination was normal
- Serum creatinine 1.2mg/dl
- RBS 109mg/dl
- Chest radiograph Normal
- ECG Normal
- MP and PF were negative
- Dengue NS1 Ag and Ab negative

DD
Dengue fever
Leptospirosis
Pneumonia with sepsis

- Started on IV antibiotics Inj Ceftriaxone 1 gram IV BD
- Paracetamol
- Rabeprazole

However

- Delirious, sick looking, hypotension,
- Respiratory system
  -Tachypnea
  -Revealed bilateral crepitations more on right side.
- Spo_2 on room air-89%
- No focal neurologic deficits noted.
- Developed hematuria and malena.

2. Clinical Approach to prescribing antimicrobials

Laboratory Investigations

- RBS 122mg/dl
- Serum Creatinine 1.5 mg/dl
- SGOT 363 IU/dl
- SGPT 278 IU/dl
- ALP 345 IU/dl
- Total bilirubin - 2.2
  –Conjugated bilirubin 1.2
- S protein 5.5 g/dl, S Alb 2.9
- TT 9 sec
- Fibrinogen 241 mg/dl
- D dimer 10.79
- PT 14 sec
- APTT 31
- Platelets 20,000

- Pf HRP2 -negative
- NS1 antigen was negative
- Dengue serology was done thrice-negative
- Blood culture –sterile
- Urine culture sterile
- Serology for Brucella abortus and melitensis- negative
- Leptospira serology - negative
- ASO titre <200
- Urine culture -no growth
- Second set of blood culture negative
- IgM RF 55(normal <40)
- ANA- negative

2. Clinical Approach to prescribing antimicrobials

Final Diagnosis

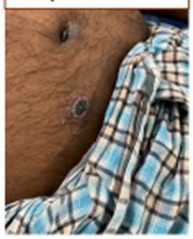
- Hepatitis
- Thrombocytopenia-bleeding manifestations
- Delirium
- Pneumonia
- Renal failure

Final clue

- Weil felix
  - OX K- 1:320
  - OX 2- 1:80
  - Ig M scrub

Final Diagnosis: Scrub typhus
Doxycycline 100mg twice daily for 7 to 15days

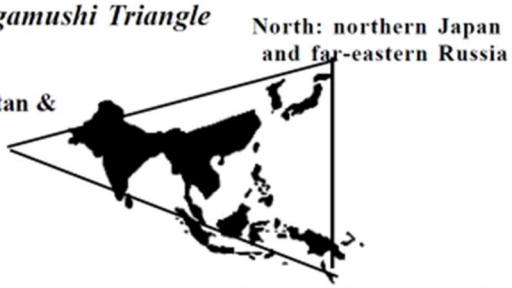
Eschar in a case of pneumonia



2. Clinical Approach to prescribing antimicrobials

Geographic Distribution

Fig 1. Tsutsugamushi Triangle

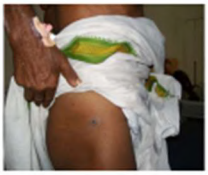


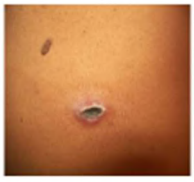
An estimated one billion people are at risk for scrub typhus and one million cases occur annually

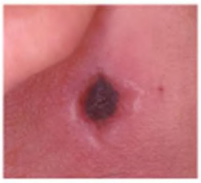
2. Clinical Approach to prescribing antimicrobials

Eschar from the bite of a Leptotrombidium mite.

Eschar in Scrub typhus







(b) High-power photomicrograph (original magnification, ×400; hematoxylin-eosin stain) shows dermal vasculitis with perivascular infiltrates that consist mostly of lymphocytes and macrophages.

Eschar from the bite of a Leptotrombidium mite.
(a) Photograph shows an epidermal ulcer covered by a black crust surrounded by an erythematous halo.

Jeong Y J et al. Radiographics 2007;27:161-172

2. Clinical Approach to prescribing antimicrobials

ii) Fever with Jaundice

- ✓ **Viral Hepatitis**: Hepatitis A, B, C and E viruses
- ✓ **Malaria**
- ✓ **Leptospirosis**
- ✓ **Typhoid Fever**
- ✓ **Scrub typhus**
- ✓ **Acute Biliary Tract Infections**
- ✓ **Every patient of jaundice do not require antimicrobials.**
- ✓ Their **blood sample should be sent to laboratory** for identifying hepatotropic virus.
- ✓ Conditions like **leptospirosis and acute biliary tract infections** are emergencies and should be treated with appropriate antibiotics.

2. Clinical Approach to prescribing antimicrobials

Liver Abscess

The most frequent **symptoms** of hepatic abscess include the following:

- Fever (either continuous or spiking), Chills, Right upper quadrant pain
- Anorexia, Malaise, Cough or hiccoughs due to diaphragmatic irritation.
- Referred pain to the right shoulder

- Individuals with solitary lesions usually have a more insidious course with
  - weight loss
  - anemia of chronic disease.
- With such symptoms, malignancy often is the initial consideration.

- Fever of unknown origin *(FUO)* frequently can be an initial diagnosis in indolent cases.

2. Clinical Approach to prescribing antimicrobials

Liver Abscess cont....

Clinical signs:

- Fever and tender hepatomegaly -most common.
- Mid epigastric tenderness, with or without a palpable mass, is suggestive of left hepatic lobe involvement.
- Decreased breath sounds in the right basilar lung zones, with signs of atelectasis and effusion on examination or radiologically, may be present.
- **pleural or hepatic friction rub** due to diaphragmatic irritation and inflammation of Glisson's capsule.
- **Jaundice** may be present in as many as 25% of cases and usually is associated with biliary tract disease or the presence of multiple abscesses

2. Clinical Approach to prescribing antimicrobials

Liver Abscess cont...

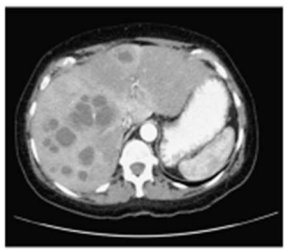
Investigations:

- Random blood sugar, CBC
- LFT
  - Elevation of alkaline phosphatase (most common liver function abnormality)
  - Hypoalbuminemia
- Elevations of transaminase and bilirubin level
- CT and ultrasound – modalities of choice and help distinguish from tumors, hemangiomas and cysts.
- CT or ultrasound-*guided aspiration* should be sent for *gram stain and culture*.
- Pyogenic abscesses are more common than amebic liver abscess
- Common organisms causing liver abscesses are E.coli, Klebsiella, pseudomonas, proteus, streptococcus, enterococci and staphylococci.
- Send blood cultures as they are positive in roughly 50% of cases
- Isolation of unusual organisms *like Burkholderia Pseudomallei* needs a prolonged treatment.

2. Clinical Approach to prescribing antimicrobials

Liver Abscess cont...

- Hepatic abscesses are usually hypodense on a CT scan and may display a rim of contrast enhancement in less than 20% of cases.
- **Percutaneous needle aspiration** Under CT scan or ultrasound guidance, needle aspiration of cavity material can be performed. Diagnostic + therapeutic.
- **Percutaneous drainage** has become the *standard* of care and should be the first intervention considered for small cysts (Seldinger or trochar technique).
- Pus should be sent for culture and sensitivity and started on antibiotics



CT abdomen showing pyogenic abscess

2. Clinical Approach to prescribing antimicrobials

Malaria

CLINICAL FEATURES

- Fever with chills and Rigors associated with headache occasionally altered sensorium
- Examination: Pallor, icterus, enlarged liver or spleen
- Labs: anemia, leucopenia and thrombocytopenia
  - **Rapid diagnostic tests:** HRP2, LDH and aldolase are produced by parasite from ring to trophozoite stage.
  - **pLDH pan detects all species**
    Rapid test for Plasmodium vivax-(pLDH)
    Sensitivity-77%, Specificity-98%
  - **Rapid test** for plasmodium falciparum-based on histidine-rich protein 2 (HRP2)- high positive predictive and negative predictive values.
    Sensitivity-98%, Specificity-88%

COMPLICATIONS

- **Cerebral malaria, DIC, ATN, ARDS and Severe hemolysis.**
- Jaundice 2.5% in severe malaria with falciparum infection but hepatitis is unusual.
- Micro occlusion of portal venous branches by parasitized red blood cells, Intrahepatic cholestasis due to reticuloendothelial blockage hepatic microvillus dysfunction
- Elevated serum bilirubin (conjugated fraction which is dominant in patients with hepatopathy)

2. Clinical Approach to prescribing antimicrobials

Management

Empiric management is some times inevitable but should not be routine

- Chloroquine combined with primaquine is the treatment of choice for chloroquine-sensitive infections.
- Uncomplicated PF Malaria-artemether plus lumefantrine, Artesunate plus amodiaquine, artesunate plus mefloquine, and artesunate plus sulfadoxine-pyrimethamine.
- Artesunate plus tetracycline or doxycycline or clindamycin; any of these combinations to be given for 7 days
- Quinine plus tetracycline or doxycycline or clindamycin; any of these combinations should be given for 7 days.
- Artemisinin and its derivatives should not be used as monotherapy.

2. Clinical Approach to prescribing antimicrobials

Enteric Fever

- Systemic infection with the *Salmonella typhi* or *S. paratyphi*.
- Transmission via food or beverages handled by an individual who chronically sheds the bacteria through stool or less commonly, urine.
- Hand-to-mouth transmission after neglecting hand hygiene.
- Oral transmission via sewage-contaminated water or eating shellfish.
- Incubation period 7-14days (3-21 days).
- The most prominent symptom is prolonged fever (101.8°–104.9°F), which can continue for up to 4 weeks if untreated.
- Many a times no specific localization of fever, sometimes associated with gastrointestinal manifestations in the form of loose motions, constipation, anorexia, nausea and abdominal pain.
- Other symptoms include headache, chills, cough, sweating, rarely arthralgia.

2. Clinical Approach to prescribing antimicrobials

Enteric Fever cont.....

PHYSICAL FINDINGS

- Mild pallor, Splenomegaly, Abdominal tenderness
- At approximately the end of the first week of illness, the fever plateaus at 103-104°F (39-40°C).
- The patient develops rose spots, which are salmon-colored, blanching, truncal, maculopapular usually 1-4 cm wide, generally resolve within 2-5 days.
- During the second week of illness, the signs and symptoms progress.
- Relative bradycardia and rarely infective endocarditis
- Gastrointestinal bleeding and intestinal perforation most commonly occur in the third and fourth weeks of illness.
- Neurologic manifestations- meningitis, Guillain-Barré syndrome and neuropsychiatric symptoms.

COMPLICATIONS

- Disseminated intravascular coagulation
- Hematophagocytic syndrome
- Hepatic and splenic abscesses and granulomas
- Endocarditis, pericarditis, myocarditis
- Hepatitis
- Glomerulonephritis
- Pyelonephritis
- Severe pneumonia
- Severe sepsis and death

2. Clinical Approach to prescribing antimicrobials

Diagnosis & Treatment

Culture:

- Blood culture is the preferred method of diagnosis. A single culture is positive in only ≈50% of cases, however multiple blood cultures increase the sensitivity
- Bone marrow culture is more invasive (and therefore less commonly performed), it increases the sensitivity to ≈80% of cases and is relatively unaffected by previous or concurrent antibiotic use.
- Stool culture is not usually positive during the first week of illness and has less diagnostic sensitivity than blood culture.
- Urine culture has a lower diagnostic yield than stool culture.

2. Clinical Approach to prescribing antimicrobials

Diagnosis & Treatment cont...

- **Rapid diagnostic tests:** available for typhoid fever, but their sensitivity and specificity are not optimal.
- The Widal test measures elevated antibody titers; it is unreliable but widely used because of its low cost.
- Serologic tests do not distinguish acute from past infection or vaccination and lack specificity; thus, blood culture remains the preferred method to diagnose acute infections.

Treatment:

- Includes Intravenous ceftriaxone 1 gram IV twice a day for 14 days or switch to oral medicines as per susceptibility reports.
- All strains that have intermediate susceptibility to fluoroquinolones on disk testing (as defined by national guidelines) should be considered fluoroquinolone-resistant.

2. Clinical Approach to prescribing antimicrobials

iii) Fever with Neurologic Manifestations

- **Meningitis**:
  Triad of Fever, severe headache, neck stiffness, altered mental status, photophobia, seizures, abnormal movements, weakness of limbs, behavioural changes, nausea, vomiting -Raised ICT causes altered sensorium
- Etiology: bacterial- S.pneumoniae, N.meningitidis, Gr B streptococci, Listeria spp and H. influenzae.
- Viral, Rickettsial, fungal infections, Tubercular (TBM can have acute presentation)
- Medical emergency-Ct brain and MRI
- Diagnosis by CSF examination
  - PMN >100 cells/µl
  - Decreased glucose
  - Increased protein
  - Increased opening pressure
  - Grams stain and CS

2. Clinical Approach to prescribing antimicrobials

Fever with Neurologic Manifestations cont...

- **Encephalitis**: Inflammation of the brain: Bacterial, Rickettsial infections like scrub typhus, Diphtheria, viral infections such as Herpes simplex virus, Japanese Encephalitis virus rarely rabies

- **Cerebral Malaria**: a severe form of malaria
  P. falciparum can be diagnosed early by rapid diagnostic tests, malarial parasite in the blood smear and initiate of antimalarials appropriately

2. Clinical Approach to prescribing antimicrobials

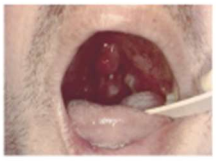
iv) Fever with Respiratory Symptoms

- Common respiratory symptoms include: Fever, throat pain, cough, running nose, sputum, breathlessness, haemoptysis, chest pain.
- Associated symptoms like wheezing, fatigue may be present
- Common aetiologies - influenza, RSV, Rhino, adeno or COVID 19.

Most of the respiratory illnesses do not require antimicrobials.

However respiratory viral infections can cause lower respiratory infections

- Diagnosis by nasal swab for RTPCR
- Treatment : Oseltamivir for Influenza,
- Specific antivirals for COVID 19
- Streptococcal pharyngitis needs antibiotics
- Throat swab for aerobic culture can identify organism



2. Clinical Approach to prescribing antimicrobials

Categorization of Pneumonia by Clinical Setting

Community-acquired pneumonia	Typical (i.e. classic) pneumonia	Nosocomial pneumonia	Hospital-acquired pneumonia
	Atypical pneumonia		Ventilator-associated pneumonia (VAP)
	Aspiration pneumonia		Healthcare-associated pneumonia (HCAP)
Pneumonia in the elderly	Community acquired pneumonia	Cystic fibrosis and anatomic disorders	Bronchopulmonary sequestration, tracheomalacia, or bronchomalacia
	Nursing home residents		

2. Clinical Approach to prescribing antimicrobials

Categorization of pneumonia by causative agents

Typical pneumonia	Atypical pneumonia
Streptococcus pneumonia (M/C)	Legionella spp
Haemophilus influenza	Mycoplasma pneumoniae
Moraxella catrrhalis	Chlamydia pneumoniae
Staphylococcus aureus	Chlamydia psittaci
Aerobic gram negative bacteria (E.coli, Klebsiella…)	Coxiella burnetii
Micro-aerophillic bacteria and anaerobes	Respiratory viruses- influenza-A,B; parainfluenza virus, SARS-CoV2, Rhinovirus, Adenovirus, Respirator syncytial virus, Human metapneumo/boca virus

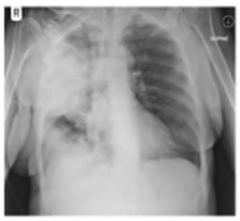
2. Clinical Approach to prescribing antimicrobials

Clinical & Investigational findings of Typical vs Atypical Pneumonia

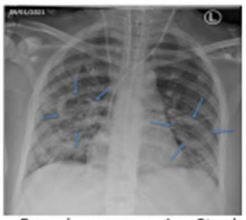
Pneumonia	Atypical	Typical
Clinical course	Subacute onset Protracted disease	Abrupt onset
Symptoms	Extrapulmonary and pulmonary (flu-like illness, myalgias, rhinorrhea, odynophagia, diarrhea, prominent headache) Dry cough; scant sputum	Confined to the lung, Pleuritic chest pain Productive cough with colored sputum
Leucocytosis	Absent	Present
Gram stain, blood and sputum cultures	No evidence of a pathogen	*S. pneumoniae (or K. pneumoniae, S. aureus…)*
Chest X-ray	Patchy, ill-defined infiltrates, scattered on both lungs	Lobar pneumonia, pleural effusion
Prognosis	Often favorable, even without antibiotics	Significant mortality despite penicillin

2. Clinical Approach to prescribing antimicrobials

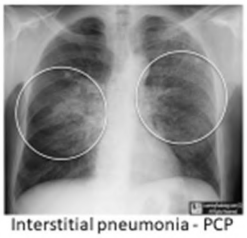
Chest x-ray findings



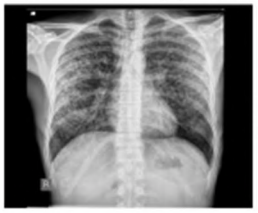
Lobar pneumonia –Strep pneumoniae



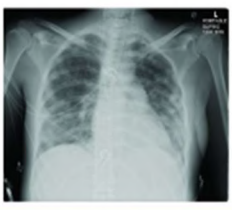
Bronchopneumonia – Staph. Aureus



Interstitial pneumonia - PCP



Miliary pneumonia - TB



Nodular infiltrates–
Round pneumonia–
Septic emboli

2. Clinical Approach to prescribing antimicrobials

Community Acquired Pneumonia -OPD based treatment

STATUS	STANDARD REGIMEN
No co-morbidities or risk factors for antibiotic resistance[a]	Combination therapy with **amoxicillin (1 g tid) +** either a macrolide[b] or doxycycline (100 mg bid) *Or*
	Monotherapy with doxycycline (100 mg bid) *Or*
	Monotherapy with a macrolide[b,c]
With comorbidities[d] ± risk factors for antibiotic resistance[a]	Combination therapy with
	Amoxicillin/clavulanate[e] or a cephalosporin[f] + either a macrolide[b] or doxycycline (100 mg bid)
	Or
	Monotherapy with a respiratory fluoroquinoloe[g]

[a]Antibiotic treatment within the past 3 months or contact with the health care system. [b]**Azithromycin (500 mg on day 1, then 250 mg/d for 4 days)**, clarithromycin (500 mg bid), or clarithromycin ER (1000 mg/d). [c]If local prevalence of pneumococcal resistance is <25%. [d]Including chronic heart, lung, liver, or kidney disease; diabetes mellitus; alcoholism; malignancy; or asplenia. [e]500/125 mg tid or 875/125 mg bid. [f]Cefpodoxime (200 mg bid) or cefuroxime (500 mg bid). [g]Levofloxacin (750 mg/d), moxifloxacin (400 mg/d), or Gemifloxacin (320 mg/d).

Community Acquired Pneumonia –Inpatient treatment

DISEASE SEVERITY, RISK STATUS	REGIMEN
Non- severe	
No risk factors	A β-lactam[a] + a macrolide[b] *or* A respiratory fluoroquinolone[c]
Prior respiratory isolation	Add coverage for MRSA[d] or Pseudomonas aeruginosa[e]
Recent hospitalization, antibiotic treatment, ± LV[f]	Add coverage for MRSA[d] or P. aeruginosa[e] only if cultures are positive
Severe	
No risk factors	A β-lactam[a] + a macrolide[b] *or* A β-lactam[a] + respiratory fluoroquinolone[c]
Prior respiratory isolation	Add coverage for MRSA[d] or P. aeruginosa[e]
Recent hospitalization, antibiotic treatment ± LV[f]	Add coverage for MRSA[d] or P. aeruginosa[e]

[a]Ampicillin-sulbactam (1.5-3 g q6h). [b]Azithromycin (500 mg/d) or clarithromycin (500 mg bid). [c]Levofloxacin (750 mg/d), moxifloxacin (400 mg/d), or Gemifloxacin (320 mg/d). [d]Vancomycin (15 mg/kg q12h, with adjustment based on serum levels) or linezolid (600 mg q12h). [e]Piperacillin-tazobactam (4.5 g q6h), cefepime (2 g q8h), ceftazidime (2 g q8h), imipenem (500 mg q6h), meropenem (1 g q8h), or aztreonam (2 g q8h). [f]Obtain cultures. MRSA rapid nasal PCR can also be used if available.
Abbreviations: LV, local validation (local prevalence, resistance, risk factors); MRSA. Methicillin-resistant Staphylococcus aureus.

v) Fever with GI symptoms: Acute Gastroenteritis

- History of recent travel.
- Recent consumption of potentially unsafe food.
- Recent antibiotic exposure (risk of C. difficile).
- Immunosuppression.
- Organisms (bacterial, parasitic or viral)
- Investigations: Stool culture, Stool microscopy (for parasites), Vibrio cholerae antigen (e.g. in outbreaks), Test for C. difficile (if recent antibiotic exposure)
- Treatment: Rehydration and electrolyte replacement is the main treatment for acute infectious diarrhea.
- Antibiotics are needed only if host is immunocompromised or there is blood in stool due to shigella or amoebic dysentery.

vi) Fever with Urinary Symptoms

- Uncomplicated UTI:
- **Cystitis:** Frequency of micturition, urgency, dysuria, haematuria and suprapubic discomfort.
  - Morning mid-stream urine sample should be collected and sent for microscopic and culture examination.
  - Antimicrobials may be initiated empirically in situations like pregnancy, diabetes and other immunocompromised conditions to be modified as per available reports.
  - Nitrofurantoin and Fosfomycin, TMP-SMX and quinolones.
- **Pyelonephritis**: Fever, flank pain, urinary symptoms, sometimes altered sensorium. Antibiotics have to be started in suspected cases after sending complete urine examination, urine culture and blood cultures.

2. Clinical Approach to prescribing antimicrobials

Fever with Urinary Symptoms cont....

- Organisms: E coli, Klebsiella, Proteus, Staphylococci and Enterococcus.
- Pyelonephritis can cause **Acute kidney injury (AKI) and sepsis.**
- Treatment: IV antibiotics-IV ceftriaxone, Piperacillin and tazobactam, Carbapenem.

AKI can be **caused by other Infectious agents**: Leptospirosis, Scrub typhus, Complicated malaria and gram negative bacterial infections.

- Autoimmune diseases like SLE affect kidney causing chronic kidney disease need to be differentiated.
- Clinicians should be aware of increasing number of ESBL producing organisms
- Avoid using quinolones like Levofloxacin and Moxifloxacin in our country.

2. Clinical Approach to prescribing antimicrobials

Acute febrile illness with CVS involvement

- Myocarditis,
- infective endocarditis,
- pericarditis,
- Kawasaki disease,
- viral haemorrhagic fevers- such as dengue fever, yellow fever, Ebola fever present with cardiovascular involvement including vascular leakage, haemorrhage and shock.

2. Clinical Approach to prescribing antimicrobials

Steps of antimicrobial prescription

- **Step 1:** Making a clinical diagnosis based on accurate history and clinical examination helps in selecting the right test for the right patient.
- A clinical diagnosis also helps in predicting most likely organism causing a clinical syndrome. The sample must be collected before the start of antimicrobials.
- **Step 2:** The empiric antibiotic therapy must be limited to seriously ill patients. This choice should be based upon institutional/local antibiograms.
- **Step 3:** Choose the appropriate antibiotic based on clinical evaluation and most likely pathogen keeping antibiogram in mind.

2. Clinical Approach to prescribing antimicrobials

THANK YOU

2. Clinical Approach to prescribing antimicrobials

3

Microbiological Diagnostic Stewardship

NMC Module on AMR for Prescribers

3. Microbiological Diagnostic Stewardship

Learning Objectives

On completion of this chapter, the prescriber should be able to:

- define diagnostic stewardship
- understand the difference between infection and colonizers
- describe the sample collection techniques, precautions, transport and rejection criteria of common samples.

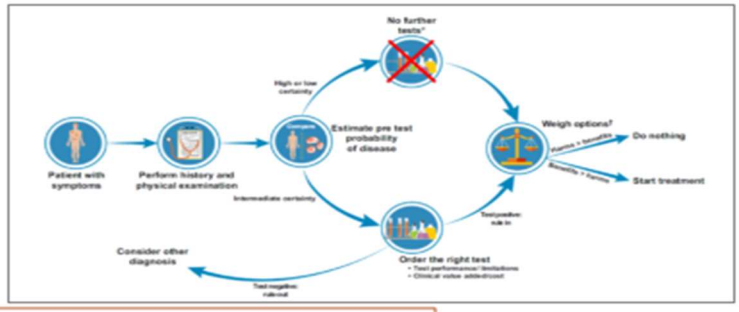
3. Microbiological Diagnostic Stewardship

What is Diagnostic Stewardship?

"Co-ordinated guidance and interventions to improve appropriate use of microbiological diagnostics to guide therapeutic decisions. It should promote appropriate, timely diagnostic testing, including specimen collection, and pathogen identification and accurate, timely reporting of results to guide patient treatment."

Diagnostic stewardship means ordering the right tests for the right patient at the right time to ensure optimal clinical care.

3. Microbiological Diagnostic Stewardship



The 4 Ts of diagnostic stewardship

- Choosing the right **Test** for
- right **Type** of sample,
- collected at the right **Time,** in order
- to guide **Treatment** decisions.

https://doi.org/10.1016/j.jmoldx.2020.06.012

3. Microbiological Diagnostic Stewardship

Specimen collection: key issues

- Consider differential diagnoses.
- Decide on test(s) to be conducted.
- Decide on clinical samples to be collected to conduct these tests
  - consultation between Microbiologist & the Clinicians - a must.

3. Microbiological Diagnostic Stewardship

Correct sample for Correct report

- Appropriate selection of samples
- Proper collection
- Transport
- Turn-around time for laboratory investigations.
- Distinguish between viral and bacterial infection

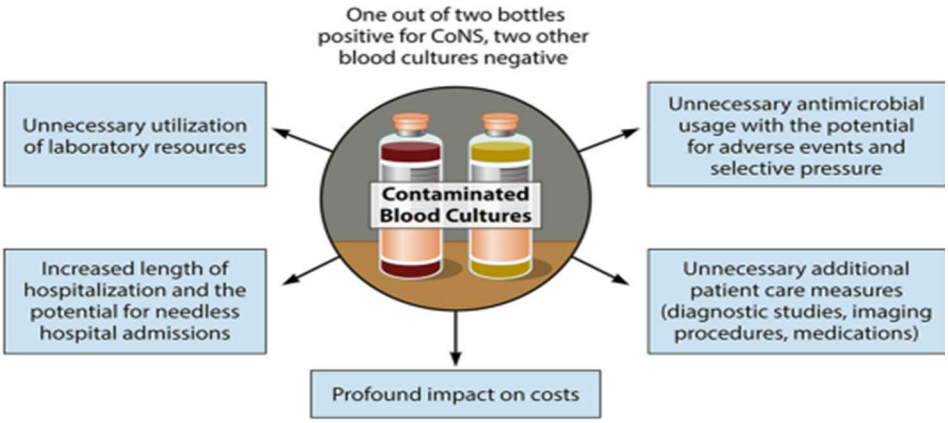
3. Microbiological Diagnostic Stewardship

General precautions while collecting samples

- **Bacterial culture** must be collected prior to antimicrobial therapy.
- Always choose **correct container** as per case definition.
- Collection should be done by **trained staff** after precise instructions to the patient.
- Transported **within 2 hours** after collection, in the correct package.
- Blood and CSF should never be refrigerated.
- All samples must be **accompanied by completely filled request form**.

3. Microbiological Diagnostic Stewardship

Aseptic Precautions



3. Microbiological Diagnostic Stewardship

Infection v. colonization

- Most organisms which colonize are **harmless commensals and should not be treated.**
- An organism isolated from a sample taken from a normally sterile site like the CSF, blood, pleural fluid etc. is likely to be a **true invader and the causative pathogen.**
- An organism isolated from a non-sterile specimen like sputum or a wound swab **may be a colonizer.**
- If the organism is persistently isolated despite 'effective' systemically administered therapy, careful clinical decision must be taken keeping in mind the organism may be a multidrug resistant pathogen or simply a colonizer.

3. Microbiological Diagnostic Stewardship

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3. Microbiological Diagnostic Stewardship

SAMPLE COLLECTION TECHNIQUES

3. Microbiological Diagnostic Stewardship

1. Blood

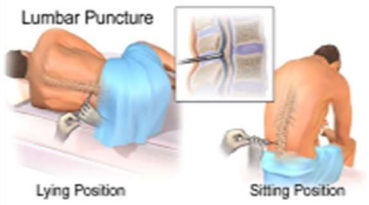
- Preferably collect paired blood samples for culture from two different sites (e.g. right and left ante cubital fossa).
- Dilution ratio: 1 ml of blood to 10 ml of culture media.
  - Wear gloves, thoroughly disinfect the venepuncture site.
  - Cleanse an area about 50 mm in diameter with 70% ethanol and allow it to air-dry.
  - Apply 2% tincture of iodine or chlorhexidine/ alcohol based disinfectant in a circular action, swab the area beginning at the point where the needle will enter the vein.
  - Allow the disinfectant to dry on the skin for at least 1 minute.
  - Wipe the top of the bottle cap using an ethanol swab and allow it to dry before injecting the sample aseptically into the bottle.
  - Inoculated blood culture bottles should be transported to the laboratory immediately or held at room temperature until they reach the laboratory.

3. Microbiological Diagnostic Stewardship

2. Cerebrospinal Fluid

Lumbar puncture

a. Disinfect the puncture site with antiseptic solution and alcohol
b. Insert a needle with stylet at the L3-L4, L4-L5, or L5-S1 interspace.
c. When the subarachnoid space is reached, remove the stylet; spinal fluid will appear in the needle hub.
d. Measure the hydrostatic pressure with a manometer.

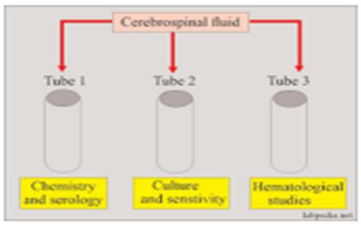


https://smartmedicalbuyer.com/blogs/smb-blog/equipment-used-in-a-lumbar-puncture

3. Microbiological Diagnostic Stewardship

Collection and transport-CSF

- Sequentially collect into three calibrated sterile tubes- routine chemistry (total protein and glucose) (tube no. 1), bacteriology (C&S) (tube no. 2), and haematology (cell count) (tube no. 3)
- Transport
- Never Refrigerate
- If delay; store at room temperature/incubator



https://labpedia.net/cerebrospinal-fluid-analysis-part-2-cerebrospinal-fluid-csf-normal abnormal-interpretations/

3. Microbiological Diagnostic Stewardship

3. Sterile body fluids

- Normally sterile body fluids such as pleural, pericardial, peritoneal, synovial, etc. should be collected with needle and syringe using sterile technique.
- The aspirated material (1-5ml) should be transferred to a sterile screw-capped tube or a paediatric Isolator tube.
- Samples should not be submitted in syringe with a needle attached.
- Swab specimens are inferior and should NEVER be used if fluid specimens can be obtained.

3. Microbiological Diagnostic Stewardship

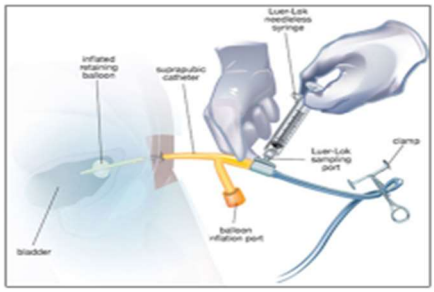
4. Urine: Midstream sample

- Preferably, early morning first midstream urine (2-5ml) in sterile, wide mouth, leak proof container.
- Instructions to patients:
  - **Female**: Wash the hands, cleanse the area around the urethral opening with soap and water,, and collect the midstream urine in a sterile container with the labia held apart.
  - **Male**: Wash the hands, retract the foreskin, cleanse the glans with soap and water, collect midstream urine in the sterile container.
- Transport to the laboratory within 2 hours of collection. Refrigerate if delayed.

3. Microbiological Diagnostic Stewardship

Urine: Catheterized Patient

- Clamp the catheter, clean the catheter wall vigorously with 70% ethanol and aspirate 5 to 10 ml of urine via a sterile needle and syringe above the clamp.
- Never collect urine sample from the urine collection bag or by disconnecting the catheter from the tube of the urine collection bag.



https://lerablog.org/health/services/when-a-suprapubic-catheter-is-necessary/

3. Microbiological Diagnostic Stewardship

Urine: Suprapubic aspiration

- The skin above the bladder is disinfected and a sterile needle and syringe is plunged into the bladder.
- Urine is aspirated and placed in a sterile container.
- It is collected primarily from infants and comatose patients.

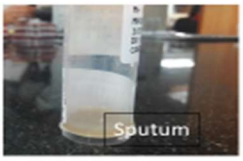
https://basicmedicalkey.com/suprapubic-catheter-insertion-andor-change/

3. Microbiological Diagnostic Stewardship

5. Sputum

- Use a clean, wide-mouthed leak-proof container,
- Collect preferably during early morning after rinsing mouth with water but before brushing, fluid or food intake.
- Instruct patient to cough deeply after taking a deep breath.
- External soiling of container with sample: Clean with phenol-containing disinfectant to wipe the outside of the container.

Specimen must be sputum, not Saliva.



ET tip, suction tip- not recommended

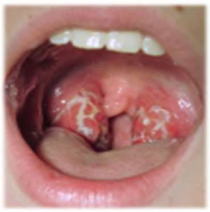
Transport

- Send within 2 hours of collection.
- Refrigerate if delay (except in case if *S. pneumoniae* and/or *H. influenzae* infection suspected).

3. Microbiological Diagnostic Stewardship

Case 1

A 10 year old boy with H/o of sore throat, fever, malaise since 1 day visits a pediatrician accompanied by his parents. O/E cervical lymph nodes are enlarged and tonsils inflamed.



3. Microbiological Diagnostic Stewardship

6. Endotracheal aspirate (ETA)

- Endotracheal aspiration is done with a sterile technique using a 22-inch, 12F suction catheter.
- The catheter is introduced through the endotracheal tube for at least 30 cm. Gentle aspiration is then performed without instilling saline solution.
- The first aspirate is discarded, the second aspirate is collected after tracheal instillation of 5 ml saline in a mucus collection tube.
- If very little secretion is produced by the patient, chest vibration or percussion for 10 min is used to increase the retrieved volume (> 1mL).
- Send the specimen to the laboratory as soon as possible.

3. Microbiological Diagnostic Stewardship

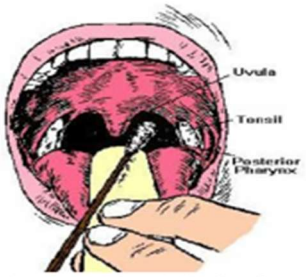
7. Bronchoalveolar lavage (BAL)

- In this procedure 100-300 ml volume of saline is infused to a lung segment through the bronchoscope
- to obtain cells and protein of the pulmonary interstitium and alveolar spaces and a portion of it to be sent to the laboratory as soon as possible.

3. Microbiological Diagnostic Stewardship

8. Throat swab (posterior pharyngeal swab)

- Hold tongue away with tongue depressor
- Locate areas of inflammation and exudate in posterior pharynx, tonsillar region of throat behind uvula.
- Avoid swabbing soft palate; do not touch tongue.
- Rub area back and forth with cotton or Daron swab. Replace it in the tube.

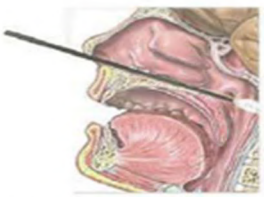


https://idsp.mohfw.gov.in/WriteReadData/l892s/2990029786156525276 9.pdf

3. Microbiological Diagnostic Stewardship

Nasopharyngeal swab

- Tilt head backwards.
- Insert flexible fine-shafted polyester swab into nostril and back to nasopharynx.
- Leave in place for a few seconds.
- Withdraw slowly in a rotating motion and place in the transport medium.

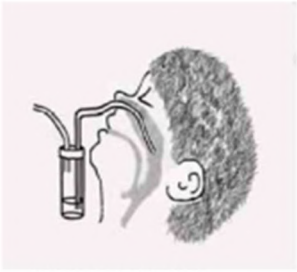


https://idsp.mohfw.gov.in/WriteReadData/l892s/2990029786156525276 9.pdf

3. Microbiological Diagnostic Stewardship

Nasopharyngeal aspirate

- Tilt head slightly backward
- Instill 1-1.5 ml of VTM /sterile normal saline into one nostril
- Use aspiration trap
- Insert silicon catheter in nostril and aspirate the secretion gently by suction in each nostril.
- Transfer in the transport medium.



WHO/CDS/EPR/ARO/2006.

3. Microbiological Diagnostic Stewardship

Triple packaging system for transport

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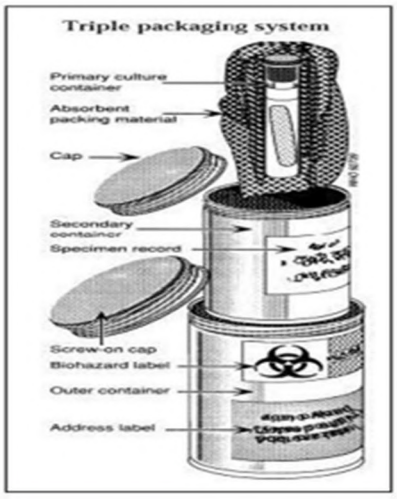


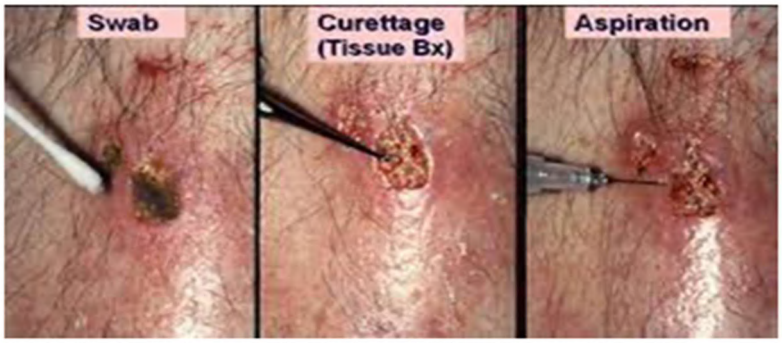
3. Microbiological Diagnostic Stewardship

9. Stool

- Use a clean, wide-mouthed leak-proof container, to collect the stool sample.
- NEVER collect from the bedpan/toilet bowl.
- Collect at least 5 ml of sample in case of liquid stool, approximately 1 g (walnut-sized) sample in case of semi-formed or formed stool.
- Transport immediately for microscopy.

3. Microbiological Diagnostic Stewardship

10. Pus/tissue biopsy



https://www.vicniss.org.au/media/1926/1500-rod-james-skin-and-soft-tissue-swabs-2.pdf

3. Microbiological Diagnostic Stewardship

Pus/tissue biopsy aspirate

Open wounds

- Debride to clear overlying debris with scalpel and swabs or sponges, and thoroughly rinse with sterile saline prior to collection of sample.
- Collect biopsy or curette sample from base or advancing margin of the lesion. The specimen must never be sent in formalin for culture.

Closed wounds

- Disinfect the area as for collection of blood sample collection before aspiration.
- Pus from an abscess is best collected at the time the abscess is incised and drained, or after it has ruptured naturally. At least 1ml of pus should be collected.

Swab is not an appropriate/ preferred sample for culture.

3. Microbiological Diagnostic Stewardship

11. Genital swabs

- Excess mucus is cleaned with cleaning swab and discarded.
- Swab is inserted into the cervical canal and rotated for 15-30 seconds.
- Swab should be Immediately broken off swab into the transport tube.

3. Microbiological Diagnostic Stewardship

Sample rejection criteria

- Samples collected in incorrect containers or in broken, poorly sealed and leaking containers.
- Unlabelled specimens or mismatch between sample requisition form and container.
- Unacceptable delay between specimen collection and arrival at laboratory
- Sample stored incorrectly before or during transport.
- Inadequate quantity of specimen.
- 24 hours urine collection.
- Foley's catheter tips and endotracheal tube tips.
- Urine from the bag of a catheterized patient.

3. Microbiological Diagnostic Stewardship

Follow up cultures

- 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.

3. Microbiological Diagnostic Stewardship

Rapid tests

PCR for respiratory viruses in children with LRTI

- help to monitor response to therapy,
- Guide the duration of antimicrobial therapy.

Inflammatory markers such as **Procalcitonin, C- Reactive Protein** etc.

- Guide prescribers to institute rational therapy especially in sepsis cases.
- Useful to differentiate between a bacterial and a viral infection and therefore is a potential guide to initiate antimicrobial therapy.
- Confirm the presence of a bacterial pathogen or help to rule out a bacterial infection rapidly.

Used for selection of appropriate therapy.

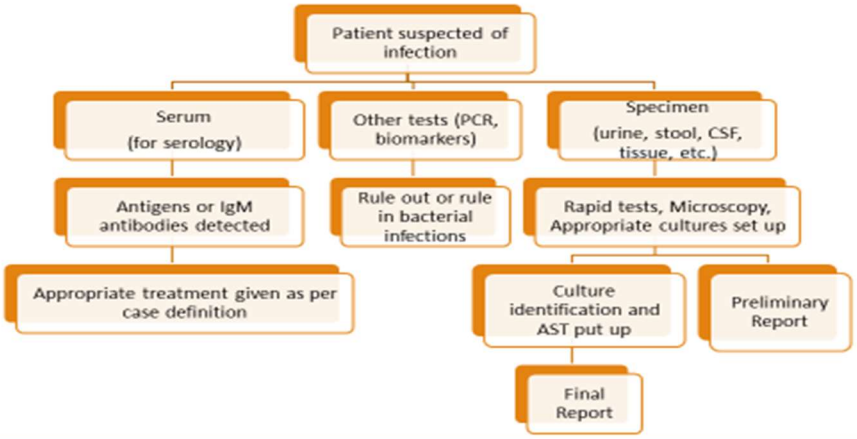
3. Microbiological Diagnostic Stewardship

Summary of sample collection and transport

Sample	Collection	Transport	Remarks
Blood	1ml blood per 10ml media	Immediately or at room temperature	
CSF	1-3 ml in sterile container	Immediately or at room temperature	Never refrigerate
Sterile body fluids (Pleural, Pericardial, peritoneal etc)	1-5 ml sterile container	Immediately or refrigerate if delay up to 4 hours	Do not transport in capped syringe
Urine	2-5ml	Immediately or refrigerate if delay up to 2 hours	Give proper instructions for collection and transport to patient
Sputum	Mucoid sample coughed up into container	Immediately or at room temperature	
Throat/ oropharyngeal swabs	Two swabs (culture and microscopy)	Immediately before drying, in VTM for viral diagnostics	Wear Appropriate PPE
Stool	1g (formed stool) to 5ml (liquid stool)	Immediately or at room temperature	Sample to be sent to the laboratory within 15 minutes for trophozoites
Pus/ Tissue biopsy/ aspirates	Sterile wide mouth container	Immediately or refrigerate if delay up to 4 hours	Do not add formalin or saline
Genital swabs	Dacron or rayon swabs	Immediately	Add to VTM if viral diagnostics is required.

3. Microbiological Diagnostic Stewardship

Choosing the right test



3. Microbiological Diagnostic Stewardship

THANK YOU

3. Microbiological Diagnostic Stewardship

4

Interpretation of Antimicrobial Susceptibility Results

NMC Module on AMR for Prescribers

Learning Objectives

On completion of this chapter, the prescriber should be able to:

- understand the importance of quality assured antimicrobial susceptibility testing (AST).
- interpret the antimicrobial susceptibility testing report.
- interpret the surrogate and cascade reporting.

4. Interpretation of Antimicrobial Susceptibility Results

Round the Clock -Microbiology Laboratory

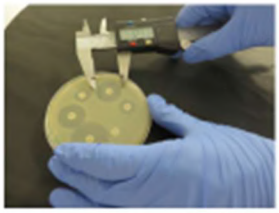
Prompt and rapid issue of reports so that the therapeutic interventions can be made in the desired time frame.

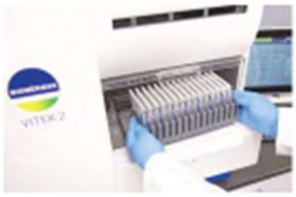
➢The results of AST are used to:

- Choose the most appropriate antimicrobial agent
- Establish antimicrobial prescription policies
- Predict upcoming resistance
- Assess the efficacy of newly developed antimicrobial agent

4. Interpretation of Antimicrobial Susceptibility Results

Antimicrobial Susceptibility Testing





Conventional Methods

Automated Methods

MIC within 12-18 hours

CLSI

EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING

European Society of Clinical Microbiology and Infectious Diseases

4. Interpretation of Antimicrobial Susceptibility Results

Case Scenario-1

(Objective: Interpretation of AST)

A 60 year Male, hypertensive, diabetic, presents to the OPD with H/O high grade fever with chills since 3 days, dysuria, abdominal pain associated with nausea, vomiting & pedal edema with decreased urine outputs since 1 day.

- WBC- 18,900/mm³
- Creatinine – 1.8 mg/dl,
- Abg – Metabolic acidosis.
- CUE - plenty of pus cells/HPF with bacteria++

4. Interpretation of Antimicrobial Susceptibility Results

DEPARTMENT OF MICROBIOLOGY
CULTURE & ANTIBIOTIC SUSCEPTIBILITY REPORT

Name: XX	Age/Sex: XX
IP Number:XX	OP/IP:XX
Sample:Midstream Urine	Sample received on:01.01.2024
Lab ID:X	Reporting date: 03.01.2024

Microscopy: Urine wet mount shows plenty of inflammatory cells(10<HPF)
Organism isolated: *Klebsiella pneumoniae* isolated in culture(>10^5 CFU/ml) Significant bacteriuria
Susceptibility pattern:

Antibiotic	Susceptibility pattern	Antibiotic	Susceptibility pattern
Cefotaxime	R	Gentamicin	S
Ceftriaxone	R	Amikacin	S
Ceftazidime	R	Ciprofloxacin	R
Cefepime	SDD	Cotrimoxazole	R
Aztreonam	R	Nitrofurantoin	R
Amoxicillin/ Clavulanic acid	S	Norfloxacin	R

'S':Susceptible, 'I': Intermediate, 'R': Resistant, 'SDD':Susceptible Dose Dependent

Comments:
Intrinsic Resistance: *Klebsiella pneumoniae* is intrinsically resistant to Ampicillin,Amoxycillin and Ticarcillin.
Advisory note:

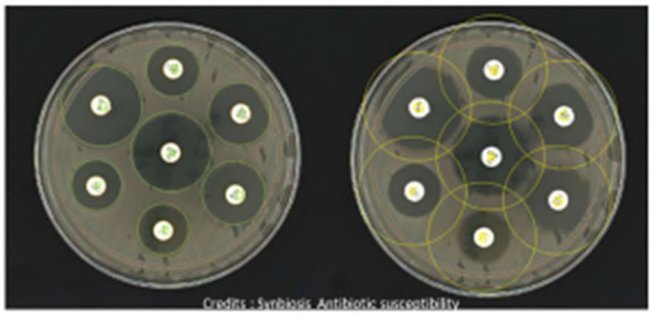
- If Carbapenem Resistant Enterobacteriaceae (CRE) is isolated, monotherapy with colistin is not advisable
- Kindly provide the provisional diagnosis, complete clinical history and antibiotic history in the requisition form.
- Cascade reporting is being followed. Second line drugs are being reported only if all the first line drugs are resistant

XXXXX
Signature of the Microbiologist

AST by conventional DD method

4. Interpretation of Antimicrobial Susceptibility Results

Interpretation of AST Result



4. Interpretation of Antimicrobial Susceptibility Results

S. I. R ??

- Interpretive criteria of susceptibility are based on standard dosing in a patient with normal renal function tests and in the absence of co-morbidities. The results of AST are reported as:

Susceptible
Bacteria are inhibited by the usually achievable concentrations

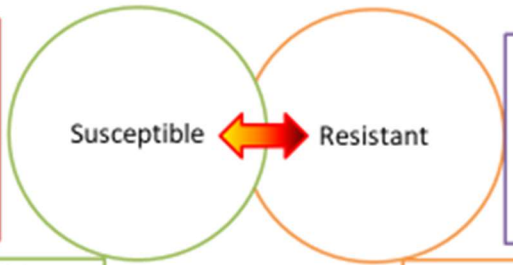
Intermediate
Buffer zone between the susceptible and resistant categories.

Resistant
Bacteria which are not inhibited by the usually achievable concentrations

4. Interpretation of Antimicrobial Susceptibility Results

One size does not fit all!

Susceptible-dose dependent
Susceptibility of the bacteria depends on the dosage regimen that is used in the patient.



Non-susceptible (NS)
Only a susceptible breakpoint is designated because of the absence or rare occurrence of resistant strains

Treatment success more likely
- Dose increased
- Dosing regimen is changed
- Infection is at a site where antimicrobials concentrate

INTERMEDIATE

Treatment success is less likely
- Dose used for "S" category is administered
- Infection is at a site where antimicrobials does not concentrate

4. Interpretation of Antimicrobial Susceptibility Results

Case Scenario 2

(Objective: Interpretation of Indicator antimicrobials)

A 46 year old gentleman presented to the hospital with complaints of right paraspinal back pain since 2 months with increasing intensity. MRI of the lumbar and thoracic spine revealed a large multiloculated abscess with osteomyelitis. A pig tail catheter drain was inserted and pus was sent for culture and sensitivity.

Gram stain showed moderate inflammatory cells and plenty of Gram positive cocci in clusters .

Culture showed growth of *Staphylococcus aureus.*

4. Interpretation of Antimicrobial Susceptibility Results

DEPARTMENT OF MICROBIOLOGY
CULTURE & ANTIBIOTIC SUSCEPTIBILITY REPORT

Name: XX	Age/Sex: XX
IP Number:XX	OP/IP:XX
Sample:Catheter Drain	Sample received on:01.01.2024
Lab ID:X	Reporting date: 03.01.2024

Microscopy: Grams stain shows moderate inflammatory cells and plenty of Gram positive cocci arranged in clusters

Organism isolated: Culture shows growth of *Staphylococcus aureus*

Susceptibility pattern:

Antibiotic	Susceptibility pattern	Antibiotic	Susceptibility pattern
Penicillin	R	Tetracycline	R
Cefoxitin	R	Ciprofloxacin	S
Cotrimoxazole	S	Gentamicin	S
Erythromycin	R	Vancomycin	S
Clindamycin	S → R	Linezolid	S

'S':Susceptible, 'I':Intermediate, 'R':Resistant, 'SDD':Susceptible Dose Dependent

**Methicillin Resistant Staphylococcus aureus(MRSA)

**Inducible Clindamycin Resistant:Positive

Comments: All beta lactam drugs including BL/BLI combinations will fail against MRSA

Intrinsic Resistance:

- All Staphylococcus aureus isolates are untrinsically resistant to Aztreonam,Ceftazidime, Nalidixic acid, Polymyxin B and Colistin
- MRSA indicates presence of mutation of the target binding site for the beta lactam drugs (Penicillin Binding Protein 2a)

XXXXX
Signature of the Microbiologist

AST by conventional DD method

4. Interpretation of Antimicrobial Susceptibility Results

Interpretation of AST Result

Indicator / Surrogate drugs:

- Indicates resistance not only to the indicator, but also to related agents (Table in next slide).

Equivalent Agents:

- One antimicrobial can be used to predict results for the other antimicrobials.
- For Example susceptibility to erythromycin can be used to predict susceptibility to clarithromycin or azithromycin.

4. Interpretation of Antimicrobial Susceptibility Results

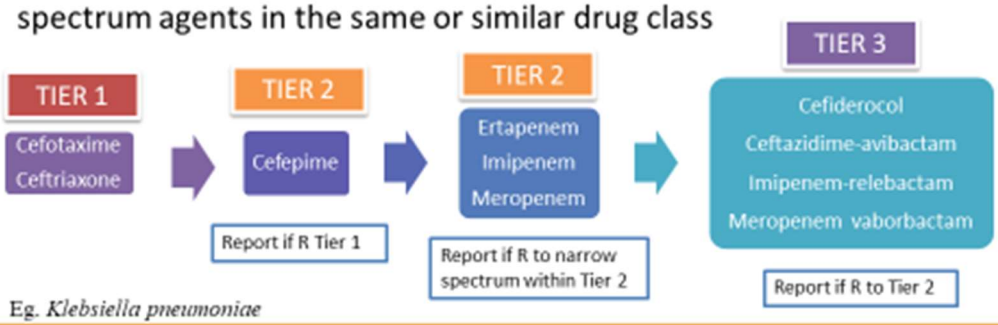
Indicator/surrogate/equivalent antimicrobials used in AST reports

Organism	Susceptibility Result	Inference / Action / Conclusion
Staphylococcus	Cefoxitin R (35 °C)	Report as Oxacillin R (Not Fox R), target Based Resistance, R to All Beta lactams (except Ceftaroline)
	Erythro R (15-26 mm) Clinda D+ve	Inducible Clindamycin Resistance +ve. Avoid Clindamycin. Report as R
Pneumococcus	Oxa zone ≥20mm i.e. S	Isolates of pneumococci with oxacillin zone sizes ≥20 mm are susceptible (MIC ≤0.06 µg/mL) to penicillin
Enterococcus	Penicillin Susceptibility	Enterococci susceptible to penicillin are predictably susceptible to ampicillin, amoxicillin, ampicillin-sulbactam, amoxicillin-clavulanate, and piperacillin-tazobactam for non–β-lactamase producing Enterococci
	Ampicillin Susceptibility	Same as above but Enterococci susceptible to ampicillin cannot be assumed to be susceptible to penicillin.

4. Interpretation of Antimicrobial Susceptibility Results

Cascade Reporting

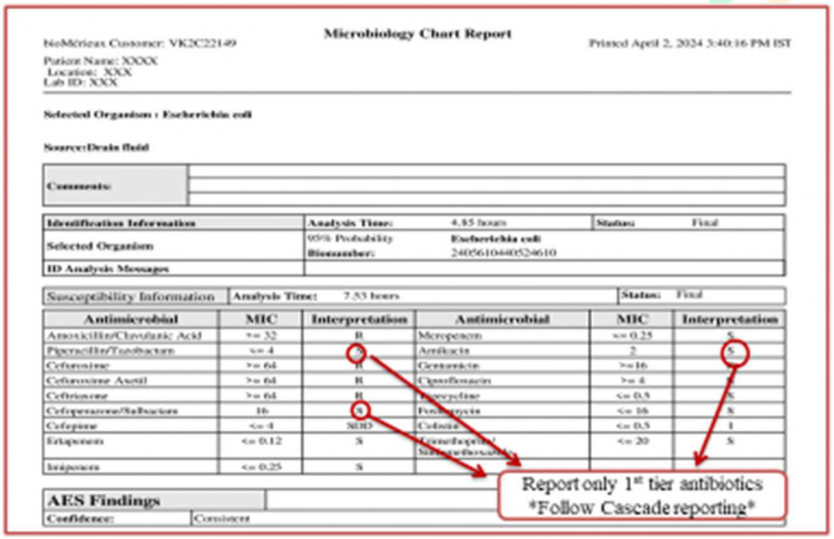
Results for broader spectrum or secondary agents are only reported if the isolate tests resistant to primary or narrower spectrum agents in the same or similar drug class



Eg. *Klebsiella pneumoniae*

4. Interpretation of Antimicrobial Susceptibility Results

Cascade Reporting



4. Interpretation of Antimicrobial Susceptibility Results

Case Scenario 3

(Objective: Role of MIC & BMQ ratio)

A 45 year old lady from Mizoram, post TKR of left knee 15 days back presented with pain, inflammation and pus discharge at the site of operation

- Patient denied any associated features of fever or chills
- Blood cultures were sent which were sterile after 48 hours of incubation
- Pus cultures showed growth of *Escherichia coli* with the following susceptibility pattern:
- What would be the preferred antimicrobial agent?

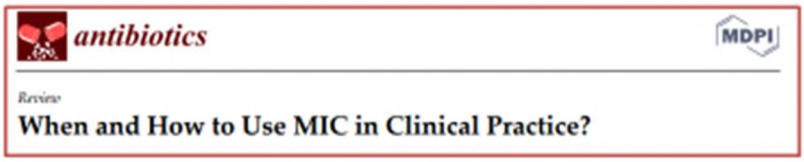
AST Pattern	Antibiotic
Susceptible	Piperacillin tazobactam, Cefoperazone sulbactam, Meropenem, Imipenem, Amikacin, Gentamicin, Tigecycline
Resistant	Ceftazidime, Cefuroxime, Ceftriaxone, Cefepime,Ciprofloxacin.

4. Interpretation of Antimicrobial Susceptibility Results

The minimal inhibitory concentration (MIC) may help to choose the most appropriate treatment.

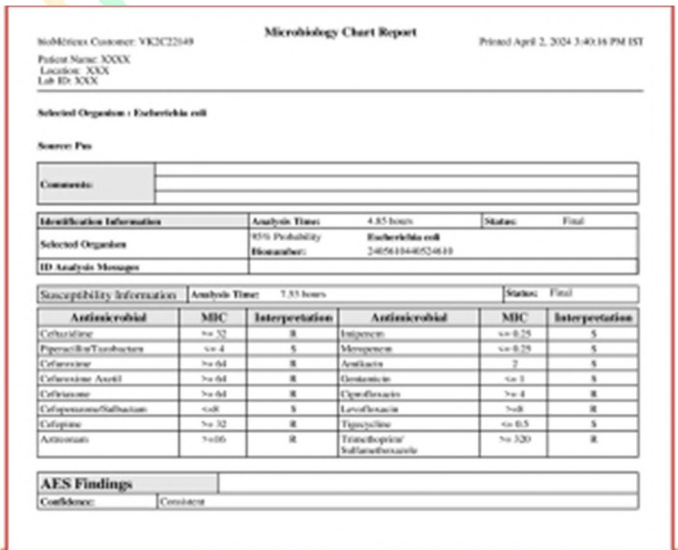
It defines the in vitro levels of susceptibility or the resistance of specific bacterial strains to a targeted antibiotic.

Reliable assessment of MIC has a significant impact on the choice of a therapeutic strategy, which affects efficiency of an infection therapy.



Magréault, Sophie & Jourdigu, Françoise & Carbonnelle, Etienne & Zahar, Jean-Ralph. (2022). When and How to Use MIC in Clinical Practice?. Antibiotics. 11. 1748. 10.3390/antibiotics11121748.

4. Interpretation of Antimicrobial Susceptibility Results



Microbiology Chart Report

Printed April 2, 2024 3:40:16 PM IST

Patient Name: XXXX
Location: XXX
Lab ID: XXX

Selected Organism : Escherichia coli

Source: Pus

Comments:	

Identification Information	Analysis Time: 4.85 hours	Status: Final
Selected Organism	95% Probability	Escherichia coli
ID Analysis Messages	Biomarker:	

Susceptibility Information	Analysis Time: 7.33 hours				Status: Final
Antimicrobial	MIC	Interpretation	Antimicrobial	MIC	Interpretation
Ceftazidime	>= 32	R	Imipenem	<= 0.25	S
Piperacillin/Tazobactam	<= 4	S	Meropenem	<= 0.25	S
Cefuroxime	>= 64	R	Amikacin	2	S
Cefuroxime Axetil	>= 64	R	Gentamicin	<= 1	S
Ceftriaxone	>= 64	R	Ciprofloxacin	>= 4	R
Cefoperazone/Sulbactam	<=8	S	Levofloxacin	>=8	R
Cefepime	>= 32	R	Tigecycline	<= 0.5	S
Aztreonam	>=16	R	Trimethoprim/ Sulfamethoxazole	>= 320	R

AES Findings	
Confidence:	Constant

Which antibiotic can be preferred??

Meropenem
MIC <0.25

OR

Tigecycline
MIC <0.5

OR

Any other Antimicrobial???

4. Interpretation of Antimicrobial Susceptibility Results

Should I Choose the Antibiotic With the Lowest MIC?

Michael J. Postelnick, BSPharm
DISCLOSURES | August 14, 2009

Lower the MIC value; the better is the Antibiotic??

4. Interpretation of Antimicrobial Susceptibility Results

MIC Therapeutic Index(BMQ ratio)

BMQ Ratio: Susceptible BP/MIC

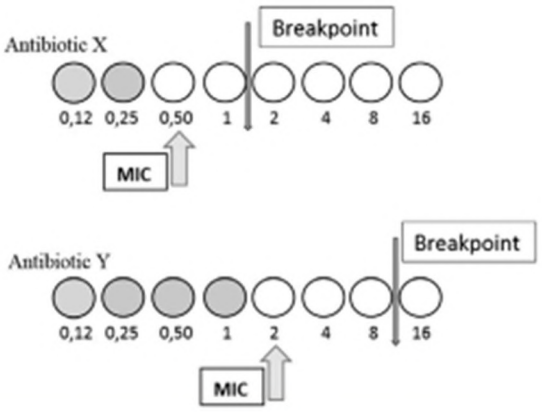
BMQ ratio for Antibiotic X

1/0.5= 2

BMQ ratio for Antibiotic Y

8/2= 4

The higher the BMQ the higher the therapeutic efficacy



4. Interpretation of Antimicrobial Susceptibility Results

MIC Therapeutic Index cont...

The Break point to MIC quotient of an antimicrobial refers to the ratio of susceptible breakpoint divided by MIC of the test isolate. The higher the BMQ the better the therapeutic efficacy.

MIC value should be assessed in relation to the distance from the breakpoint value of susceptibility.

There is an antibiotic X with a MIC of 0.5 mg/L and breakpoint 2 mg/L, and an antibiotic Y with a MIC of 2 mg/L but breakpoint of 16 mg/L: the drug with a MIC
more favorable is the antibiotic Y (Figure 2).

4. Interpretation of Antimicrobial Susceptibility Results

MIC Guiding Table

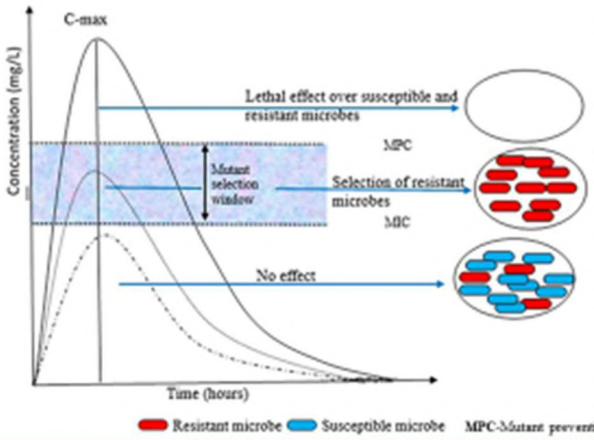
Antibiotic	Detectable MIC Range lower than Susceptible MIC BP					S	I	R	Detectable MIC Range lower than Susceptible MIC BP	
Ceftazidime	0.12	0.25	0.5	1.0	2.0	4.0	8.0	16.0	32.0	64.0
Ciprofloxacin				0.06	0.12	0.25	0.5	1.0	2.0	4.0
Levofloxacin						0.12	0.25-1	2.0	4.0	8.0
Gentamicin			0.5	1.0	2.0	4.0	8.0	16.0		
Cotrimoxazole					20.0	40.0		80.0	160.0	320.0
Cefepime		0.12	0.25	0.5	1.0	2.0	4.0-8.0	16.0	32.0	64.0
Piperacillin tazobactam					4.0	8.0	16.0	32.0	64.0	128.0
Cefoperazone Sulbactum					8.0	16.0	32.0	64.0		
Amikacin		1.0	2.0	4.0	8.0	16.0	32.0	64.0		
Aztreonam				1.0	2.0	4.0	8.0	16.0	32.0	64.0
Imipenem				0.25	0.5	1.0	2.0	4.0	8.0	16.0
Meropenem				0.25	0.5	1.0	2.0	4.0	8.0	16.0
Tigecycline			0.25	0.5	1.0	2.0	4.0	8.0		

4. Interpretation of Antimicrobial Susceptibility Results

Antimicrobial agent	Line	MIC(µg/ml)	Interpretation	BMQ
Ceftazidime	First line	32	R	NA
Ciprofloxacin	First line	>=4	R	NA
Levofloxacin	First line	>=8	R	NA
Gentamicin	First line	<=0.5	S	8
Trimethoprim/Sulfamethoxazole	First line	>=320	R	NA
Cefepime	2nd line	>=32	R	NA
Piperacillin tazobactam	2nd line	<=4	S	2
Cefoperazone sulbactam	2nd line	<=8	S	2
Amikacin	2nd line	2	S	8
Aztreonam	Restricted	16	R	NA
Imipenem	Restricted	<=0.25	S	4
Meropenem	Restricted	<=0.25	S	4
Tigecycline	Restricted	<=0.5	S	4

High BMQ i.e. Greater Distance b/w Susceptible BP & MIC, Better Bug Kill

Reason Why We Need MIC Values & High BMQ



Mutant Selection Window(MSW) is an antimicrobial concentration range extending from the MIC required to block the growth of wild-type bacteria up to that required to inhibit the growth of the least susceptible, single-step mutant

When Cmax ≥ 4xMIC, it usually covers the MPC as well.

Tilahun, Hidanna & Mathewos, Macfie et al (2023). Potential Causes of Spread of Antimicrobial Resistance and Preventive Measures in One Health Perspective-A Review. Infection and drug resistance. 16. 7113-7143.

Selective Reporting

Reporting results for specific antimicrobial agents based on defined criteria unrelated to the AST results

The Criteria may be:

- Sample specific
- Organism specific
- Site specific
- Based on mechanism of resistance, clinical setting, patient demographics and availability of breakpoints.

4. Interpretation of Antimicrobial Susceptibility Results

Selective Reporting - Sample specific

AST results are provided only if clinical assessment suggests infection in the following situations:

- **Urine:** The urine of patients with indwelling catheters frequently becomes colonized. Unless clinically indicated, treatment is not required.
- **Sputum:** Antimicrobial therapy may be indicated if clinical or radiological evidence of lower respiratory tract infection is present. Rule out colonization.
- **Pus:** Antimicrobial therapy may be indicated in case of cellulitis or deep-seated infection only.

4. Interpretation of Antimicrobial Susceptibility Results

Selective Reporting - Organism specific

Enterococcus sp	*Staphylococcus sp*	*Salmonella* and *Shigella* species
• Cephalosporins, clindamycin, and trimethoprim-sulfamethoxazole may appear active in vitro but are not effective clinically and should not be reported.	• Methicillin (oxacillin)-resistant staphylococci are resistant to all currently available β-lactam antimicrobial agents, with the exception of ceftaroline.	• Aminoglycosides, first- and second-generation cephalosporins and cephamycins may appear active in vitro but are not effective clinically and should not be reported as susceptible.

4. Interpretation of Antimicrobial Susceptibility Results

Selective Reporting - Site specific

Antibiotic	Selective reporting
Nitrofurantoin	Only in Uncomplicated lower UTI
Tigecycline	Skin, soft tissue and abdominal infections only. Not to be reported in Blood. High volume of distribution
Aminoglycosides	Never given for Abscess and anaerobic infections
Daptomycin	Not effective in lung infections
1st and 2nd Generation Cephalosporins, Carbapenems, Clindamycin, Tetracyclines and Flouroquinolones	Should not be reported in CSF samples

4. Interpretation of Antimicrobial Susceptibility Results

Selective Reporting based on

Mechanism of Resistance

- If inducible clindamycin is positive Clindamycin should be reported resistant regardless of interpretation

Clinical setting

- IV drugs suppressed for OPD patients
- Renal impairement Aminoglycosides, colistin and vancomycin are suppressed from reporting.

Patient demographics

- Suppression of antimicrobials known to cause adverse drug reactions in children such as ciprofloxacin, tetracycline and chloramphenicol.

Breakpoints not available

- Tigecycline breakpoints for *Acinetobacter baumannii are not available..*

4. Interpretation of Antimicrobial Susceptibility Results

Antibiotic-Should not be Reported

Site / Patient	Antibiotic
Blood	Tigecycline (High Volume of distribution: Doesn't Stay in Blood)
Abscesses	Aminoglycosides (Never for AnO2 Infections & Salmonella / Shigella)
Lungs	Daptomycin
Urine	Macrolides, Tigecycline, Chloramphenicol, Clindamycin
Children	Fluoroquinolones, Tetracyclines, Chloramphenicol, Cotrimoxazole(infants)
Pregnancy	Tetracyclines, Fluoroquinolones, Aminoglycosides, Metronidazole

4. Interpretation of Antimicrobial Susceptibility Results

Comments as Foot Notes in the AST: Don't overlook!

Resistant to all tested antimicrobials	Consider 90-60 rule-suggests that 90% of susceptible results predict success, while 60% of resistant results still have successful treatment outcomes
Susceptible dose dependant (SDD)	If MIC is 4µg/ml, recommended dose of Cefepime is 1gm thrice daily or 2 gm twice daily & If MIC is 8µg/ml, recommended dose of Cefepime is 2gm thrice daily
Vancomycin Resistant Enterococci(VRE)	Kindly ensure appropriate infection control measures.
Colistin reported as susceptible	*Colistin Warning comments* If planning to start colistin as therapeutic option kindly remember, clinical and Pk/Pd data demonstrate colistin is of limited efficacy Use in combination with one or more active antimicrobials Renal dose adjustments required

4. Interpretation of Antimicrobial Susceptibility Results

Comments on Intrinsic Resistance

A 60-year Male, diabetic (poorly controlled), presented with H/O high grade fever and chills for 3 days associated with dysuria, flank pain,nausea & vomiting

- Initial Lab parameters -WBC- 18,900/mm3;
- Creatinine – 1.8 mg/dl,
- CUE - plenty of pus cells/hpf with bacteria++;
- Urine C/S report –*Providentia* sp >10^5 CFU/ml
- Considering the following susceptibility pattern the patient was started on combination of Colistin and Meropenem.

Colistin susceptibility not mentioned

AST Pattern	Antibiotic
Susceptible	Tigecyline
Resistant	Meropenem Amikacin,Gentamicin, Norfloxacin

Failure to mention comments on "intrinsic resistance" would result in improper choice of antimicrobial agent.

4. Interpretation of Antimicrobial Susceptibility Results

Case Scenario 4

(Objective: Reporting based on patient symptoms)

Asymptomatic bacteriuria (ASB) is a common finding in many populations, including healthy women and persons with underlying urologic abnormalities.

In healthy premenopausal, nonpregnant women or healthy postmenopausal women, IDSA recommends against screening for or treating ASB **(strong recommendation, moderate-quality evidence).**

Lindsay E Nicolle, Kalpana Gupta, Suzanne F Bradley et al.Clinical Practice Guideline for the Management of Asymptomatic Bacteriuria: 2019 Update by the Infectious Diseases Society of America, Clinical Infectious Diseases, Volume 68, Issue 10, 15 May 2019, Pages e83–e110

4. Interpretation of Antimicrobial Susceptibility Results

Points to Remember…

- ✓ Infants, children, healthy non pregnant females and diabetics should not be screened or treated for asymptomatic bacteriuria.
- ✓ Presence of indwelling catheter is not an indication for antimicrobial therapy.

4. Interpretation of Antimicrobial Susceptibility Results

Case Scenario 5

(Objective: Reporting based on Clinical correlation)

- Biopsy on HPE showed Squamous cell Carcinoma (high grade)
- Sputum microscopy -Many pus cells , no bacteria
- Bacterial culture - Burkholderia Cepacia (Moderate)

Antibiotic	Sensitivity
Amikacin	Resistant
Ceftazidime	Resistant
Meropenem	Susceptible
Piperacillin Tazobactam	Intermediate
Colistin	Resistant
Cotrimoxazole	Susceptible

Plan of Treatment?

Treat bacterial infection and start ATT simultaneously as clinical features are highly s/o of Tuberculosis ?

4. Interpretation of Antimicrobial Susceptibility Results

Points to Remember…

- ✓ Always remember the syndrome of presentation
- ✓ Put effort to confirm the diagnosis
- ✓ Don't treat colonizers

4. Interpretation of Antimicrobial Susceptibility Results

Case Scenario 6

(Objective: Reporting based on appropriate sample)

A 57 year old diabetic patient following below knee amputation presented with wound infection. Wound swab showed growth of Carbapenem resistant *Acinetobacter baumanii*

-

Microbiology Chart Report

Printed: April 2, 2024 3:40:16 PM IST

Patient Name: XXXX
Location: XXX
Lab ID: XXX

Selected Organism : Acinetobacter baumanii MDR/Other

Source: Wound swab

Comments	

Identification Information	Analysis Time: 4.83 hours	Status: Final
Selected Organism	95% Probability: Acinetobacter baumanii Biomarkers: 2485630440524633	
ID Analysis Messages		

Susceptibility Information	Analysis Time: 7.33 hours	Status: Final

Antimicrobial	MIC	Interpretation	Antimicrobial	MIC	Interpretation
Piperacillin/Tazobactam	>= 128	R	Amikacin	>= 64	R
Ceftazidime	>= 64	R	Gentamicin	>= 16	R
Cefoperazone-sulbactam	>= 64	R	Ciprofloxacin	>= 4	R
Cefepime	>= 32	R	Levofloxacin	>=8	R
Aztreonam	>= 64	R	Minocycline	>= 32	R
Cefoperazone/Sulbactam	>= 64	R	Colistin	<=0.5	I
Imipenem	>= 16	R	Trimethoprim/ Sulfamethoxazole	>= 320	S
Meropenem	>=16	R			

AES Findings	
Confidence:	Consistent

Case Scenario 6 cont...

(Objective: Reporting based on appropriate sample)

What is the most appropriate management?

1. Treat with Colistin
2. Treat with combination of Colistin and Carbapenem therapy
3. Go ahead with wound closure followed by antibiotic therapy
4. None of the above

Points to Remember...

- ✓ Appropriate sample collection: Rule out surface contamination and colonization as swabs are considered to be inferior to tissue samples.
- ✓ Look for signs of sepsis
- ✓ Wound inspection (Prescence of pus/healthy granulation tissue)

Points to Remember

- Commence therapy with Narrow spectrum agents.
- Be hasty in De-escalation whenever possible.
- Take note of Organism, Site and Patient Profile before prescribing antibiotics.
- Treat only when clinically significant or if a True pathogen is isolated.
- Read comments with caution.
- Appropriate sample collection is the fundament of a good susceptibility report..

4. Interpretation of Antimicrobial Susceptibility Results

THANK YOU

4. Interpretation of Antimicrobial Susceptibility Results

5

Antimicrobial Resistance - Principle and Implications

NMC Module on AMR for Prescribers

Learning Objectives

On completion of this chapter, the prescriber should be able to:

- define and explain the differences between antimicrobials and antibiotics
- outline the drivers for resistance
- Explain the intrinsic and acquired resistance
- outline the global epidemiology of key antimicrobial resistant pathogens and antimicrobial consumption

5. Antimicrobial Resistance - Principle and Implications

Introduction

- 'Antimicrobials' is a broad term that is used for all agents that act against different types of microorganisms namely bacteria (antibacterial), viruses (antiviral), fungi (antifungal) and parasites (antiparasitic).
- Antibiotic refer to compounds that are produced by microorganisms and act against bacteria.

5. Antimicrobial Resistance - Principle and Implications

Antimicrobials pose special challenges

- **Limited shelf life**: The efficacy of antimicrobials wanes over time.
- **Multispecialty usage**: They are used for prophylaxis and treatment of various conditions in a variety of situations.
- **Inappropriate use**: May harm other people who are not even exposed to the antimicrobial.
- **Limited drug development**: Past three decades have not seen significant development and licensing of antimicrobials.
- **Change in natural bacterial flora**: Overuse of antimicrobials tend to select bacteria with resistance to proliferate in the environment and body.

5. Antimicrobial Resistance - Principle and Implications

Overview of Antimicrobial Resistance (AMR)

Antimicrobial Resistance (AMR) occurs when bacteria, viruses, fungi and parasites change over time and no longer respond to medicines making infections harder to treat and increasing the risk of disease spread, severe illness and death.

- It makes standard treatments ineffective, prolonging infections that can increase the risk of spread to others.
- The resistant microbes are able to grow/multiply in the presence of drug that would normally kill them or limit their growth.

5. Antimicrobial Resistance - Principle and Implications

Antimicrobials- Mechanism of Action

- Inhibition or disruption of:
  - Cell wall or cell membrane synthesis of microbes
  - Protein synthesis of microbes
  - Nucleic acid synthesis in microbes
  - Metabolism or enzyme

Bactericidal	Bacteriostatic
Beta lactams	Macrolides
Glycopeptides	Clindamycin
Cyclic lipopeptides	Tigecyclines
Aminoglycosides	Tetracyclines
Fluoroquinolones	Linezolid

5. Antimicrobial Resistance - Principle and Implications

Mechanism of AMR

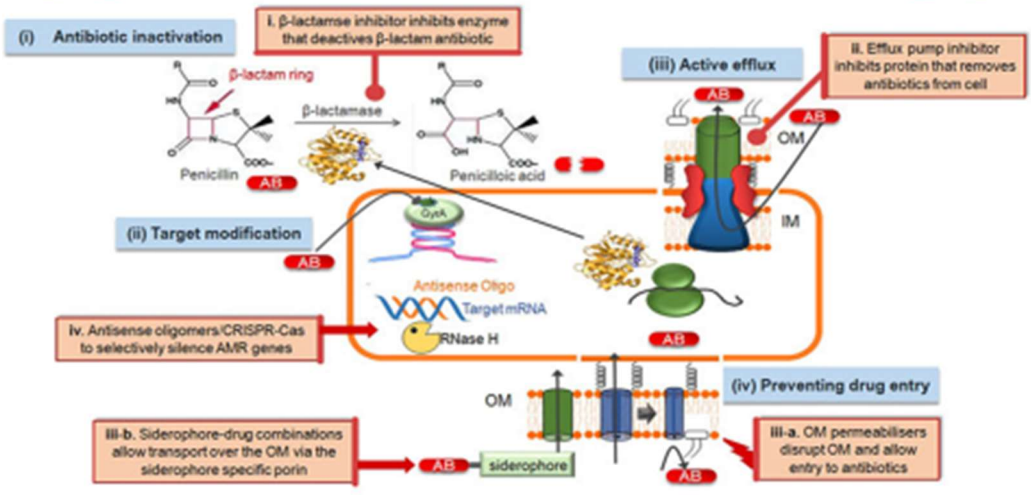
Some bacteria inherently do not respond to certain drugs (intrinsic resistance) while others may stop responding to a drug to which it is originally sensitive (acquired resistance).

Bacteria	Examples of Intrinsic resistance exhibited against drugs
Gram positive	Aztreonam
All Gram negative	Glycopeptides, Lipopeptides
Klebsiella species	Amoxicillin-clavulanate, Cefazolin
Citrobacter species	1st & 2nd generation cephalosporins, Cephamycins
Proteus species	Colistin, Cefazolin, Tetracycline, Nitrofurantoin
Pseudomonas aeruginosa	Amoxi-clav, Co-trimoxazole, I and II gen cephalosporins, Cefotaxime, Ceftriaxone, Ertapenem, Chloramphenicol, Tetracycline
Acinetobacter species	amoxicillin-clavulanate, aztreonam, chloramphenicol, Fosfomycin, ertapenem
Enterococcus	Aminoglycosides, Cephalosporins, clindamycin, many β-lactams

Mechanism of AMR cont..

Acquired resistance: Bacteria may stop responding to a drug to which it is originally sensitive by any of the following actions:

- Production of enzymes that destroy the antibacterial drug (e.g., beta-lactamases)
- Expression of efflux systems that prevent the drug from reaching its intracellular target (e.g., fluoroquinolone resistance)
- Reduction of permeability of drug through mutation of porin proteins (aminoglycosides)
- Modification of the drug's target site (e.g., penicillin-binding protein)
- Production of an alternative metabolic pathway that evades the action of the drug (e.g., folate metabolism).



Source: Biosci Rep.2019;39(4):BSR20180474. doi:10.1042/BSR20180474.

Drivers of AMR

- The development of AMR is multifactorial.
- The risk factors most commonly found to be associated with development of antimicrobial resistance are:
  - Excessive and irrational prescriptions of antimicrobials in community and hospitals
  - Increase in invasive procedures, transplants surgeries and immunosuppressive therapy.
  - Increase use of prosthetic devices amenable to superinfection and resistant bacteria.

5. Antimicrobial Resistance - Principle and Implications

Drivers of AMR

Risk factors (continued):

- Lack of effective preventive infection control measures such as hand hygiene, isolation procedures of patients with multi drug resistant organisms.
- Lack of effective antimicrobial stewardship programs restricting antimicrobial usage in community and hospitals.
- Use of antimicrobial in agriculture sector, animal husbandries and fisheries.
- Improper disposal of antimicrobials and antimicrobial residues which leads to finding their way in community and entering food chain through food, animals and water.

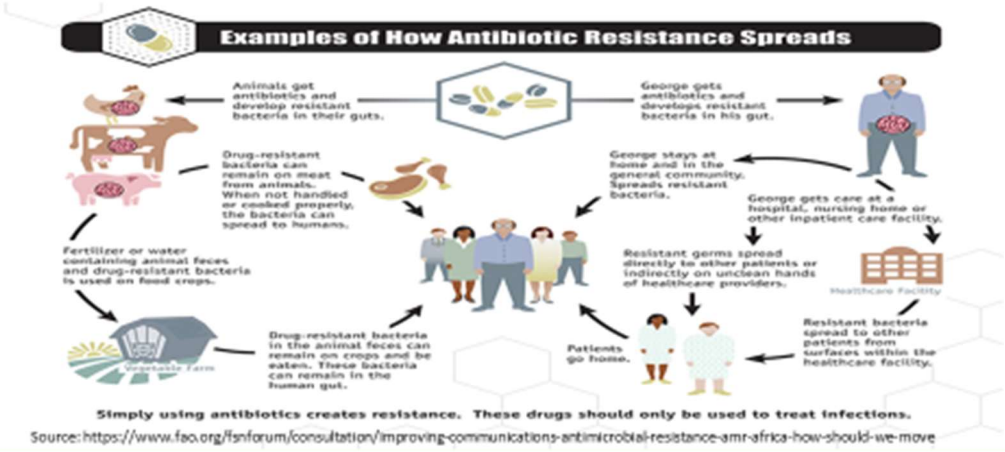
5. Antimicrobial Resistance - Principle and Implications

Drivers of AMR

Source: CDC - Drivers of resistance in healthcare settings and community level

5. Antimicrobial Resistance - Principle and Implications

Drivers of AMR



Source: https://www.fao.org/fsnforum/consultation/improving-communications-antimicrobial-resistance-amr-africa-how-should-we-move

Drug Resistance in Bacteria

- For common bacterial infections, high rates of resistance against antibiotics have been observed world-wide, indicating that we are running out of effective antibiotics.
- For eg. The rate of resistance to ciprofloxacin, varied from 8.4% to 92.9% for E. coli.
- K. pneomoniae for ciprofloxacin from 4.1% to 79.4% in countries reporting to the Global AMR and use Surveillance System (GLASS).

Drug Resistance in Bacteria cont..

- Resistance in K. pneumoniae to last resort treatment (carbapenem antibiotics) has spread to all regions of the world.
- K. pneumoniae is a major cause of hospital acquired infections such as pneumonia, blood stream infections, infection in newborns and in ICU patients.
- Resistance to fluoroquinolone antibiotics in E. coli , used for the treatment of UTI, is widespread.
- Colistin is the only last resort treatment for life-threatening infections caused by carbapenem resistant Enterobacteriaceae (e.g. E. coli, Klebsiella etc.)

Drug Resistance in Bacteria cont..

- Bacteria resistant to colistin have also been detected in several countries and regions, causing infections for which there is no effective antibiotic treatment available.
- Staphylococcus aureus are part of skin flora and are also common cause of infectious both in the community and in health care facilities.
- People with Methicillin – resistance S. aureus (MRSA) infections are more likely to die than people with drug sensitive infections.

5. Antimicrobial Resistance - Principle and Implications

Key antimicrobial resistant pathogens

- WHO priority list 2024 lists drug resistant pathogens that pose a critical threat to human health due to their resistance to antimicrobials.
- **Carbapenem resistant Enterobacterales (CRE)** These include *Klebsiella* spp. and *Escherichia coli* that are resistant to carbapenems and are placed atop in the critical list of priority pathogens.
- **Third generation cephalosporin-resistant Enterobacterales (3GCREB)** - Gram-negative bacteria resistant to third-generation cephalosporins, a broad class of antibiotics used to treat many different types of infections.
- **Carbapenem resistant Acinetobacter baumannii (CRAB)** - The emergence of CRAB poses a formidable challenge due to limited treatment options particularly in ICU settings.

5. Antimicrobial Resistance - Principle and Implications

- **Methicillin-resistant *Staphylococcus aureus* (MRSA)** – *S. aureus* resistant to many common antibiotics, making it difficult to treat skin infections, pneumonia, and bloodstream infections.
- **Vancomycin-resistant *Enterococcus* (VRE)** - one of the last-resort antibiotics used to treat serious infections.
- **Fluoroquinolone-resistant bacteria** - This includes strains of *E. coli*, *Salmonella* and *Campylobacter* that are resistant to fluoroquinolones, commonly used to treat urinary tract infections, diarrhea, and respiratory infections.

5. Antimicrobial Resistance - Principle and Implications

Global Epidemiology of AMR

Antimicrobial Consumption

- The overuse and misuse of antimicrobials are major drivers of AMR. This includes:
  - Using antibiotics for viral infections, which are ineffective.
  - Taking antibiotics for an incomplete course of treatment.
  - Using antibiotics for non-medical purposes, such as promoting growth in livestock.

5. Antimicrobial Resistance - Principle and Implications

Impact of AMR

- Increased morbidity and mortality from infections.
- Longer hospital stays and higher healthcare costs.
- Limited treatment options for common infections.
- The emergence of untreatable "superbugs."

5. Antimicrobial Resistance - Principle and Implications

Clinical Impact

- **Drug resistant infections**
  - Increased mortality
  - Treatment delays
  - Limited treatment options
  - Increased length of hospital stay
- **Hospital acquired infections**
  - Increased mortality
  - Antibiotic resistance
  - Increased complications like pneumonia, sepsis, and organ failure.
  - Psychological impact in form of anxiety, stress, and depression in patients

5. Antimicrobial Resistance - Principle and Implications

Economic impact

- **Increased costs:** due to longer hospital stays, more costly antibiotics, need for additional treatments for complications.
- **Reduced productivity:** due to longer recovery times → lost workdays and decreased productivity.
- **Strain on healthcare systems:** due to increased demand for resources to treat DRIs and HAIs limited resources available for other patients.
- **Global economic impact:** The World Bank estimates that AMR alone could push an additional 10 million people into poverty by 2030.

5. Antimicrobial Resistance - Principle and Implications

THANK YOU

5. Antimicrobial Resistance - Principle and Implications

6

Antimicrobial Policy

NMC Module on AMR for prescribers

Learning Objectives

On completion of this session, the prescriber should be able to:

- describe the attributes and features of antimicrobial policy
- understand the key elements of developing hospital antimicrobial policy
- assist in developing antimicrobial policy

6. Antimicrobial Policy

Aim of Antimicrobial Policy

- Reduce morbidity and mortality due to antimicrobial resistance in hospitalized patients.
- Preserve the effectiveness of antimicrobial agents in the treatment and prevention of communicable diseases.
- Provide uniform guidance for use of antimicrobials for treatment and prophylaxis.

6. Antimicrobial Policy

Antimicrobial Policy

- Empirical
- Specific
- Prophylaxis

The policy must incorporate specific recommendations for the treatment of different high-risk/special groups such as immunocompromised hosts; hospital-associated infections and community-associated infections.

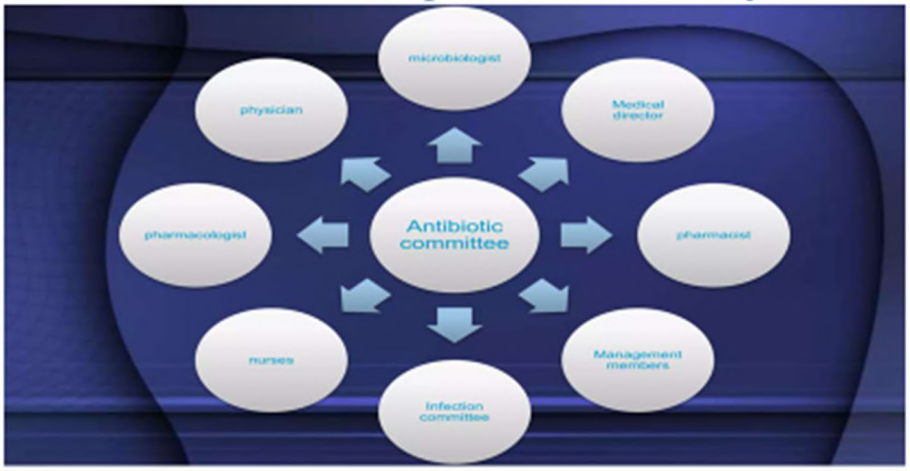
6. Antimicrobial Policy

Objectives of Antibiotic policy/Antimicrobial policy

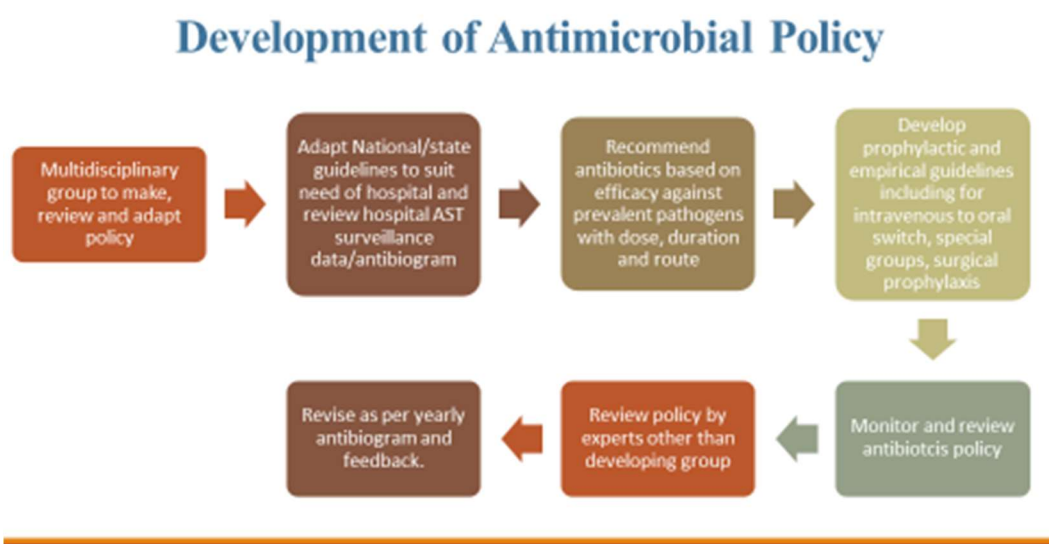
- Prescribing strategies to optimise the indication
- Selection and dosing
- Route of administration
- Duration and timing of antibiotic therapy to maximise clinical cure or prevention of infection whilst limiting the unintended consequences of antibiotic use, including toxicity and selection of antimicrobials

6. Antimicrobial Policy

Team to Develop Antibiotic Policy



6. Antimicrobial Policy



6. Antimicrobial Policy

THANK YOU

6. Antimicrobial Policy

Antimicrobial Stewardship in Humans 7

NMC Module on AMR for Prescriber

Learning Objectives

On completion of this chapter, the prescriber should be able to:

- define Antimicrobial stewardship
- outline the goals, strategies and interventions of Antimicrobial stewardship
- describe the core and supplemental interventions
- outline the pharmacokinetics and pharmacodynamics approach to antimicrobial prescription
- describe and interpret antibiogram
- understand the utility of antibiogram in formulating empirical therapy

Definition

Antimicrobial stewardship has been defined as *"coordinated interventions designed to improve and measure the appropriate use of antimicrobial agents by promoting the selection of the optimal antimicrobial drug regimen including dosing, duration of therapy, and route of administration"*.

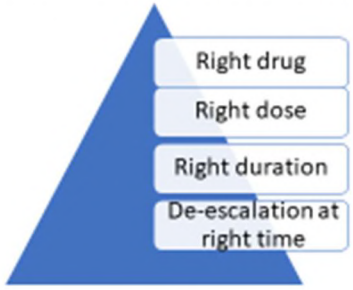
Goals of Antimicrobial Stewardship

- Ensure the best clinical outcome, for treatment or prevention of infection
- Minimize unintended consequences of antimicrobial use such as adverse drug reactions, emergence of clones of antimicrobial resistance
- Minimize healthcare costs without compromising quality of care
- Accurate diagnostics and diagnostic pathways

7. Antimicrobial Stewardship in Humans

"4Ds" of Prescribing Antimicrobials

Antimicrobial stewardship program (AMSP) have a direct responsibility to ensure prudent antimicrobial prescribing.



4Ds of prescribing antimicrobials

7. Antimicrobial Stewardship in Humans

AMSP Interventions

- Interventions can be introduced in a phased manner or in the whole hospital depending upon the facilities and motivation. Broadly the interventions that can be introduced are given below:

Core interventions	Supplemental interventions
Prospective audit	Dose optimization and combination therapies
Antimicrobial timeouts	Streamlining or de-escalation of therapy
Antimicrobial consumption analysis	Parenteral to oral conversion
Formulary restriction	Laboratory surveillance and feedback
Guidelines and clinical pathways	Information, education and communication

7. Antimicrobial Stewardship in Humans

Core Interventions

1. **Prospective audit**

- Regular bedside review of the patients to be done to analyse the prescriptions related to antimicrobial prescribing.
- After reviewing, feedback should be provided to the prescriber advising change if required on the optimal antimicrobial therapy.

7. Antimicrobial Stewardship in Humans

Core Interventions cont..

2. **Antimicrobial "Time outs"**

- Antimicrobials are often started empirically in hospitalized patients while diagnostic information is being obtained.
- All prescribers should review antimicrobials prescription after 48 hours to assess all 4Ds of antimicrobial stewardship.

7. Antimicrobial Stewardship in Humans

Core Interventions cont..

3. **Antimicrobial consumption analysis**

- **Quantitative analysis of antimicrobial consumption:** It should be collected from pharmacy purchase stores which will give proxy data of overall consumption of antimicrobials by the population (antimicrobial consumption surveillance).
- **Qualitative analysis of appropriateness of prescription:** Information regarding which patients are being given what antibiotics, their indications, dose and duration is collected using point prevalence surveys.
- It gives antimicrobial use surveillance.

7. Antimicrobial Stewardship in Humans

Core Interventions cont..

4. Formulary Restriction

- Antimicrobials included on the hospital formulary should be divided into three groups:

(i) **Unrestricted:** may be prescribed by any clinician
(ii) **Consultant only:** may only be prescribed by a consultant
(iii) **Restricted:** may only be prescribed following prior discussion with, and approval by, the antimicrobial stewardship team

- This list should be reviewed periodically preferably every year on the basis of antimicrobial usage data and rates of antimicrobial resistance.

7. Antimicrobial Stewardship in Humans

Core Interventions cont..

5. Guidelines and clinical pathways

- Every hospital must develop antimicrobial prescription guidelines based on principles of rational antimicrobial prescription.
- In absence of local guidelines, National Antimicrobial prescription guidelines may be adopted.

7. Antimicrobial Stewardship in Humans

Supplemental Interventions

1. Dose optimization and combination therapies

Antimicrobial must be given at the optimal:

- Dose
- Frequency and duration
- Based on individual patient characteristics such as age, weight, renal function
- Likely causative organism
- Site of infection, and
- Pharmaco-kinetic and pharmaco-dynamic characteristics of the antimicrobial agent(s)

7. Antimicrobial Stewardship in Humans

Supplemental Interventions cont..

1. Dose optimization and combination therapies

A few combinations are considered synergistic, such as:

- Aminoglycoside and beta–lactam antimicrobial.
- Beta –lactam antimicrobial and beta–lactamase inhibitor.
- Beta –lactam antimicrobial and glycopeptide (vancomycin/teicoplanin)
- Sulphamethoxazole and Trimethoprim

Antimicrobial drug therapy cannot be considered in isolation, it may be ineffective in cases where pus is not drained, septic shock is not treated and hypoxia/ anaemia are not corrected

7. Antimicrobial Stewardship in Humans

Supplemental Interventions cont..

2. Streamlining or de-escalation of therapy

- All empiric antimicrobial therapy should be reviewed on a daily basis by the clinician responsible for the patient's care.
- Special attention must be paid to factors such as:
  - Antimicrobial combinations with overlapping spectrum of activity.
  - Prolonged use of broad spectrum antimicrobials
  - Unauthorised use of restricted agents
  - Antimicrobial use not in accordance with hospital antimicrobial policy.
  - Clear criteria for prescribing intravenous antimicrobials.

7. Antimicrobial Stewardship in Humans

Supplemental Interventions cont..

3. Parenteral to oral conversion

- Always review intravenous prescription after 48 hours (at least) and switch to oral if possible.
- Early switch from intravenous (IV) agents to the equivalent oral preparation offers several benefits:
  - Decreased total cost of therapy,
  - Decreased potential for line associated infections,
  - Potential for decreased length of stay and patient preference,
  - Increased patient comfort and mobility,
  - Savings in nursing time spent preparing and administering intravenous doses.

7. Antimicrobial Stewardship in Humans

Supplemental Interventions cont..

4. Laboratory surveillance and feedback

- The Microbiology laboratory must share antimicrobial susceptibility data as an antibiogram with the prescribers.
- Also, feedback on follow up cultures must be promptly provided to allow timely review of antimicrobial prescriptions.

Supplemental Interventions cont..

5. Utility of antibiograms

- Empiric antimicrobial therapy is started to provide initial control of a presumed infection of unknown cause.
- Hence, local cumulative antibiograms are required to select appropriate empiric antimicrobials for patients with common infections.
- It also provides a broad overview of local antimicrobial resistance over time (e.g. the proportion of *S. aureus* isolates that are methicillin-resistant).
- Can provide an overview of the emergence of antimicrobial resistance in particular settings over time.
- It can assist in managing infections due to multidrug-resistant organisms.

Supplemental Interventions cont..

6. Information, Education and Communication (IEC)

- **Prescriber IEC**: Educational aids to guide prescribers at the point of prescribing such as:
- Clinical algorithms for the diagnosis of infection, or
- Methods to standardise documentation of treatment decisions must be displayed at important locations in hospitals by the hospital administration in consultation with the AMSP committee.

Supplemental Interventions cont..

- **Patient IEC**: Patients, their families and general public should be educated through awareness program, regarding appropriate use of antimicrobials such as:
- When antimicrobials are not needed, like in cases of upper respiratory tract infections of viral etiology.
- Inappropriate use may cause antimicrobial associated diarrhoea, allergic reaction, colonization with drug resistant bacteria, and autoimmune diseases, likely through disturbing the microbiome etc.
- They should be made aware of the importance of adherence to antimicrobial treatment

7. Antimicrobial Stewardship in Humans

Case Scenario 1

- A 40 year old female with symptoms of dysuria and lower abdominal pain from 2 days.
- Urine exam: WBCs: 20-25
  RBCs: 1-2

  Rx
- Inj. Ceftrioxone, 1gr i.v od for 5 days
- Liq. Alkalizer, 10 ml, thrice a day

7. Antimicrobial Stewardship in Humans

Case Scenario 2

- Male, 50 Years, D.M.,HTN, presents with symptoms of fever, breathlessness , tachypnea from 2 days.
- CBC: TLC: 20,000
- Chest X ray: shows consolidation rt side

  Rx
- Ceftriaxone 1 gr , twice daily
- Patient shows no improvement and deteoriates and succumbs to his illness.

7. Antimicrobial Stewardship in Humans

Principles of Rational Prescription

The general principles guiding antimicrobial prescription must be followed for all patients. Some of these principles are given below:

- **Do NOT use antimicrobials:**
  - To treat colonization or contamination unless there is clear indication such as immunosuppression or post splenectomy.
  - As a general prophylaxis or "Feel good" factor.
  - To treat infections which have high suspicion of viral causes such as influenza

7. Antimicrobial Stewardship in Humans

Principles of Rational Prescription cont..

- **Use Antimicrobials only:**
  - In cases of high degree of suspicion of infection.
  - After a treatable infection has been recognized
  - Prevention of infection where evidence has demonstrated that the potential benefits outweigh the risks.
- Empirical therapy must be based on local/national prescribing guidelines.

7. Antimicrobial Stewardship in Humans

Principles of Rational Prescription cont..

- Use targeted therapy instead of broad-spectrum antimicrobials unless there is a clear clinical reason (for example, mixed infections or life-threatening sepsis).
- Review broad spectrum antimicrobials as early as possible and promptly switch to narrow spectrum agents when sensitivity results become available.
- Choose antimicrobials as determined by the sensitivity of identified causative organisms.

7. Antimicrobial Stewardship in Humans

Principles of Rational Prescription cont..

- The indication for which the patient is being prescribed the antimicrobials should be documented in the drug chart and case notes by the prescriber.
- Always have a stop/review date on antimicrobial order form/patient chart. No antimicrobial should be written for indefinite time.
- Pre-surgical prophylaxis guidelines must be followed.

7. Antimicrobial Stewardship in Humans

Strategic Approach for Development and Intervention of AMSP

The strategic approach must be as per the availability of resources in the local settings:

Committee preparation: An AMS committee is required to provide leadership and overall coordination of the AMS programme.

- Committee must include Administrative leader, Clinicians from each clinical department, Clinical pharmacist, Microbiologist, Nursing officer etc. as per standard guidelines.
- **Clinicians education:** The policy-makers and health care administrators to provide opportunities for physicians to address information gaps through clinical education and continuing professional development.

7. Antimicrobial Stewardship in Humans

Strategic Approach cont..

Development of Institution-specific guidelines and interventions:

Institution-specific guidelines or algorithms can be adapted from national or international evidence-based guidelines to reflect local epidemiology, access to diagnostic testing and drug availability.

7. Antimicrobial Stewardship in Humans

THANK YOU

7. Antimicrobial Stewardship in Humans

8

Infection Prevention & Control (IPC)

NMC Module on AMR for Prescribers

Learning Objectives

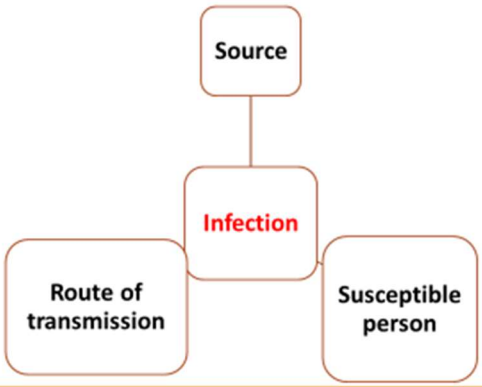
On completion of this chapter, the prescriber should be able to:

- define standard precautions
- describe the elements of standard precautions
- describe moments and steps of hand hygiene
- define and describe transmission-based precautions.
- define and describe biomedical waste management
- describe various segregation methods of biomedical waste and their disposal as per BMW rules.
- define device associated infections
- define and describe preventive care bundles for device associated infections

Need for IPC Program

- Healthcare Associated Infections (HAI) common adverse events
- Increase morbidity & mortality
- Increase duration of hospital stay
- Increase antibiotic use & increase AMR
- Increase overall treatment costs
- Economic burden
- Bad publicity for hospital

Infection Cycle



Inter-relationship of AMR & IPC

AMR & IPC

AIM OF IPC PROGRAM

- Prevention & stopping transmission of hospital acquired infections (HAI)
- Reduce Antibiotic Use
- Reduce Antimicrobial Resistance

8. Infection Prevention & Control (IPC)

Route of Transmission

Infections are spread by following routes-

- Contact (Direct/ Indirect)
- Airborne (aerosol)
- Respiratory (droplet nuclei)
- Fomite (surface)
- Inoculation or parenteral
- Faeco-oral
- Health care transmission

8. Infection Prevention & Control (IPC)

Modes of Transmission of Disease

- Transmission is the process by which a pathogen spreads from one host to another. Diseases or infections are transmitted in many ways.
- **Direct transmission:** This occurs when the pathogen is transmitted directly from an infected person. Direct transmission are-
  - Person to person
  - Droplet transmission
  - Spread by Skin
  - Spread through body fluids or blood

8. Infection Prevention & Control (IPC)

Modes of Transmission of Disease cont..

- **Indirect transmission:** Contact occurs from a reservoir to contaminated surfaces or objects, or to vectors such as mosquitoes, flies, mites, fleas, ticks, rodents or dogs.

Indirect transmission are-

- Airborne transmission
- Contaminated objects
- Vector borne diseases
- Food and drinking water
- Through animals
- Environmental factors

8. Infection Prevention & Control (IPC)

Strategies for Prevention of Hospital Acquired Infections (HAIs)

- **Standard precautions:** are the minimum standard of IPC practices that should be used by **all** health-care workers, during the care of **all** patients, at **all** times, in **all** settings.

Includes-

- **Transmission based precautions:**

-are used in addition to standard precautions for patients with known or suspected infection or colonization with transmissible and/or epidemiologically significant pathogens.

-The type of transmission-based precautions assigned to a patient depends on the transmission route of the microorganism: contact, droplet, or airborne

8. Infection Prevention & Control (IPC)

Strategies for Prevention cont..

Standard Precautions components

- Risk assessment
- Hand hygiene
- Respiratory hygiene and cough etiquette
- Patient placement
- Personal protective equipment
- Aseptic technique
- Safe injections and sharps injury prevention
- Environmental cleaning
- Handling of laundry and linen
- Waste management
- Decontamination and reprocessing of reusable patient care items and equipment.

8. Infection Prevention & Control (IPC)

Hand Hygiene

Hand Hygiene-

- A general term that applies to either -handwashing, antiseptic handwash, antiseptic handrub, or surgical hand antisepsis
- Alcohol-based handrubs reduce bacterial counts on hands more effectively than plain soaps, and in a majority of studies more effectively than antimicrobial soaps.

Hand Hygiene

- It is one of the basic measures of standard precaution
- Hand hygiene is the simplest, most effective measure for preventing nosocomial infections, however it is the most neglected one too.

Hand Hygiene

Hand Rub

- Alcohol based Hand sanitizers
- 20-30 seconds

Hand wash

- Using Soap & Water
- 40-60 seconds
- Hands soiled

(Source: https://openwho.org/courses/IPC-HH-en)

Routine Hand Washing Tips

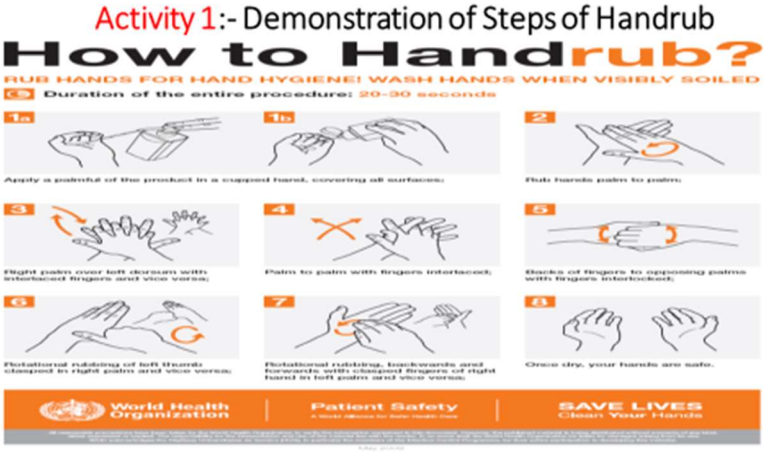
Jewelry

- **Rings should either be removed or moved to ensure washing underneath them.**
- **Rings can make donning gloves more difficult and may cause gloves to tear more readily.**

Condition of Nails and of Hands

- Artificial nails should be avoided.
- Nails should be kept short, rounded, and unvarnished, and the routine use of nail brushes should be avoided.
- The hands, including the nails, should be inflammation free

Activity 1:- Demonstration of Steps of Handrub



(Source: Guideline on Hand Hygiene in Health Care in the Context of Filovirus Disease Outbreak Response, WHO, 2014)

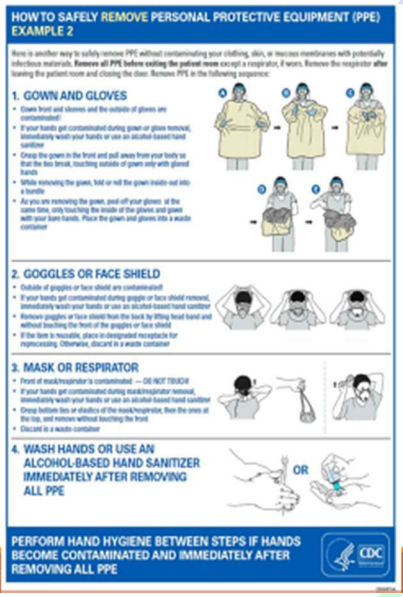
Donning of PPE

(source: https://www.cdc.gov>hai>pdfs>ppe-sequences)

Activity 2:- Donning of PPE

Doffing of PPE

source: https://www.cdc.gov>hai>pdfs>ppe-sequences



Activity 3:- Doffing of PPE

Inoculation Precautions

- Rational/ Safe Injection Practices
- Safe procedures for handling sharps
- Recapping of needle should be avoided
- Metallic waste disposed into a puncture resistant container.
- Have maximum visibility & properly position the patient during exposure-prone procedures such as phlebotomy.
- Fingers must be protected from injury by using forceps for holding suturing needles.

Spill Management

- Cordon off the area of spill.
- Open spill kit and wear PPE. Use forceps, tongs or scooper to pick broken glass pieces and discard in cardboard box.
- Put absorbent paper over the spill. For large spill cover with large size gauze pad or newspapers.
- Pour fresh hypochlorite over the recovered spill and leave for 20 minutes.
- Put another paper covering the soaked paper and then remove the soaked paper and put it in the yellow bag.

8. Infection Prevention & Control (IPC)

Activity 4- Demonstration of Spill Management

- You are the medical officer in hospital emergency. A RTA victim is brought to the emergency with an open left femur fracture and was bleeding profusely. After initial investigations & treatment the patient was stabilized and transferred to the Orthopaedics department for further management.
- You observe that about 50-60 ml spilled blood is present in the cubicle where this patient was received.
- What instructions would you like to give regarding management of this blood spill?

8. Infection Prevention & Control (IPC)

Airborne precautions

- These are to be followed for droplet nuclei <5µm, e.g., tuberculosis, chicken pox, measles and influenza. This requires:
- Isolation of patients in individual room with adequate ventilation: This includes, where possible, negative pressure; door closed; at least twelve air exchanges per hour; exhaust to outside placed away from intake ducts
- Staff wearing high-efficiency masks in room

8. Infection Prevention & Control (IPC)

Droplet precautions

- These are to be followed for droplet nuclei >5 µm, e.g., meningococcal meningitis, diphtheria, respiratory syncytial virus. The following procedures are required:
- Individual room for the patient, if available
- Surgical mask for healthcare workers
- Restricted circulation for the patient; patient wears a surgical mask if leaving the room
- Teach the patient to follow respiratory hygiene/cough etiquette.

8. Infection Prevention & Control (IPC)

Contact precautions

- Direct contact occurs when performing patient- care activities that require touching the patient's skin. Indirect contact occurs when touching potentially contaminated environmental surfaces or equipment in the patients' environment Individual room for the patient if available; grouping patients if possible
- Staff wear gloves on entering the room; a gown for patient contact or contact with contaminated surfaces or material
- Wash hands before and after contact with the patient, and on leaving the room
- Restrict patient movement outside the room
- Appropriate environmental and equipment cleaning, disinfection, and sterilisation

8. Infection Prevention & Control (IPC)

Summary

Type	Isolation room or cohorting	Hand Hygiene	Gloves	Gown	Mask	Eye protection	Handling of equipment	Visitors
Standard	Not required	Yes	Possible contact with blood/body fluid	If soiling likely	For aerosol generating procedures	For aerosol generating procedures	Single use or reprocessed	No additional precautions
Contact	Essential	Yes	Essential	Essential	For aerosol generating procedures	For aerosol generating procedures	Preferential single use/ patient dedicated equipment	Same as HCW's
Droplet	Essential	Yes	Possible contact with blood/body fluid	If soiling likely	Surgical mask	For aerosol generating procedures	Single use or reprocessed	Restricted visitor policy. Precautions same as HCW's
Airborne	Negative Pressure	Yes	Possible contact with blood/body fluid	If soiling likely	N 95 mask	For aerosol generating procedures	Single use or reprocessed	Restricted visitor policy. Same as HCW's

8. Infection Prevention & Control (IPC)

Biomedical Waste Management

Definition

Any waste generated while providing health care, performing research and undertaking investigations or related procedures on human beings or animals in hospitals, clinics, laboratories or similar establishments

8. Infection Prevention & Control (IPC)

Non-compliance

The occupier is liable for penalty for contravention of the provisions of the Act and the Rules, orders and directions as specified in Rule 15. of the E(P)Act,1986,

"whosoever fails to comply or contravenes any of the provisions of the Act and the Rules, orders and directions be punishable with imprisonment for a term which may extend to five years or with fine which may extend to one lakhs rupees or both"

8. Infection Prevention & Control (IPC)

Definition of Occupier

"**Occupier**" means a person having **administrative control** over the institution and the premises generating bio-medical waste, which includes a hospital, nursing home, clinic, dispensary, veterinary institution, animal house, pathological laboratory, blood bank, health care facility and clinical establishment, irrespective of their system of medicine and by whatever name they are called

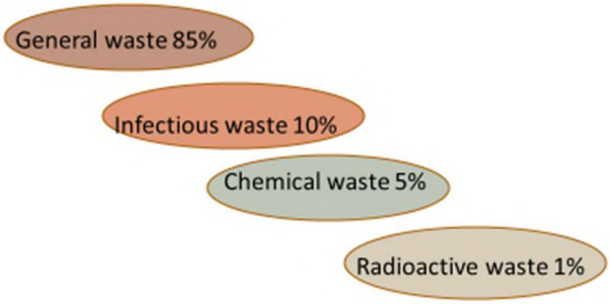
8. Infection Prevention & Control (IPC)

Authorisation

- Every occupier or operator handling bio-medical waste, irrespective of the quantity shall make an application in Form II for authorization under BMW Rules and consent under Air Act & Water Act.
- The authorisation shall be one time for non-bedded occupiers.

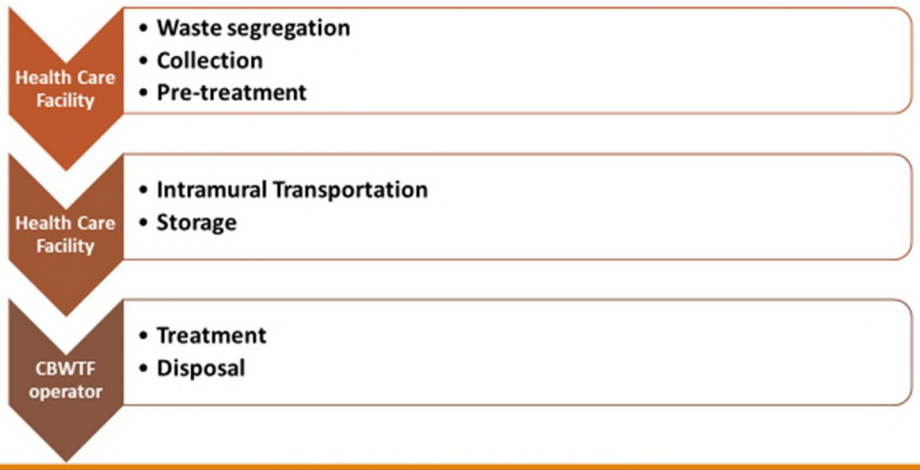
8. Infection Prevention & Control (IPC)

Generation Rate of Waste



8. Infection Prevention & Control (IPC)

Steps involved in BMW Management



8. Infection Prevention & Control (IPC)

Segregation at Source

- Segregated at the point of generation

Yellow bag and bin	Red bag and bin	Blue container or box	White puncture proof container

- Four colour coded containers/bags as per BMW guideline
- Non-chlorinated colour coded bags of 55 microns are used

8. Infection Prevention & Control (IPC)

Segregation at Source cont..

- The bags should be labelled with ward and date before placing into the bin
- All patient care areas and laboratories will be provided with appropriate colour coded bags placed in appropriate bins.
- Infection control nursing officer will be responsible to ensure that proper
- Guidelines are followed during the segregation of wastes.

8. Infection Prevention & Control (IPC)

YELLOW BAG (non-chlorinated plastic bag)	**RED COLOUR** (non–chlorinated plastic bag) Contaminated Waste (Recyclable)	**Blue** (Cardboard boxes with blue colored marking)	**White** (Translucent Puncture proof container)
(a) Human Anatomical Waste **(b)Animal Anatomical Waste** **(c) Soiled Waste** **d) Expired or Discarded Medicines** **(e) Chemical Waste** **(f) Chemical Liquid Waste** **(g) Discarded linen, mattresses, beddings contaminated with blood or body fluid.** **h) Microbiology, Biotechnology and other**	Wastes generated from disposable items such as tubing, bottles, intravenous tubes and sets, catheters, urine bags, syringes (without needles and fixed needle syringes) and Vaccutainers with their needles cut) and gloves.	**(a) Glassware:** Broken or discarded and contaminated glass including medicine vials and ampoules except those contaminated with cytotoxic wastes. **(b) Metallic Body Implants**	**Waste sharps including Metals:** Needles, syringes with fixed needles, needles from needle tip cutter or burner, scalpels, blades, or any other contaminated sharp object that may cause puncture and cuts. This includes both used, discarded and contaminated metal
			

YELLOW BAG (non-chlorinated plastic bag)

(a) Human Anatomical Waste:
Human tissues, organs, body parts and foetus below the viability period (as per the Medical Termination of Pregnancy Act 1971, amended from time to time).

(b) Animal Anatomical Waste :
Experimental animal carcasses, body parts, organs, tissues, including the waste generated from animals used in experiments or testing in veterinary hospitals or colleges or animal houses.

(c) Soiled Waste:
Items contaminated with blood, body fluids like dressings, plaster casts, cotton swabs and bags containing residual or discarded blood and blood components.

(d) Expired or Discarded Medicines:
Pharmaceutical waste like antibiotics, cytotoxic drugs including all items contaminated with cytotoxic drugs along with glass or plastic ampoules, vials etc.

(e) Chemical Waste:
Chemicals used in production of biological and used or discarded disinfectants.

(f) Chemical Liquid Waste :
Liquid waste generated due to use of chemicals in production of biological and used or discarded disinfectants, Silver X-ray film developing liquid, discarded Formalin, infected secretions, aspirated body fluids, liquid from laboratories and floor washings, cleaning, house-keeping and disinfecting activities etc.

(g) Discarded linen, mattresses, beddings contaminated with blood or body fluid.

(h) Microbiology, Biotechnology and other clinical laboratory waste: Blood bags, Laboratory cultures, stocks or specimens of microorganisms, live or attenuated vaccines, human and animal cell cultures used in research, industrial laboratories, production of biological, residual toxins, dishes and devices used for cultures.

8. Infection Prevention & Control (IPC)

RED COLOUR (non–chlorinated plastic bag)

- **Contaminated Waste (Recyclable)**

(a) Wastes generated from disposable items such as tubing, bottles, intravenous tubes and sets, catheters, urine bags, syringes (without needles and fixed needle syringes) and Vaccutainers with their needles cut) and gloves.

8. Infection Prevention & Control (IPC)

White (Translucent Puncture proof container)

Waste sharps including Metals:

- Needles, syringes with fixed needles, needles from needle tip cutter or burner, scalpels, blades, or any other contaminated sharp object that may cause puncture and cuts. This includes both used, discarded and contaminated metal sharps

8. Infection Prevention & Control (IPC)

Blue (Cardboard boxes with blue colored marking)

(a) Glassware:

Broken or discarded and contaminated glass including medicine vials and ampoules except those contaminated with cytotoxic wastes.

(b) Metallic Body Implants

8. Infection Prevention & Control (IPC)

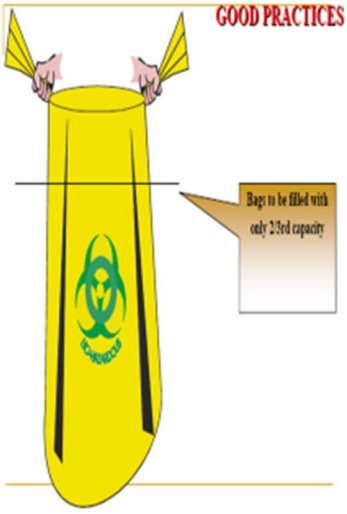
Handling and Transport

- The staff handling and transporting the bio-medical waste should wear appropriate PPE including boots and to prevent occupational hazard.
- All bins containing BMW should have biohazard label on them in accordance with Schedule IV Part A.
- Posters indicating waste segregation will be made available at all areas of patient care.
- Microbiology and all other clinical laboratory waste should be pre-treated by sterilisation before packing and sending to the common bio-medical waste treatment facility.

8. Infection Prevention & Control (IPC)

Handling and Transport cont..

- When waste bag/containers are ¾th full, they should be sealed.
- Foot operated or lidded bins should be used and in good working condition.
- Plastic waste bags should be fully enclosed within the bins.
- Origin of the waste is marked on the waste bag.



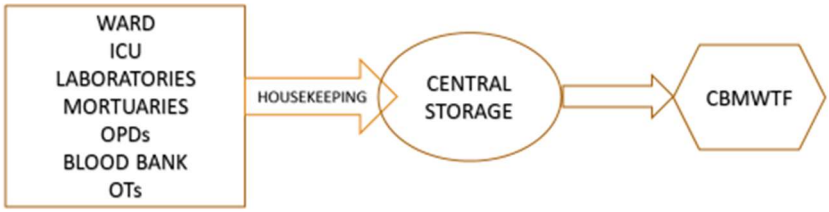
8. Infection Prevention & Control (IPC)

Storage

- A dedicated, well ventilated and clean area for storage of BMW within the hospital premises should be there.
- No untreated Bio medical waste will be kept stored beyond a period of **48 hours.**
- Each bag/container is weighed and the weight recorded in record sheet which has to be signed by appropriate personnel.
- At the end of month the record sheet will be submitted to the waste management committee for record keeping.

8. Infection Prevention & Control (IPC)

Transport



- Transport to be carried out on daily basis from central storage to CBMTF.
- Closed type transport vehicle
- Trained driver in basic handling of BMW.

8. Infection Prevention & Control (IPC)

Preventive Bundles for Device Associated Infections

8. Infection Prevention & Control (IPC)

Device Associated Infections

- These healthcare–associated infections are infections that can be associated with the devices used in medical procedures , such as catheters or ventilators .

8. Infection Prevention & Control (IPC)

Care Bundles

- These are a **set of interventions** that when applied together result in better prevention of device associated infections than individual elements implemented alone.
- Some recommended preventive bundles are given below. The hospital may modify these bundles according to their availability of resources and other logistics.

8. Infection Prevention & Control (IPC)

Care Bundles cont..

These include

- Bundles for the prevention of central line-associated bloodstream infections (CLABSI)
- Bundle for the prevention of catheter-associated urinary tract infections (CAUTI)
- Bundle for the prevention of ventilator associated pneumonia (VAP)

8. Infection Prevention & Control (IPC)

Checklist for Prevention of CLABSI

For Clinicians

1. Follow proper insertion practices

- Perform hand hygiene before insertion.
- Adhere to aseptic technique.
- Use maximal sterile barrier precautions (i.e., mask, cap, gown, sterile gloves, and sterile full body drape).
- Choose the best insertion site to minimize infections and noninfectious complications based on individual patient characteristics.

8. Infection Prevention & Control (IPC)

Checklist for Prevention of CLABSI

- Avoid femoral site in obese adult patients.
- Use Subclavian rather than Jugular veins.
- Prepare the insertion site with >0.5% chlorhexidine with alcohol.
- Place a sterile gauze dressing or a sterile, transparent, semipermeable dressing over the insertion site.

8. Infection Prevention & Control (IPC)

Checklist for Prevention of CLABSI cont..

- For patients 18 years of age or older, use a **chlorhexidine impregnated dressing** with an FDA cleared label that specifies a clinical indication for reducing CLABSI for short term non-tunneled catheters unless the facility is demonstrating success at preventing CLABSI with baseline prevention practices.

8. Infection Prevention & Control (IPC)

Checklist for Prevention of CLABSI cont..

2. Handle and maintain central lines appropriately

- ✓ Comply with **hand hygiene** requirements.
- ✓ Bathe ICU patients over 2 months of age with a chlorhexidine preparation on a daily basis.
- ✓ Scrub the access port or hub with friction immediately prior to each use with an appropriate **antiseptic** (chlorhexidine, povidone iodine, an iodophor, or 70% alcohol).

8. Infection Prevention & Control (IPC)

Checklist for Prevention of CLABSI cont..

- Use only sterile devices to access catheters.
- Immediately replace dressings that are wet, soiled, or dislodged.
- Perform routine dressing changes using aseptic technique with clean or sterile gloves.
  - Change gauze dressings at least every two days or semipermeable dressings at least every seven days.

8. Infection Prevention & Control (IPC)

Checklist for Prevention of CLABSI cont..

- Change administrations sets for continuous infusions no more frequently than every 4 days, but at least every 7 days.
  - If blood or blood products or fat emulsions are administered change tubing every 24 hours.
  - If propofol is administered, change tubing every 6-12 hours or when the vial is changed.
  - Perform daily audits to assess whether each central line is still needed.

8. Infection Prevention & Control (IPC)

Catheter Associated Urinary Tract Infections (CAUTI)

8. Infection Prevention & Control (IPC)

Definition

Catheter-associated UTI (CAUTI): A UTI where an indwelling urinary catheter (IUC) was in place for more than **two consecutive days** in an inpatient location on the date of event or the day before, with day of device placement being Day 1.

8. Infection Prevention & Control (IPC)

1. Core Prevention Strategies

- Insert catheters only for appropriate indications
- Leave catheters in place only as long as needed
- Ensure that only properly trained persons insert and maintain catheters
- Insert catheters using aseptic technique and sterile equipment (acute care setting)
- Following aseptic insertion, maintain a closed drainage system
- Maintain unobstructed urine flow.
- Hand hygiene and Standard (or appropriate isolation) Precautions.

8. Infection Prevention & Control (IPC)

2. Supplemental Prevention Strategies

- Consideration of alternatives to indwelling urinary catheterization
- Use of portable ultrasound devices for assessing urine volume to reduce unnecessary catheterizations
- Use of antimicrobial/antiseptic-impregnated catheters (after first implementing core recommendations for use, insertion, and maintenance)

8. Infection Prevention & Control (IPC)

Ventilator Associated Pneumonia (VAP)

8. Infection Prevention & Control (IPC)

Definition

Ventilator Associated Pneumonia (VAP):

A pneumonia where the patient is on mechanical ventilation for > 2 consecutive calendar days on the date of event, with day of ventilator placement being Day 1 AND the ventilator was in place on the date of event or the day before.

8. Infection Prevention & Control (IPC)

Maintenance Care Bundle for Mechanical Ventilation

- Adherence to hand hygiene
- Elevation of head of the bed to 30-45°
- Daily oral care with Chlorhexidine 2% solution
- Need of Peptic ulcer disease prophylaxis to be assessed daily- If needed sucralfate should be given
- DVT prophylaxis should be provided
- Daily assessment of readiness to remove mechanical ventilator must be documented.

8. Infection Prevention & Control (IPC)

Suggested Practices

- Bundles are not **'silver bullet'** solutions for all infection risks and should be implemented in a targeted group of patients, in a common hospital location, so that the elements of the bundle can be delivered as part of a single process of care.
- Ensure the elements of the care bundle are concise, simple, and prescriptive since numerous, complex bundle elements may hinder the success and effectiveness of frontline adoption and implementation.

8. Infection Prevention & Control (IPC)

Suggested Practices cont..

- Identify members of the healthcare team to test the implementation of the proposed bundle elements. It is recommended that these team members are early adopters of change.
- Bundle elements should not be static, but must adapt to changing evidence and best practices as new evidence emerges.
- Create awareness through the necessary training and education and provide the team with the applicable guidelines, evidence, toolkits and supplies (if any) to execute the implementation of a bundle.
- Once an appropriate methodology has been established, implement the interventions of each bundle element every time for every eligible patient.

8. Infection Prevention & Control (IPC)

Suggested Practices cont..

- Track compliance to the care bundle as an **"all or none"** measure and feedback results to frontline teams. Feedback should be delivered frequently (weekly or monthly if possible) to encourage improvement and sustainability.
- IHI improvement methods to re-design care processes and improve quality of care should be adopted when gaps or system breakdowns.
- The most effective programs include those with robust leadership, stringent protocols, participation of all members of the available healthcare team.

8. Infection Prevention & Control (IPC)

THANK YOU

8. Infection Prevention & Control (IPC)

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