Antimicrobial Resistance a Global threat and its Rational Management at Hospital Level

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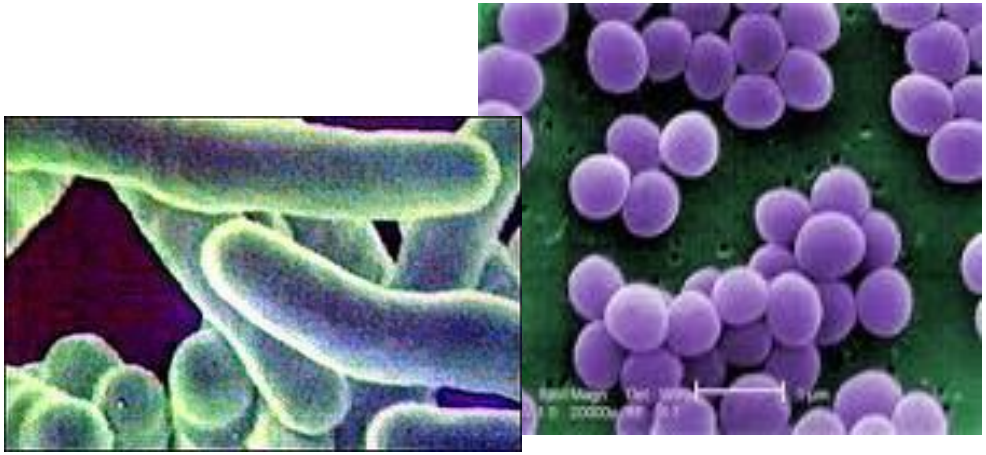


- **Situation analysis**
- **Impact of antimicrobial resistance**
- **Rational use of antimicrobials & Role of Hospitals**

- **Antibiotics** are a **class of drugs/medicines used specifically against bacteria** and are often used in treatment of bacterial infections
- Also called **antibacterial**
- They may either kill or inhibit the growth of bacteria
- **Generally antibiotics are not effective against viruses, fungus, parasites, etc**

- Antibiotics are substances produced by microorganisms, which suppress the growth of or kill other microorganisms at very low concentration

Examples-

Penicillin

Cephalosporins

Sulfanomides

Chloramphenicol

Tetracycline

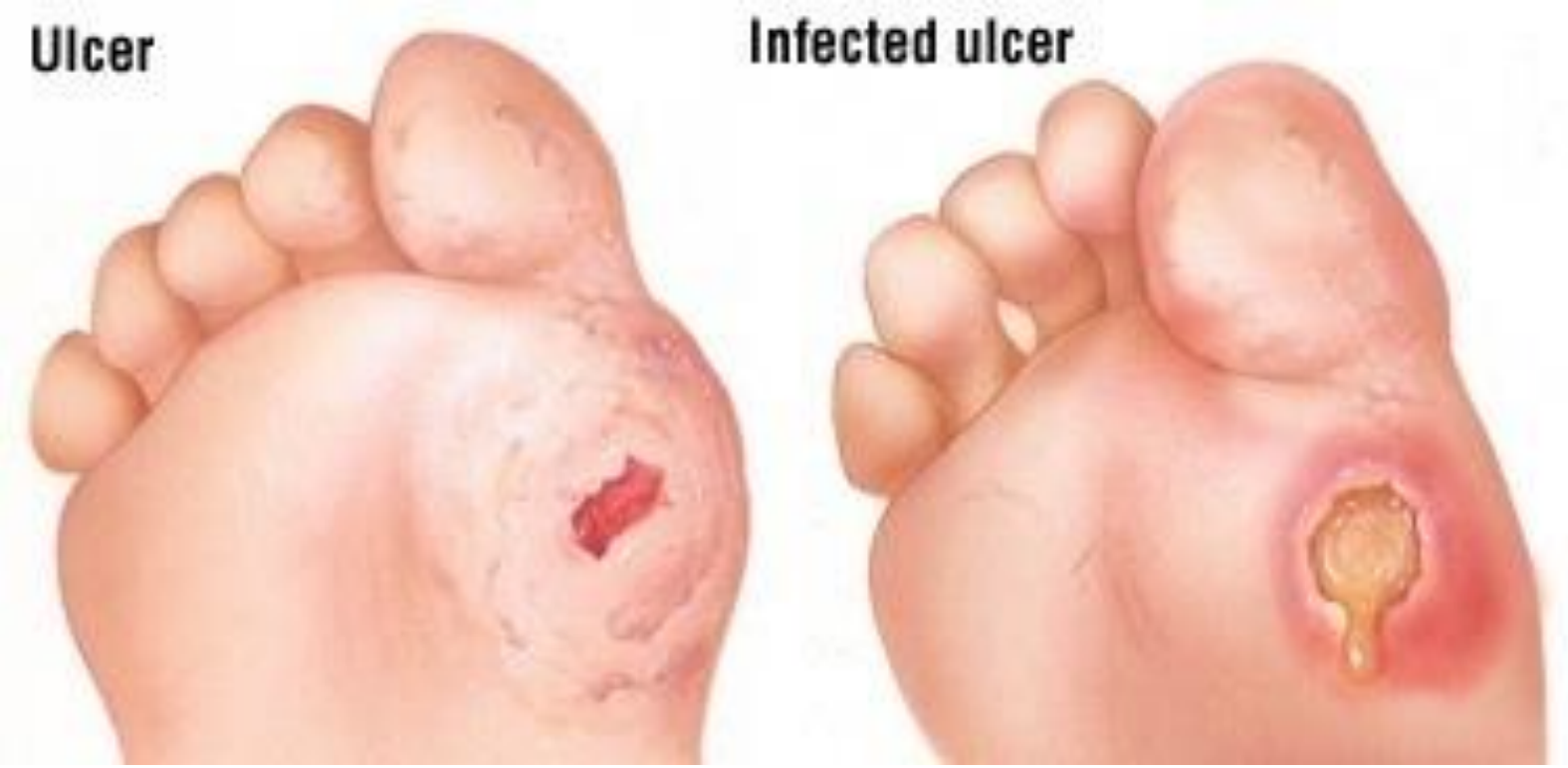
- **Antimicrobial Agent** (AMA) is a group of drug (both synthetic & natural) which are effective against microorganisms.
- These includes antibiotics as well as antivirals, antifungals, etc.

In neonatal fnfections

In the treatment of burn

Transplant patients

Diabetic foot ulcer



Antimicrobials continue to save lives every day…

- Neonatal care
- Transplantation
- Chemotherapy for malignancy
- Immunosuppression
- Safe surgery
- Safe obstetric care
- Intensive care interventions

Antibiotics are very popular: Outpatient antibiotic purchases from retail outlets in India

Year	2005	2006	2007	2008	2009	2018
Purchases in crore rupees (INR)	3,763	4484	5,075	5,886	6,414	14,554

"Anne Miller & Penicillin"

In 1999, the **New York Times** published an article about **Anne Sheafe Miller**….

"…who made medical history as the first patient ever saved by penicillin…died on May 27 in Salisbury, Conn. She was 90….."

"Anne Miller & Penicillin"

- In March 1942 - Mrs Miller was near death, suffering from a **Streptococcal infection**. Doctors had tried everything available (Sulfa drugs, blood transfusions, surgery)
- **All treatments failed**
- Desperate, doctors obtained a tiny amount of what was still an obscure, experimental drug and injected Mrs Miller with it
- Her hospital chart (now an exhibit at the Smithsonian Institution), registered a sharp overnight drop in temperature, and by the next day she was rapidly recovering.

"Anne Miller & Penicillin"

- **Mrs Miller's life was saved by antibiotics**
- **57 years life as bonus**

- Penicillin also saved thousands of lives of bacterial infection patient (with Streptococci, Staphylococci and Pneumococci)
- Saved an untold number of servicemen and civilians wounded in **World War II**

Emergence of antibiotic resistance: *Sir Alexander Fleming*

In 1945

“It is not difficult to make microbes resistant to Penicillin in the laboratory by exposing them to concentrations not sufficient to kill them, and the same thing has occasionally happened in the body”

What is antimicrobial resistance?

- **Antimicrobial resistance** happens when microorganisms (such as bacteria, fungi, viruses, and parasites) **change when they are exposed to antimicrobial drugs** (such as antibiotics, antifungals, antivirals, antimalarials, and anthelmintics).
- **As a result, the medicines/drugs become ineffective and infections persist in the body, increasing the risk of spread to others.**

- **The issue of antimicrobial resistance was recognised early in the ‘antibiotic era’**
- It threatens our ability to control infection from that time
- **Because, development of resistance is a natural phenomena for microbes**

- It is an increasingly serious threat to global health that requires action across all government sectors and society
- AMR is present in all parts of the world & new resistance mechanisms emerge and spread globally
- There are high proportions of antibiotic resistance in bacteria that cause common infections (e.g. urinary tract infections, pneumonia, bloodstream infections) in all regions of the world
- A **high percentage of hospital-acquired infections** are caused by highly resistant bacteria such as **methicillin-resistant *Staphylococcus aureus*** (**MRSA**) or multidrug-resistant Gram-negative bacteria

Situation Analysis

- Antibiotics are necessary in many life-threatening cases
- On the other hand, **overuse, underuse, misuse of antibiotics** can be disastrous in the long run
- Judicious use of antibiotics is required, but acceptable strategies to achieve this goal and to address the challenges must be devised and communicated

Status of resistance

- **More than 5 million Indian children** under five years get pneumonia or sepsis, and half die annually from infections from two bacterial pathogens: ***Streptococcus pneumoniae*** *(S. pneumoniae) and* ***Haemophilus influenzae*** *type b (Hib)*

- ***Staphylococcus aureus***
  - >50% isolates in hospitals are methicillin -resistant
  - 48% of patients with bacteraemia died in **Thailand**
- ***Acinetobacter baumannii***
  - >50% of patients infected with resistant strains die
- ***Pseudomonas, Klebsiella, Serratia***
  - Multidrug-resistance, persist in hospital settings, and cause huge mortality, morbidity

Status of resistance

- **Cholera**
  - Resistance to Nalidixic acid, fluorazolidone, Cotrimoxazole, Tetracycline: **India**
- **Shigellosis**
  - Multidrug resistant, causing extensive outbreaks
- **Typhoid fever**
  - **MDR *Salmonella typhi* prevalent all over the globe**
  - Causing 10% Case Fatality Rate (CFR) in children (preantibiotic era: 12.8%)

Status of resistance in South-East Asia

- **Tuberculosis**
- India- 2012, 450 000 new cases of multidrug-resistant tuberculosis (**MDR-TB**)
- Extensively drug-resistant tuberculosis (**XDR-TB**)-92 countries
- MDR-TB around 3% cases annually
- **XDR-TB: Reported from Bangladesh, India, Indonesia, Thailand**

- 2012, virtually all influenza A viruses circulating in humans were resistant to drugs frequently used for the prevention of influenza (**Amantadine** and **Rimantadine**)

- Frequency of resistance to the drugs in **HAART** therapy (**NRTI/NNRTI/PI**) are increasing rapidly

- **HIV and STIs**

  - Data on HIV resistance are alarming
  - Frequency of resistance to the drugs in **HAART** therapy (**NRTI/NNRTI/PI**) are increasing rapidly
  - STIs: Multi drug resistance Gonorrhoea

- **Malaria**

  - 400 million people at risk of infection with resistant parasites

Resistant organisms move rapidly across borders through humans and the food-chain

- Methicillin-resistant *Staph. aureus* (MRSA) in hospitals
- Multidrug-resistant typhoid fever even in USA
- MDR *Salmonella*
- Multidrug resistant *Mycobacteria*
- Resistant malaria
- Resistance in H1N1 and HIV are global concerns

Antimicrobial Resistance: Reasons

- Antibiotics are **fed to pigs** to speed up growth
- Antibiotics are used to increase the efficiency of their digestion
- Antibiotics are **fed to chicken** to increase muscle mass
- Antibiotics are **added to food pellets** and dropped to salmon in cages in the seas

Antimicrobial Resistance: Reasons

- **Approximately 80% of antibiotics in the United States are consumed in agriculture and aquaculture**
- Antibiotics are **sprayed on fruit trees** in India
- Antibiotics are even **embedded in marine paint** to inhibit the formation of barnacles

Antimicrobial Resistance: Reasons

- Every body can purchase any antibiotic/antimicrobial OTC and can use
- Therapeutic and non-therapeutic (e.g. as growth promoters)
- Same antimicrobials are used irrationally for humans as well as animals & plants
- In community acquired infections
- In hospital-associated infections
- **There is little regulation in their use**

Resistance & irrational use of antibiotics

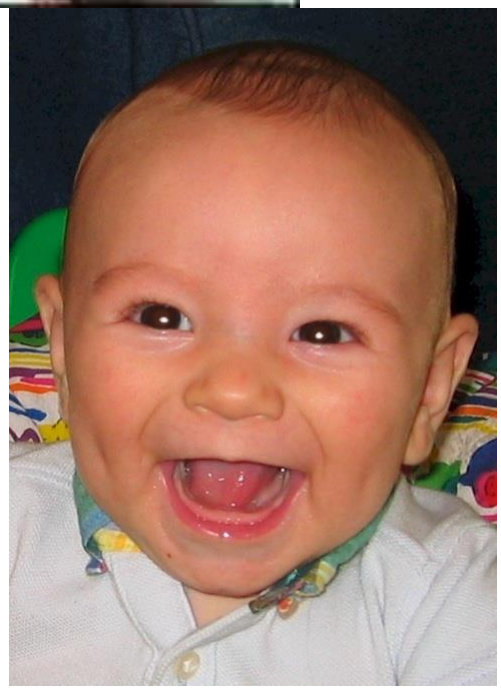
- **Irrational use of antibiotics is the greatest driver of resistance**
  - **50%** of antibiotics are prescribed inappropriately
  - **50%** of patients have poor compliance
  - **50%** of populations do not have access to essential antibiotics

Resistance & inappropriate use of antibiotics

- Standard treatment guidelines not provided to physicians
- Provided but not adhered to
- Accessible but poor quality
- Inadequate monitoring
- Irrational self-administration

Resistance & its impact on health

- Longer duration of illness
- Longer treatment
- Higher mortality/morbidity
- Treatment with expensive drugs
- Increased burden on health system
- Negates technological advances in medical sector
  - Complex surgeries
  - Transplantations and other interventions
- Patient acts as reservoir of resistant organisms which are passed to community and health-care workers
- Huge economic impact



Antibiotics are a precious resource

We need to preserve this resource by working together

Combating antimicrobial resistance:

No action today, no cure tomorrow

Rational Use of Antibiotic

What is inappropriate use ?

- Unnecessary prescription of antibiotics, such as for viral infections (colds) or for prolonged prophylaxis
- Using broad-spectrum antibiotics (such as third generation **Cephalosporins, Carbapenems**) when narrow-spectrum antibiotics are effective
- Prescribing too low or too high a dose
- Continuing treatment for longer than necessary
- Not prescribing according to microbiology results
- Omitting or delaying administration of doses
- Prescribing intravenous therapy when oral therapy is known to be effective and clinically safe

- **Right Drug**
- **To Right person**
- **At Right time**
- **In Right dose, duration, frequency**
- **At Right cost**

Examples

- **Examples: Diarrhoea & use of irrational antibiotic**

Diarrhoea & its Rational management


Dehydration
Sunken Fontanelle
Sunken Eyes and Cheeks
Few or no tears
Decreased Skin Turgor
Dry mouth or Tongue
Sunken Abdomen

Rational Management of Respiratory Disorders

Danger signs!!
Child aged 2mths– 5 yrs

- Not able to drink
- Convulsions , abnormally sleepy or difficult to wake
- Stridor in a calm child
- Severe malnutrition

Very severe disease

Chest indrawing

Severe pneumonia

- Fast breathing only
- No chest indrawing

Pneumonia

- No fast breathing ---- only cough / cold
- No chest indrawing

No pneumonia

Example

- **Common Fever**
- It is important to remember that **not all fevers are due to infections and not all infections are caused by bacteria**

- The majority of infections seen in general practice are of viral origin and antibiotics can neither treat viral infections nor prevent secondary bacterial infections in these patients

- Even where a bacterial etiology is established, an antibiotic may not be always necessary

- Many bacterial infections resolve spontaneously

General Principles of Antibiotic use

- Rational use of antibiotics is extremely important as injudicious use can adversely affect the patient, cause emergence of antibiotic resistance and increase the cost of health care.

Prescribing an antibiotic

- **Perception of need** - is an antibiotic necessary ?
- **Choice of antibiotic** - what is the most appropriate antibiotic ?
- **Choice of regimen** - what dose, route, frequency and duration are needed ?
- **Monitoring efficacy** - is the treatment effective ?

Is an antibiotic necessary?

- Antibiotics are generally only useful for the treatment of bacterial infections
- It is important to remember that not all fevers are due to infections and not all infections are caused by bacteria
- The majority of infections seen in general practice are of viral origin and antibiotics can neither treat viral infections nor prevent secondary bacterial infections in these patients.

Is an antibiotic necessary?

- **Even where a bacterial etiology is established, an antibiotic may not be always necessary. Many bacterial infections resolve spontaneously**
- Minor superficial skin infections may be more suitably treated with a local antiseptic
- **Collections of pus should be drained surgically and if drainage is adequate, antibiotics are often not required**

Choice of an antibiotic ?

- The successful outcome of therapy would depend very much on the choice of the antibacterial agent

- In the process of selecting an antibiotic, three main factors need to be considered; the **etiological agent, the patient and the antibiotic**

The etiological agent ?

- Determination of the etiological agent depends on a **combination of clinical acumen and laboratory support**
- In many instances an antibiotic prescription has to be made based on the clinical diagnosis (empirical therapy)
- Even where a bacteriology report is available- it is necessary to interpret the report

The etiological agent ?

- Bacterial isolates from culture specimens may represent normal flora, colonizers or contaminants rather than true pathogens
- **Sensitivity results when available are at best only a guide to treatment**
- **Laboratory reports should always be viewed in the light of clinical findings**

The patient ?

- Several patient factors have to be considered in selecting an antibiotic-
- Age is an important factor
- The very young and the very old tend to be more prone to the adverse effects of the antibiotics
- Neonates have immature liver and renal functions which affect their ability to metabolize or excrete antibiotics
- Antibiotics and their metabolites may adversely affect growing tissues and organs in children
- Elderly patients are more likely to suffer from nephrotoxicity and allergic reactions
- Dosage modifications would also have to be made in those patients with hepatic or renal impairment

The patient ?

- Antibiotics can also give rise to severe toxic reactions in patients with certain genetic abnormalities eg. **Sulphonamides** in patients with glucose-6-phosphate dehydrogenase deficiency
- Antibiotics should as far as possible be avoided in Pregnancy and when it is necessary to use an antibiotic, betalactam antibiotics and erythromycin are probably the safest
- A history of allergy to antibiotics should always be sought before administration
- Routine intradermal test doses for penicillin allergy is of little value and may even be dangerous. If in doubt avoid betalactams and use a macrolide or tetracycline (in adults) instead

The antibiotic ?

- The clinician should have adequate knowledge of the pharmacokinetic properties of the antibiotic he uses
- Antibiotics vary in their ability to be absorbed orally or to cross the blood brain barrier and these factors will affect their routes of administration
- The ability of the antibiotic to achieve therapeutic concentrations at the site of infection is another important consideration, thus antibiotics used for treating urinary infections should ideally be concentrated in urine

The antibiotic ?

- Some antibiotics have very severe toxic effects and are best avoided in certain conditions
- The clinician should also be aware of drug-drug interactions since many antibiotics can interact with other non-antibiotic drugs

The antibiotic ?

- Cost of the antibiotic is also of major concern
- In calculating costs it is perhaps more reasonable to take into account the total cost of treatment rather than just the actual cost of antibiotic per dose
- The route of administration, the necessity for monitoring antibiotic levels and the patient's length of stay in hospital can affect the cost of treatment as well
- The patient's compliance to medication is an important factor for consideration in the choice of antibiotics

Monitoring & review of response

- A routine early review (3 days after commencing treatment) of the patient's response is important in order to ensure that the patient is receiving appropriate treatment

- After review the clinician will have to decide whether to:
- i) continue with the present regimen
  ii) increase the level of treatment by changing from oral to parenteral; increasing the dose or changing to a broader spectrum antibiotic
  iii) decrease the level of treatment by changing from parenteral to oral, decreasing the dose or changing to a more specific narrow spectrum antibiotic
  iv) stopping the antibiotic if the infection has resolved; the objective of treatment is achieved or the diagnosis has been changed.

- **The word "Rational" primarily is not an adjective for antibiotic therapy but it reflects the mindset of the person prescribing antibiotics**

- Therefore **"Rational Antibiotic Therapy"** would mean antibiotic therapy given by physician and that must be evaluated by all, Pharmacist, Nursing Staffs, etc, **with a rational mindset**

What is Rational ?

- Choose the most appropriate and effective group of antibiotic based on the criteria of **efficacy, safety, suitability and cost**
- Choose an appropriate antibiotic from the chosen group
- Decide route of administration, dosage schedule and standard prescribed duration
- Write a legible prescription with name, age, sex, weight, diagnosis, drug's generic name, dose, route frequency and duration of treatment with other supportive drugs and treatment measures with signature and date

What is Rational ?

- Give relevant information, instructions and warnings. (Before food or after food, need for greater intake of water, alerting or danger signals of progression of infection and when to report again etc.)

- Monitor and review the therapeutic response and choose an alternative in case of intolerance, allergy or other adverse drug reactions or poor in vivo response (midcourse correction)

Role of Hospital

- Develop their action plans and strengthen their health and surveillance systems so that they can prevent and manage antimicrobial resistance.
- Collaborating with partners to strengthen the evidence base and develop new responses to this threat.
- Practices to avoid the emergence and spread of antibiotic resistance, including optimal use of antibiotics in humans.

Role of Hospital

- Situation analysis is very important
- To design hospital specific guidelines
- To ensure quality monitoring system
- Training of health care professionals
- Ensuring Rational Therapy
- Changes in the practices of prescribers and patients to reduce antibiotic misuse. Misuse includes prescribing the wrong antibiotic, dosage, or duration; prescribing an antibiotic unnecessarily; and patients not taking antibiotics correctly.
- Ensuring the quality of Drugs used in the hospitals
- Ensuring the rational cost of therapy
- Adequate information dissemination to the health care professionals, patients and public

Role of Hospital

- Strengthen Hospital microbiology department
- Ensure quality diagnosis
- Regular updatation of Antibiogram of the set up
- Regular information to the clinicians about the antimicrobial resistance status
- Design Drug formulary
- Follow Standard Treatment Guidelines
- Regular Prescription or Antimicrobial use audit

Rational Use of Antimicrobials ?

Thank you all

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- **Wish you a Happy learning !!!**