# Antimicrobial Resistance
# Rational Antibiotic Therapy


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**20-1-2018**

# Case scenario

- **A 80 year old man, a know case of COPD and old stroke, presented with breathlessness, cough with mucoid sputum and fever for one week.**
- **On examination, the patient was thin, frail, confused and dyspneic, febrile, bilateral crepts and rhonchi in both lung fields.**
- **Diagnosed as Infective exacerbation of COPD.**
- **Treated with Nebulised bronchodilators and Empirical antibiotics (Cefuroxime and Azithromycin) and steroids.**

- Th tum

C8

| | Ward | Lab Ref.No | Reported Date |
|---|---|---|---|
| | Medical | P201801110281 | 14/1/2018 |

**Requested for- Sputum Culture And Sensitivity**

**Type of sample** Sputum

**Macroscopic Examination**

**Microscopic Examination**

**Direct Gram stain examination** Pus cells(+)Gram negative bacilli (+)Gram positive cocci in pairs(+)

**ZN stain examination**

**Culture Result** Moderate growth of *Klebsiella pneumoniae* isolated.

| Antibiotic | S | SS | R | Antibiotic | S | SS | R |
|---|---|---|---|---|---|---|---|
| Amikacin | | | ✓ | Gentamicin | | | |
| Cefoxitin | | | | Imipenem | | | ✓ |
| Amoxycillin/Calvulanic Acid | | | ✓ | Kanamycin | | | |
| Ampicillin | | | | Levofloxacin | | | ✓ |
| Azithromycin | | | | Ticarcillin/Clavulanic Acid | | | |
| Cefepime | | | | Norfloxacin | | | |
| Cefoperazone/Sulbactam | | | ✓ | Ofloxacin | | | ✓ |
| Cefotazime | | | | Oxacillin | | | |
| Ceftazidime | | | ✓ | Penicillin | | | |
| Ceftriaxone | | | | Tetracycline | | | |
| Cefuroxime | | | | Vancomycin | | | |
| Cephalothin | | | | Piperacillin / Tazobactam | | | |
| Chloramphenicol | | | | Netilmicin | | | |
| Ciprofloxacin | | | | Cefixime | | | ✓ |
| Clindamycin | | | | NalidixicAcid | | | |
| Cotrimoxazole | | | | Linezolid | | | |
| Erythromycin | | | | Ampicillin/Sulbactam | | | |

# What is antimicrobial resistance?

- **Antimicrobial resistance is the ability of a microorganism (like bacteria, viruses, and some parasites) to stop an antimicrobial (such as antibiotics, antivirals and antimalarials) from working against it. As a result, standard treatments become ineffective, infections persist and may spread to others.**

# What causes drug resistance?

- **Drug resistance is a natural evolutionary phenomenon.**
- **When microorganisms are exposed to an antimicrobial, the more susceptible organisms succumb, leaving behind those resistant to the antimicrobial.**
- **They can then pass on their resistance to their offspring.**

# Drug Resistance

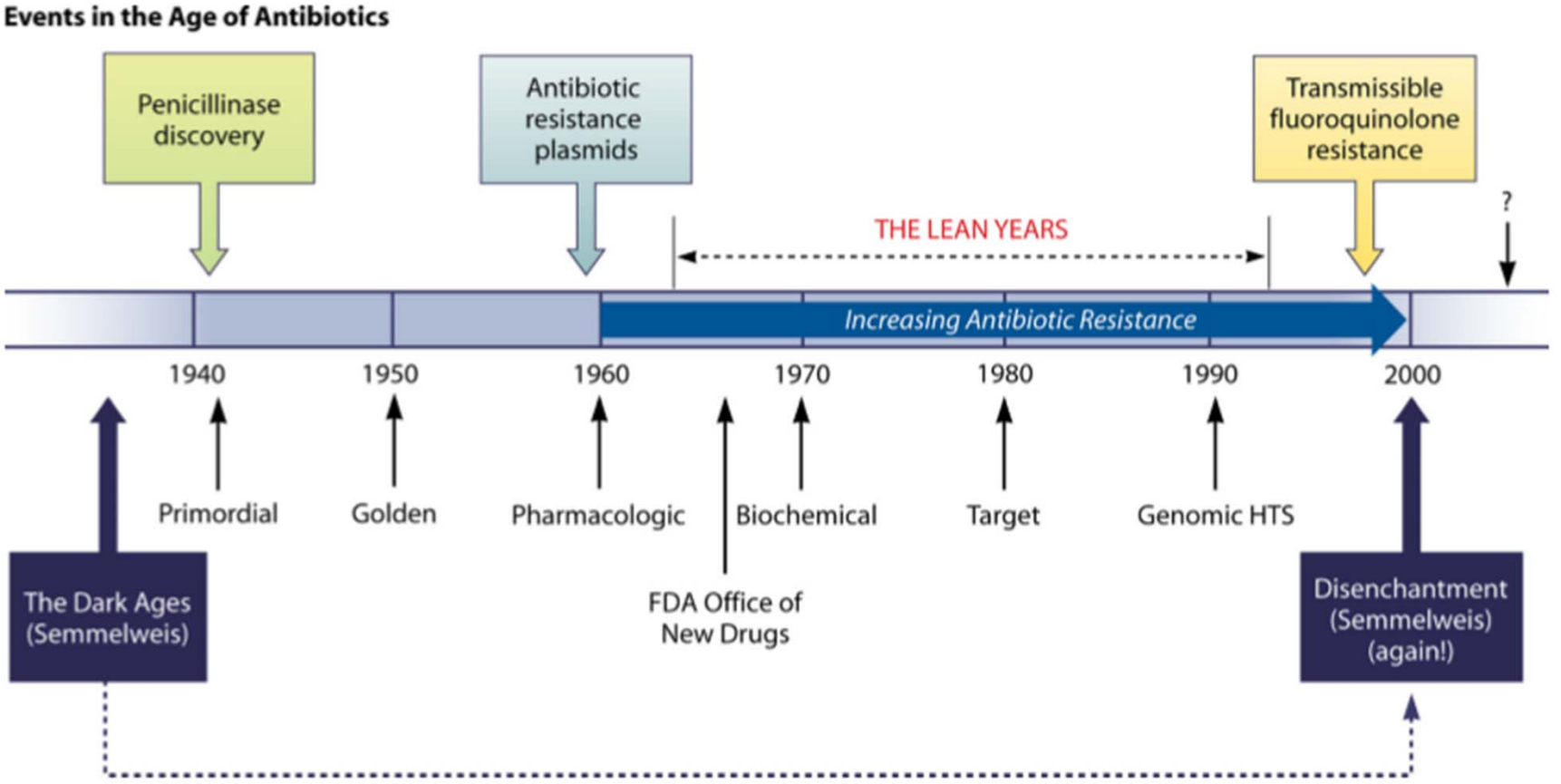
**Drug resistance occurs in**

- **Bacteria – Antibiotic resistance**
- **Endoparasites**
- **Viruses**
- **Fungi**
- **Cancer cells**

# Antibiotic Resistance

- **Defined as micro-organisms that are not inhibited by usually achievable systemic concentration of an antimicrobial agent with normal dosage schedule and or fall in the minimum inhibitory concentration (MIC) range.**

**Antibiotic resistance = MIC > Toxic plasma concentration**


Events in the Age of Antibiotics
Penicillinase discovery
Antibiotic resistance plasmids
Transmissible fluoroquinolone resistance
?
THE LEAN YEARS
Increasing Antibiotic Resistance
1940
1950
1960
1970
1980
1990
2000
Primordial
Golden
Pharmacologic
Biochemical
Target
Genomic HTS
The Dark Ages (Semmelweis)
FDA Office of New Drugs
Disenchantment (Semmelweis) (again!)

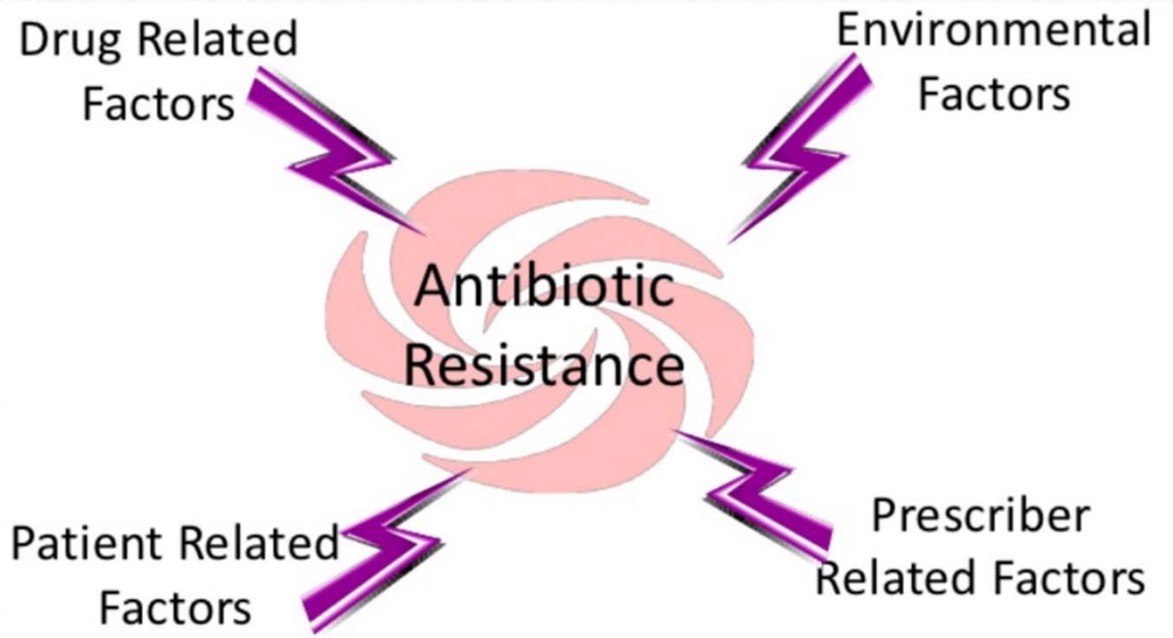
| | |
|---|---|
| The dark ages | • The preantibiotic era |
| Primordial | • The advent of chemotherapy, via the sulfonamides |
| Golden | • The halcyon years when most of the antibiotics used today were discovered |
| Pharmacologic | • Attempts were made to understand and improve the use of antibiotics by dosing, administration, etc. |
| The lean years | • The low point of new antibiotic discovery and development |

| | |
|---|---|
| Biochemical | • Knowledge of the biochemical actions of antibiotics and resistance mechanisms led to chemical modification studies to avoid resistance |
| Target | • Mode-of-action and genetic studies led to efforts to design new compounds |
| Genomic/HTS | • Genome sequencing methodology was used to predict essential targets for incorporation into high-throughput screening assays |
| Disenchantment | • With the failure of the enormous investment in genome-based methods, many companies discontinued their discovery programs. |

# Events in the age of antibiotics

- Before antibiotics were discovered, *Semmelweis* advocated hand washing as a way of avoiding infection; this practice is now strongly recommended as a method to prevent transmission.

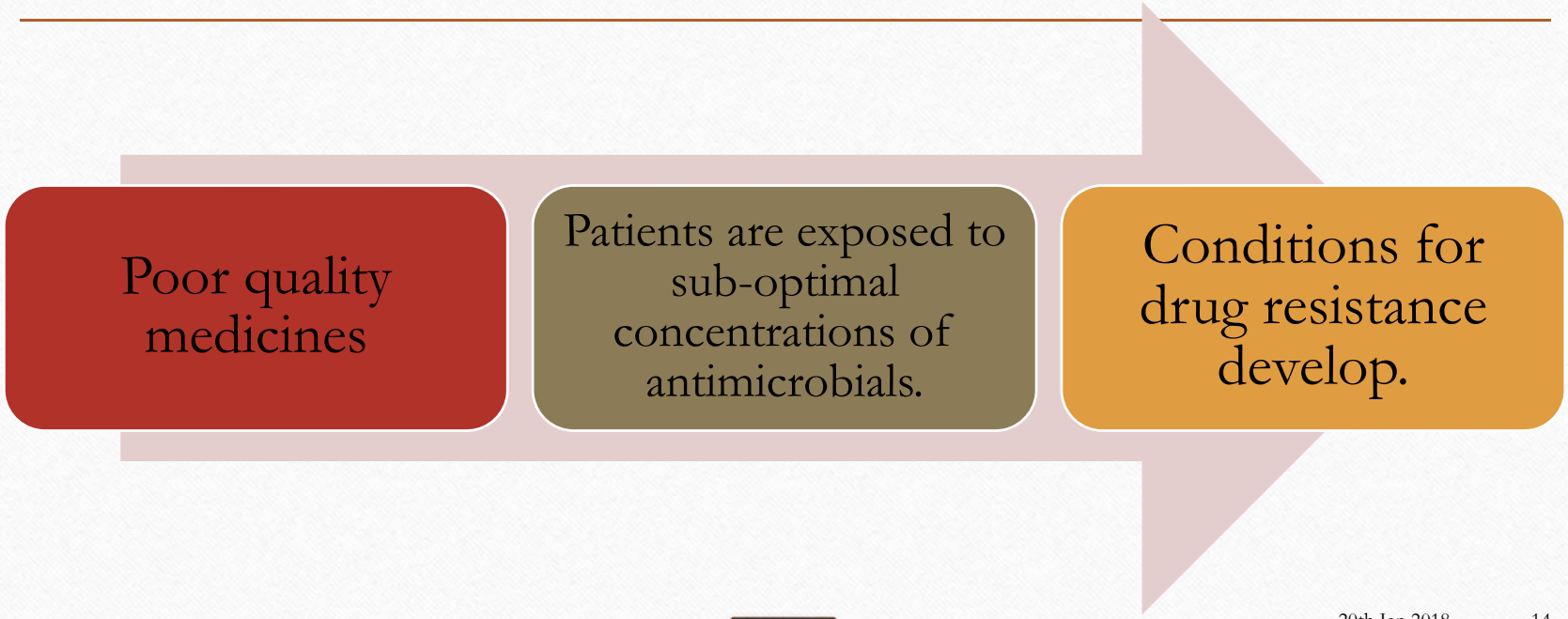
# Factors of Antibiotic Resistance



# Drug Related Factors

- **Over the counter availability of antimicrobials**
- **Counterfeit and substandard drugs causing sub-optimal blood concentration**
- **Irrational fixed dose combination of antimicrobials**
- **Soaring use of antibiotics**

# Lack of quality medicines contributes to drug resistance.



# Patient Related Factors

- **Poor adherence of dosage regimens**
- **Poverty**
- **Lack of sanitation concept**
- **Lack of education**
- **Self-medication**
- **Misconception**

- **Ensuring that patients are informed about the need to take the right dosage of the right antimicrobial requires action from prescribers, pharmacists and dispensers, pharmaceutical industry as well as the policy makers.**

# Environmental related factors

# Animal husbandry is a source of resistance to antibiotics.

- **Sub-therapeutic doses of antibiotics are used in animal-rearing for promoting growth or preventing diseases.**
- **This can result in resistant microorganisms, which can spread to humans.**

# Agriculture

# Aquaculture

# Horticulture

# Prescriber Related Factors

- **Inappropriate use of available drugs**
- **Increased empiric poly-antimicrobial use**
- **Overuse of antimicrobials (Available without prescription)**
- **Inadequate dosing**
- **Lack of current knowledge and training**

# Inappropriate use of medicines worsens drug resistance.

- **Inappropriate use of antimicrobials drives the development of drug resistance.**
- **Both overuse, underuse and misuse of medicines contribute to the problem.**

# A Guide to Antibiotic Prescribing

*Start smart:*

1 Do not prescribe[2] antibiotics in the absence of clinical evidence of bacterial infection, or for a self-limiting condition. Take time to discuss:

- why an antibiotic is not the best option
- alternative options, eg symptomatic treatment, delayed prescribing
- the views and expectations of the patient
- safety-netting advice: what the patient should do if their condition deteriorates.

- Empirical Treatment
- Definitive Treatment
- Prophylactic Treatment

# Before prescribing empirical antibiotics….

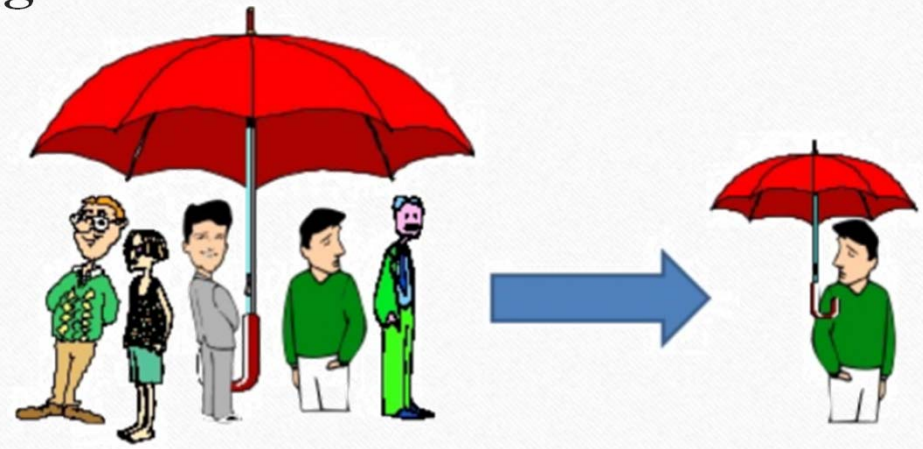
- **Clinician should first determine whether antimicrobial therapy is warranted for a given patient.**
- **Is antimicrobial agents indicated on the basis of clinical findings?**
- **Is it prudent to wait until such clinical findings become apparent?**
- **Can some simple bedside tests done to confirm your suspicion?**
  - **Microscopy**
  - **Gram staining**

# Empirical Antimicrobial Selection

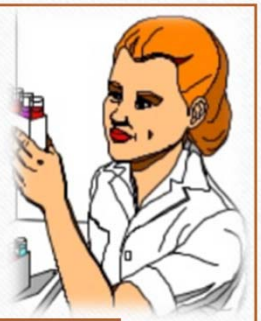
- **What are the likely etiologic agents for the patient's illness?**
- **Is there clinical evidence (from clinical trials) that antimicrobial therapy will confer clinical benefit for the patient? (Evidence based medicine)**

# Definitive Treatment

- **Can a narrower spectrum agent be substituted for initial empiric drug?**



# Principles of antibiotic selection



2 Take microbiological samples *before* prescribing,[1] especially for:
- hospital in-patients: review your prescription as soon as MC&S result is available
- recurrent or persistent infection
- non-severe infection: consider if your prescription can wait for MC&S results.

3 Follow local guidelines first: best practice is informed by local epidemiology and sensitivities.

4 Consider benefit and harm for each individual patient:

- *Allergies:* clarify the patient's reaction—the true incidence of penicillin allergy in patients who report that they are allergic is <10%. In those with a confirmed penicillin allergy, cross-reactivity with 3rd-generation cephalosporins and carbapenems is possible but rare (<1%).
- Dose adjust for renal function and weight: use ideal body weight in extremes of BMI (or ideal weight plus a % of excess weight—see local guidelines).
- Check for medication interactions.
- In pregnancy and lactation, see p17.

5 Prescribe the shortest effective course. Most antibiotics have good oral availability. Use IV antibiotics only if in line with local or national (sepsis) guidelines.

# Route of administration

- **The route of administration of an antibacterial often depends on the severity of the infection.**
- **Life threatening infections require intravenous therapy.**
- **Antibacterials that are well absorbed may be given by mouth even for some serious infections.**
- **Parenteral administration is also appropriate when the oral route cannot be used (e.g. because of vomiting) or if absorption is inadequate.**

# Duration of therapy

- **Duration of therapy depends on the nature of the infection and the response to treatment- can be assessed by procalcitonin level.**
- **Courses should not be unduly prolonged because they encourage resistance, they may lead to side-effects and they are costly.**

# Duration of therapy

- **However, in certain infections such as tuberculosis or osteomyelitis it may be necessary to treat for prolonged periods.**
- **Conversely a single dose of an antibacterial may cure uncomplicated urinary-tract infections. The prescription for an antibacterial should specify the duration of treatment or the date when treatment is to be reviewed.**

*Then focus:*

Review the clinical diagnosis and continuing need for antibiotics at 48h for all in-patients and all patients prescribed IV antibiotics:

- *Stop* antibiotics if there is no evidence of infection.
- Switch from IV to *oral* whenever possible.
- Change to a *narrower spectrum* antibiotic whenever possible.
- Continue regular clinical *review* whilst antibiotics are prescribed.

# Hospital Acquired Drug Resistance

- **Hospital Antibacterial Policy**
- **Hospital Antibiogram**
  - **Hospital specific antibacterial resistance pattern**
  - **Identification of potential pathogen most likely to cause infection**
  - **Previous antibacterial therapy**
- **Prescription auditing**

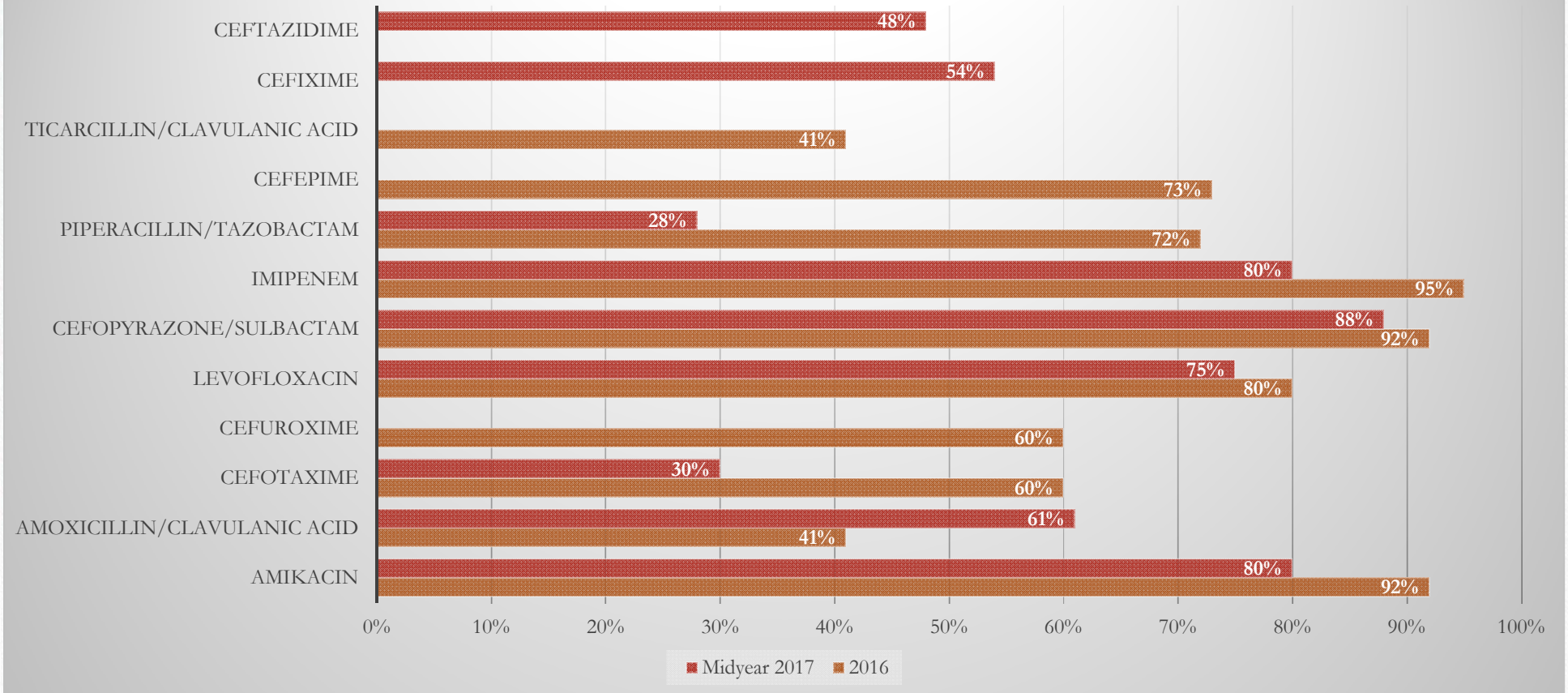
# NYGH Antibiogram

# Growth of organisms in cultured specimens from Medical ward, NYGH (2016 & Midyear 2017)

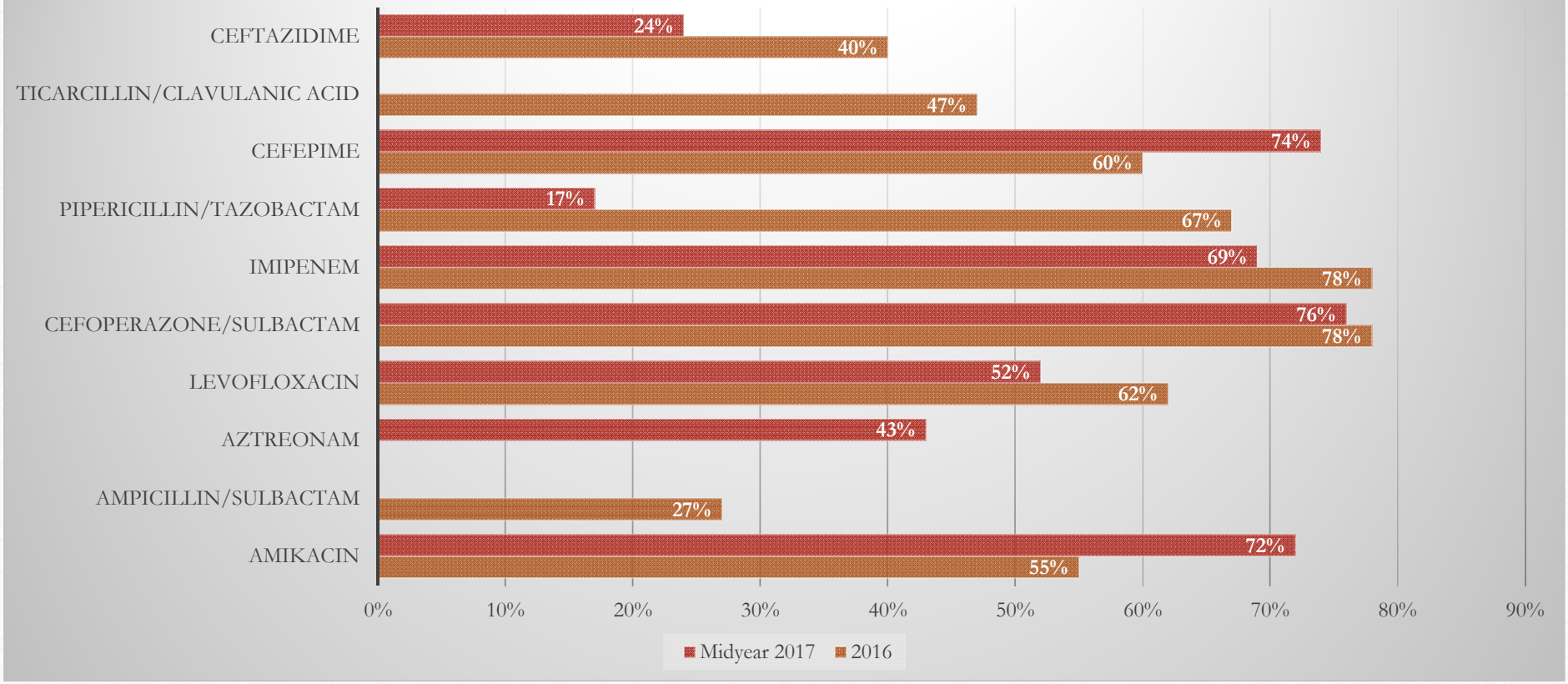
| Organisms (2016) | No of culture positive specimens |
|---|---|
| E coli | 81 |
| Klebsiella | 212 |
| Pseudomonas species | 45 |
| Proteus species | 3 |
| Acinetobacter | 0 |
| Staphlococcus species | 15 |

| Organisms (Midyear 2017) | No of culture positive specimens |
|---|---|
| E coli | 54 |
| Klebsiella | 103 |
| Pseudomonas species | 41 |
| Proteus species | 1 |
| Acinetobacter | 4 |
| Staphlococcus species | 12 |
| Citrobacter species | 22 |
| Enterobacter species | 1 |
| Coliform | 4 |

# AST profile of Klebsiella species susceptible percentage



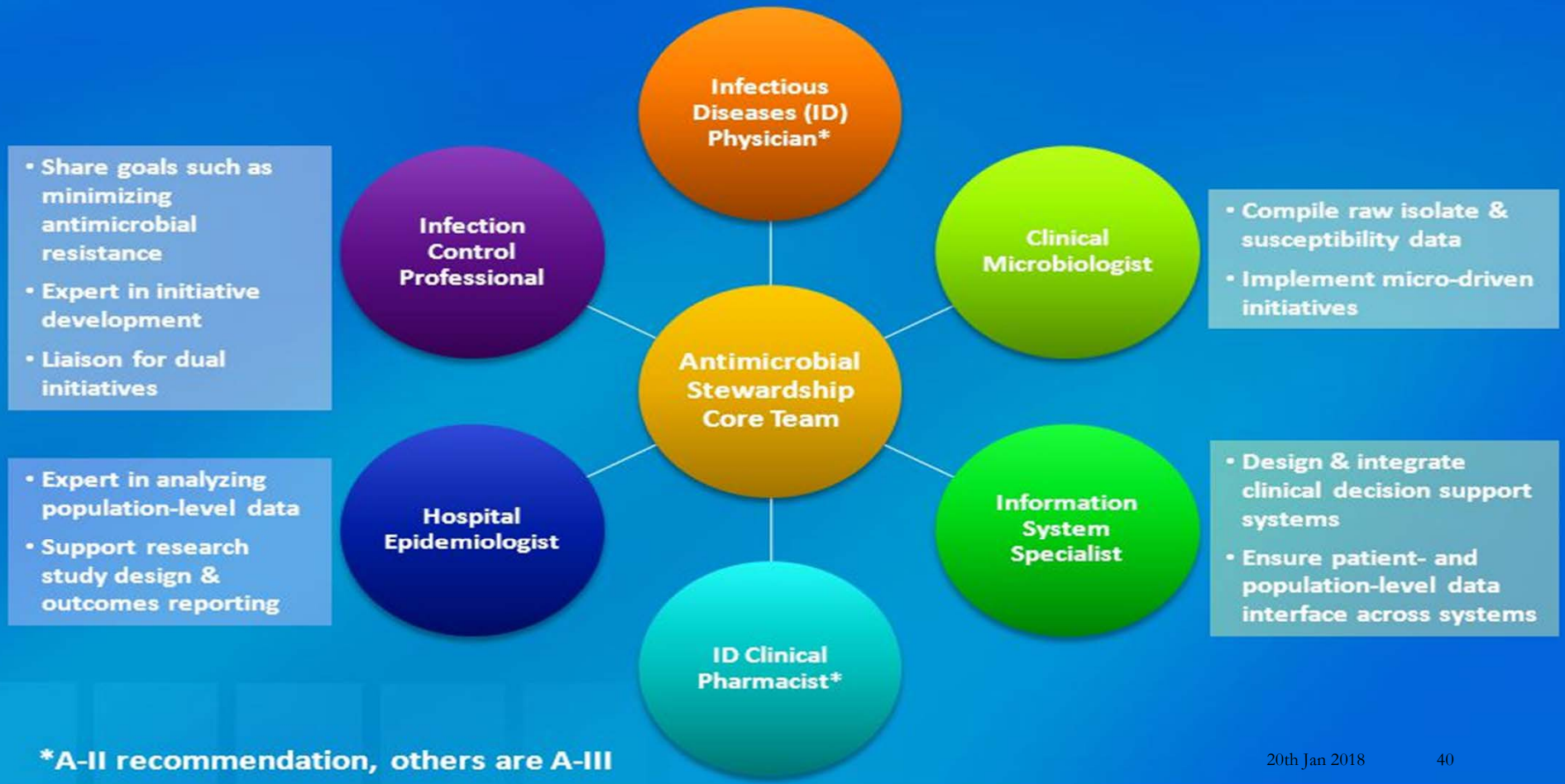
# AST profile of Pseudomonas species susceptible percentage



# Antibiotic Stewardship


- **Antibiotic stewardship refers to a set of coordinated strategies to improve the use of antimicrobial medications with the goal of enhancing patient health outcomes, reducing resistance to antibiotics, and decreasing unnecessary costs.**

# Antimicrobial Stewardship Core Team




*A-II recommendation, others are A-III



1. Dellit TH, et al. Clin Infect Dis 2007; 44: 159-177.

# Important Factors to be considered

- Commitment
- Surveillance
- Research
- Infection Control
- Rational Prescribing
- Drug Quality


COMBAT
DRUG
RESISTANCE
NO COMMITMENT
WEAK SURVEILLANCE
POOR DRUG QUALITY
IRRATIONAL DRUG USE
NO INFECTION CONTROL
LACK OF RESEARCH
DRUG RESISTANCE
THANK YOU!!
No action today,
no cure tomorrow