Antimicrobial Resistance and Antimicrobial Stewardship in Health Care Settings

Module 14


I AM NOT BLIND.
IF ANTIBIOTIC RESISTANCE
WERE A BIG ISSUE
I WOULD HAVE SEEN
IT BY NOW
ANTIBIOTIC RESISTANCE
MINISTRY OF HEALTH

Objectives

- Define antibiotic and antibiotic resistance
- Describe AMR in health care setting
- Describe the interface between IPC and AMR
- Identify the strategies to prevent the emergence of AMR.
- Describe the principles for antibiotic stewardship program
- Define antimicrobial stewardship and describe its goals
- Describe the scope of AMS and describe strategies for establishing AMS program in health care settings

Introduction to AMR

Antimicrobial resistance is the product of a complex interaction of multiple factors of which selection of resistant pathogens by antimicrobial use is probably the most important

- Ability of a microbe strain to survive and/or multiply despite the administration and absorption of a drug given in doses equal to or higher than those usually recommended but within tolerance of the subject

Definition

- Antibiotics are powerful medicines that fight bacterial infection

- When pathogens develop resistance to the antibiotics, is termed ***Antibiotic Resistance***.

AMR & IPC

Spread of AMR genes is facilitated by

- Interspecies gene transmission
- Poor sanitation and hygiene
- Appearance of successive resistant clones.

Current AMR Status

- Drug resistance is increasing globally
  - Diseases are becoming resistant to drugs faster than we can develop new treatments
  - Infections that are easily managed are transforming to life threatening ones
    - Malaria
    - TB
    - Strep pneumonia

Evolution of Antibiotic Resistance

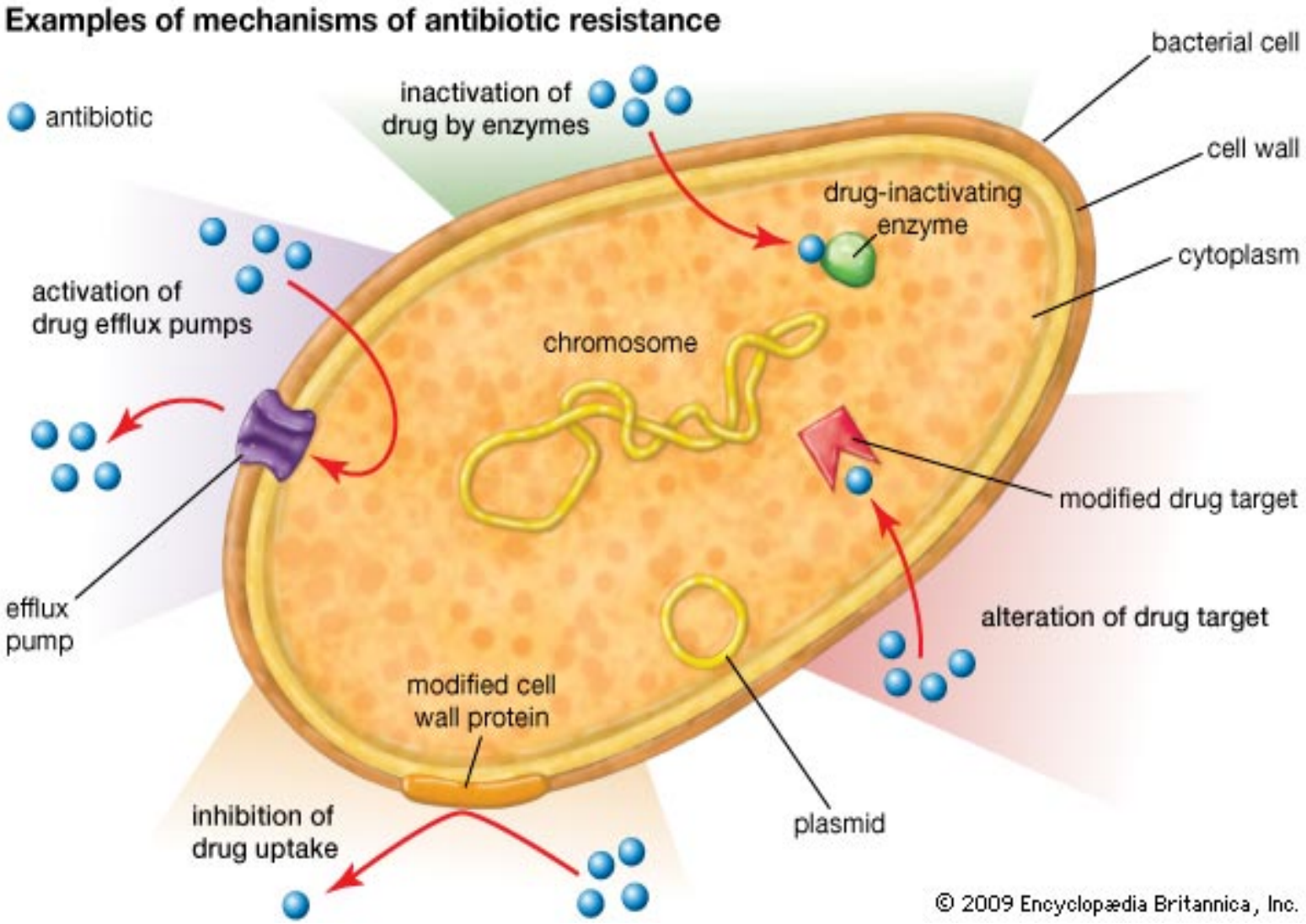
Antibiotic	Year Deployed	Resistance Observed
Sulphonamides	1930s	1940s
Penicillin	1943	1946
Streptomycin	1943	1959
Chloramphenicol	1947	1959
Tetracycline	1948	1953
Erythromycin	1952	1988
Vancomycin	1956	1988
Methicillin	1960	1961
Ampicillin	1961	1973
Cephalosporins	1960s	Late 1960s

The Burden of AMR in Kenya

	Study site	mid-80s	mid-90s	2001	2002	2003	2005	2006	2009
Streptococcus pneumonia	**Nairobi**								
Penicillins		**25%**				**43%**			
Cotrimoxazole						**50%**			
Haemophilus influenza type B	**Kilifi**								
Amoxicillin + chloramphenicol				**50%**	**32%**				
Cotrimoxazole					**66%**				
Non-typhi Salmonella	**Western Kenya**								
Ampicillin			**45%**				**94%**		
Cotrimoxazole			**45%**				**67%**		
Fluoroquinolones							**53%**		
Ampicillin + cotrimoxazole			**45%**						
Neisseria gonorrhoea	**Nairobi**								
Fluoroquinolones			**31%**			**42%**			**53%**

How Does Resistance arise?

- As a consequence of mutations in microbes and selection pressure from antibiotic use that provides a competitive advantage for mutated strains.
- The presence of antimicrobials in their environment in higher concentrations increases the pressure by natural selection.
- Suboptimum antimicrobial doses aid step-wise selection of resistance.
- Bacteria either have natural resistance to drugs, or they can develop it.
- In many cases, resistance to a certain drug from a class leads to resistance to all other drugs in that class.


Examples of mechanisms of antibiotic resistance
antibiotic
inactivation of drug by enzymes
bacterial cell
cell wall
drug-inactivating enzyme
cytoplasm
activation of drug efflux pumps
chromosome
modified drug target
efflux pump
alteration of drug target
modified cell wall protein
plasmid
inhibition of drug uptake
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Drivers of AMR

- AMR is driven by
  - Prescribers and patient behaviour
  - Health System
  - Non-human use of antimicrobials
  - Technological developments

Factors influencing prescriptions

- Patient expectation and satisfaction.
- Severity.
- Duration of illness
- Parents demands.
- Concerns about secondary bacterial infection.
- Time.

Behavioral

- Patient
  - Self medication
  - Incomplete dosing (cost?)
  - Access of medicines from informal dispensers
- Prescriber /providers
  - Lack of information to support drug selection
  - Incentives / influence from marketers

Drivers of AMR

1. Overuse

Physicians

↓

Incorrect diagnosis and Prescribing Antibiotics for Viral (Seasonal Flu) infections, 2 or more antibiotics together, unnecessary long courses of antibiotics

↓

Kills Resident Bacteria (Normal flora)

↓

Some survive

↓

Antibiotic resistant genes

↓

Passing of these genes to Pathogenic bacteria

↓

Antibiotic resistance

Drivers of AMR

2. Misuse

Patients

↓

Not finishing full course of antibiotics

↓

Misuse

↓

Leaving 1 or 2 doses

↓

Some bacteria not killed

↓

Resistance developed for future antibiotic treatment

Drivers of AMR

3. OTC antibiotics

Antibiotics

↓

Available as OTC medicines

↓

Inappropriate use

↓

Overuse or Misuse

↓

Antibiotic resistance

Drivers of AMR

4. Healthcare Workers

Hospital

↓

Healthcare Workers

↓

Not following infection control protocols

↓

Resistance transferred by bacteria swapping genes

Drivers of AMR

5. Hospitalized Patients

Hospital

↓

Immunocompromised Patients

↓

Exposed to Pathogenic organisms

↓

Increased use of different antibiotics

↓

Rapid development of Resistance

Drivers of AMR

6. Animal Feed

Animal feed

↓

Mixed with antibiotics to prevent infections and to promote growth

↓

Resistant organisms in animals

↓

Spread to Human

Non-human drug use of antibiotics

Use of antibiotics in animal health and agriculture

- Antibiotics used to
  - promote rapid growth and earlier marketing
  - Reduce incidence of disease thereby cut costs

Examples: Netherlands: 20% MRSA infections derived from animal strains

US: Use of Fluoroquinolones in poultry responsible for human resistance (banned 2005)

Antibiotics in animal feed now banned in Europe

Drivers of AMR

7. Antibiotics in food and water

Antibiotics found in beef cattle, pigs and poultry

↓

Drainage with antibiotics contaminates groundwater

↓

Same antibiotics mixed with municipal water systems

↓

antibiotics food and drinking water

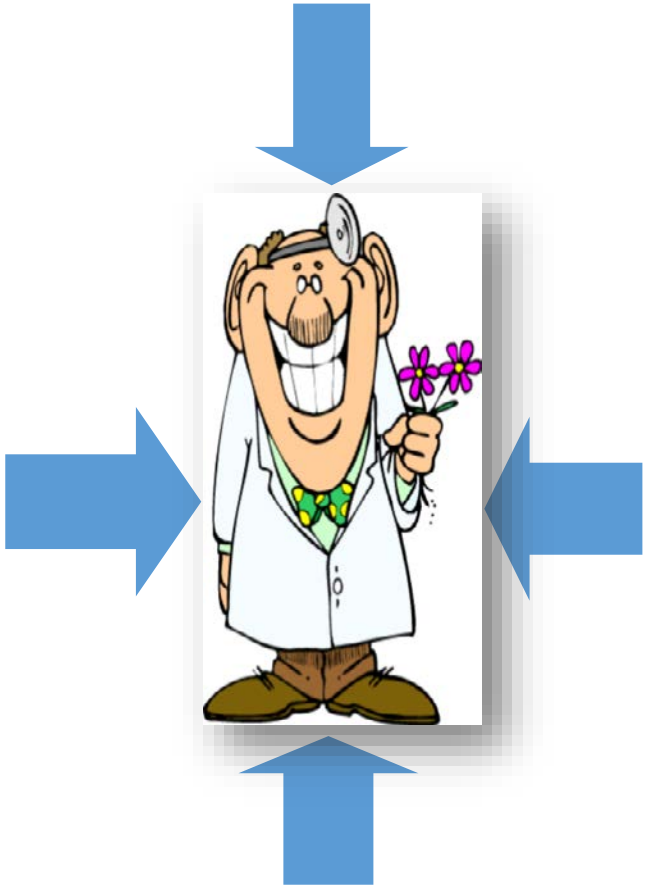
↓

promote bacterial resistance.

Peer groups /

prescribing and pharmacy advisors

Pharmaceutical representatives



Patients' or Parent's demands

Doctor's aspirations

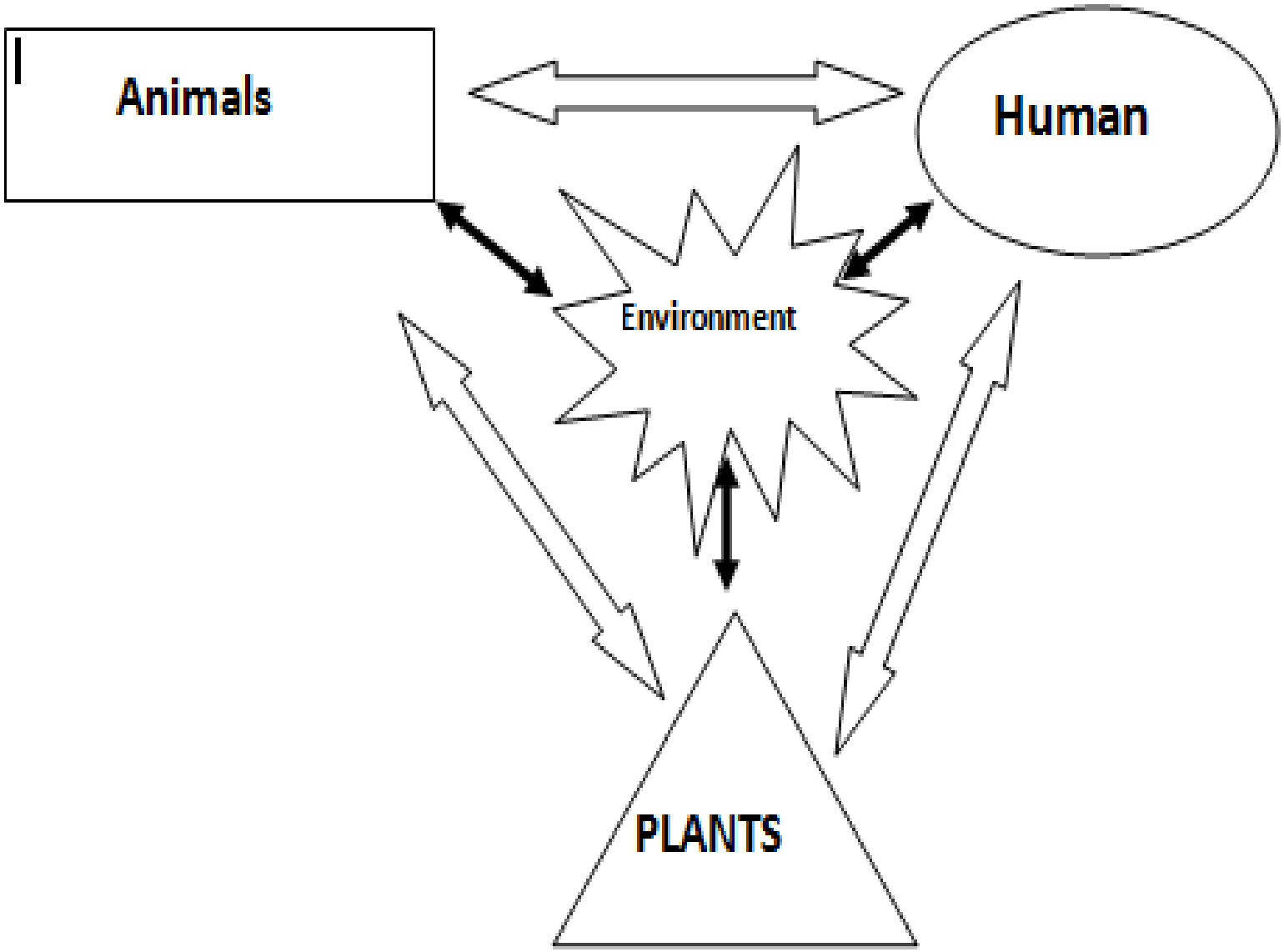
Regulatory control mechanisms

Hospital experts,

Formularies and guidelines

Health systems challenges

- Insufficient or poorly trained health care workers
- Poor drug resistance surveillance
  - Drug resistance data very limited
- Poor infrastructure
- Lack of regulation and enforcement
  - Pharmaceuticals supply chain
  - Drug quality & efficacy / post market surveillance



AMR Cycle

Dangers of AMR

- Kills
- Hampers infectious diseases control
- Threatens a return to a pre-antibiotic era
- Increases health care costs
- Jeopardizes health-care gains to society
- Threatens health security
- Damages trade and economies

Health and Economic Consequences

- Short term consequences
  - Borne by the patient/

- Long term
  - Borne by ALL
    - Reduced number of effective drugs
    - Increased cost of health care delivery

Health consequences of Resistance

- TB
  - Killed 1.6 million people in 2006
  - Treatment: 4 drugs, 6-9 months

- MDR- and XDR- TB
  - 2007: 50,000 cases were XDR-TB
  - Sept 2009: Cases of XDR-TB recorded in at least 57 countries

Economic consequences of resistance

	Avg. cost 1st line therapy (USD)	Avg. cost 2nd line therapy (USD)
HIV/AIDS	90 USD /patient/year	1,214 USD /patient/ year
TB	20 USD /course	3,500 USD/ course
MALARIA	0.25 – 0.35 USD /adult course	5 – 10 USD / adult course

Technological developments

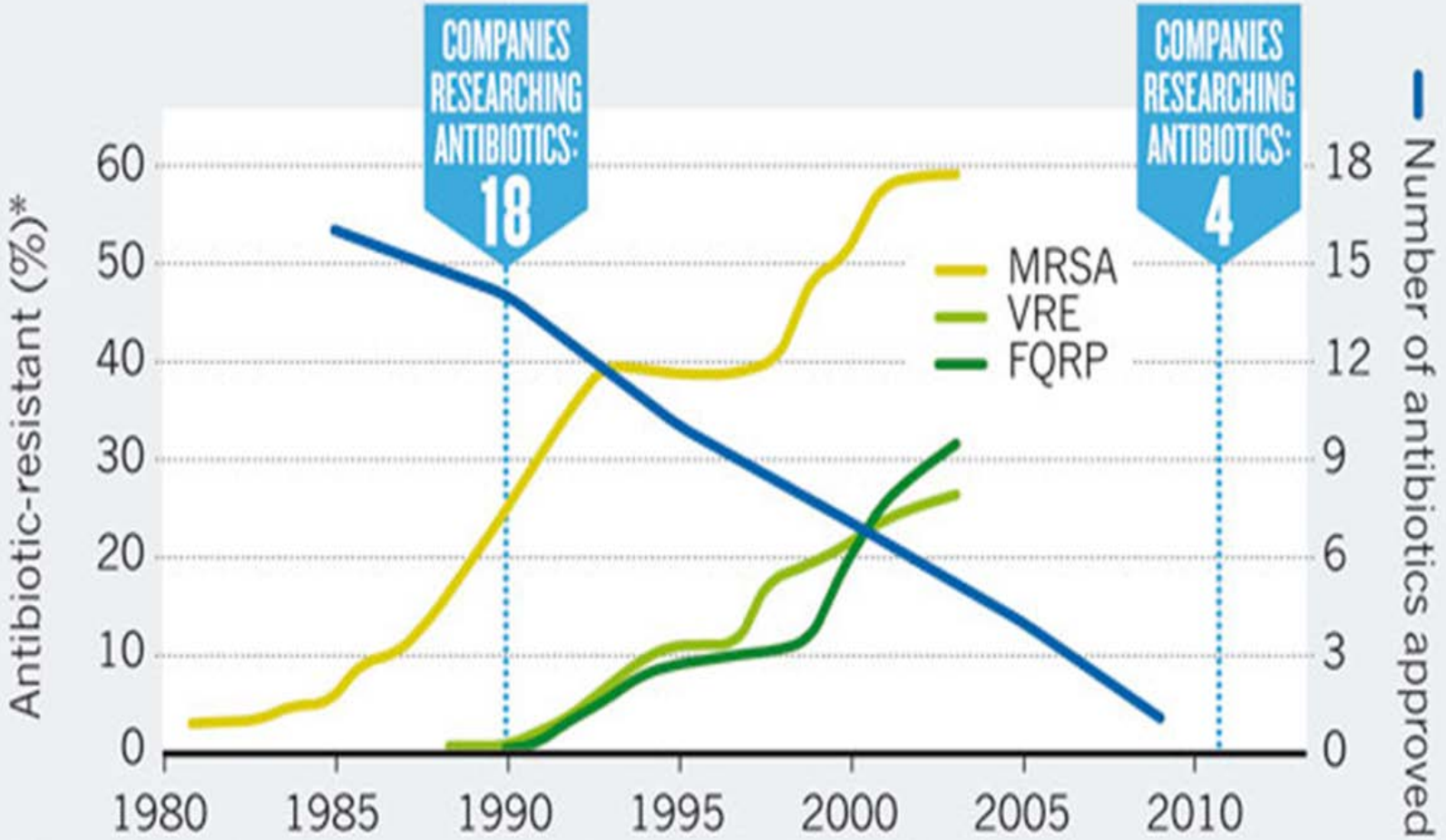
Drug resistance is a naturally occurring phenomenon

Technological innovations to manage AMR must also be developing R&D must focus on developing these technologies

Challenges: Profit margins, Motivations and Commercial rationale

A PERFECT STORM

As bacterial infections grow more resistant to antibiotics, companies are pulling out of antibiotics research and fewer new antibiotics are being approved.



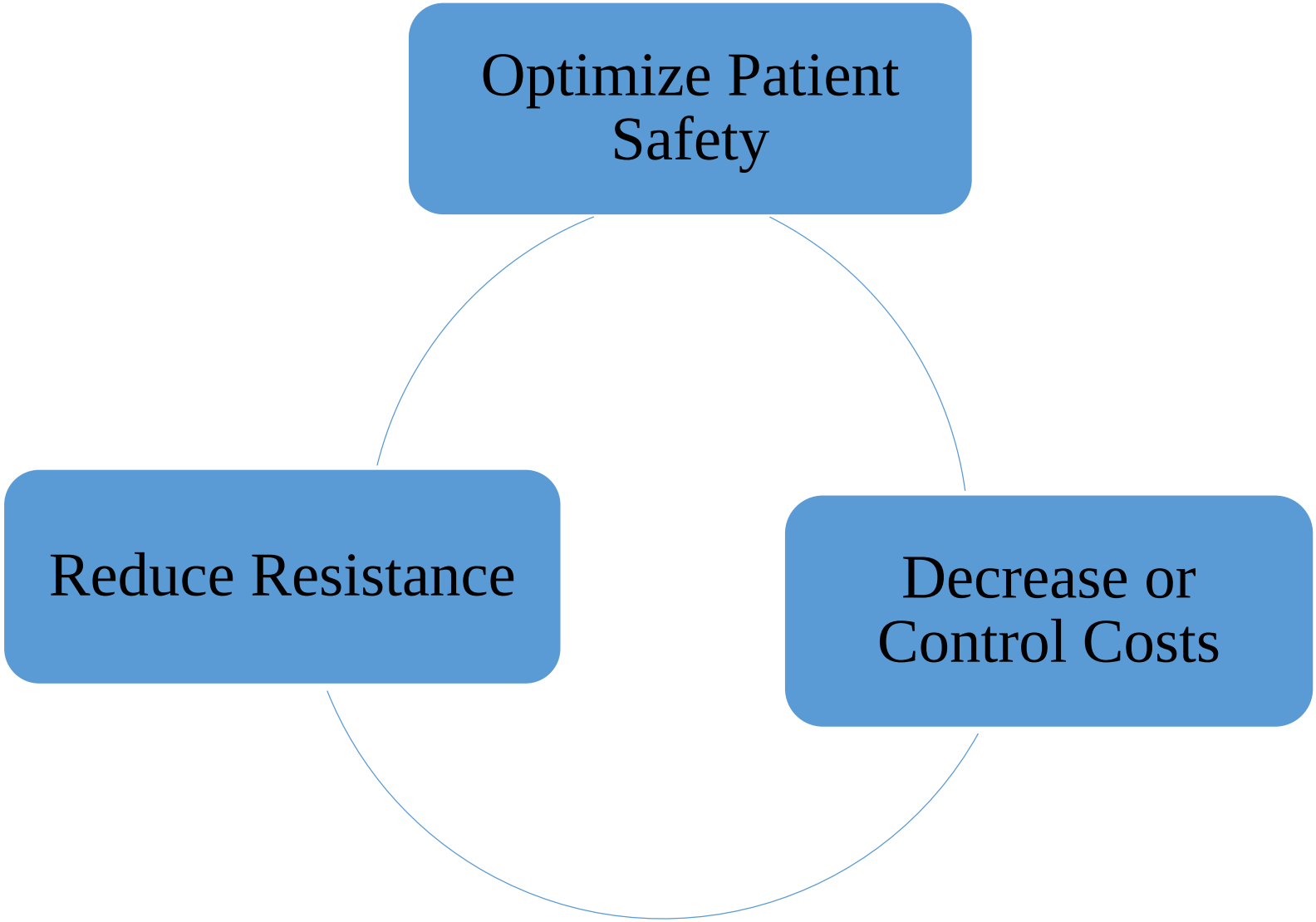
*Proportion of clinical isolates that are resistant to antibiotic. MRSA, methicillin-resistant *Staphylococcus aureus*. VRE, vancomycin-resistant *Enterococcus*. FQRP, fluoroquinolone-resistant *Pseudomonas aeruginosa*.

Antimicrobial Stewardship in Health Care Settings

Introduction to AMS

- Definition
  - AMS refers to the multifaceted approach (including policies, guidelines, surveillance, prevalence reports, education and audit of practice) that healthcare organizations have adopted to optimize prescribing
- AMS programs in hospitals seek to optimize antimicrobial prescribing in order to
  - improve individual patient care
  - reduce hospital costs
  - slow the spread of antimicrobial resistance
- Overarching role is to change and direct antimicrobial use at a health care institution

Goals of AMS


Optimize Patient Safety
Decrease or Control Costs
Reduce Resistance

Benefits of an AMS program

- Reduction in 20%- 40% of antimicrobial use, with savings of USD 200,000–USD 900,000.
- Promote patient safety and reduction in mortality
- Minimize drug-related adverse events
- Reduction in Clostridium difficile infections
- Reduction of HAIs, due to a short hospital stay.
- Reduction of global bacterial resistance
- Provide the infrastructure to preserve antimicrobials
- Can be implemented in any healthcare setting – from the smallest to the largest

IDSA Guidelines: Elements of a successful stewardship program

- Comprehensive program
  - Active monitoring of resistance
  - Fostering of appropriate use
    - Often used as a surrogate marker for impact on resistance
  - Collaboration of effective infection control to minimize secondary spread of resistance

Dellit TH. Clin Infect Dis 2007 Jan 15;44(2):159

IDSA Guidelines: **Collaborative effort-**Multidisciplinary team

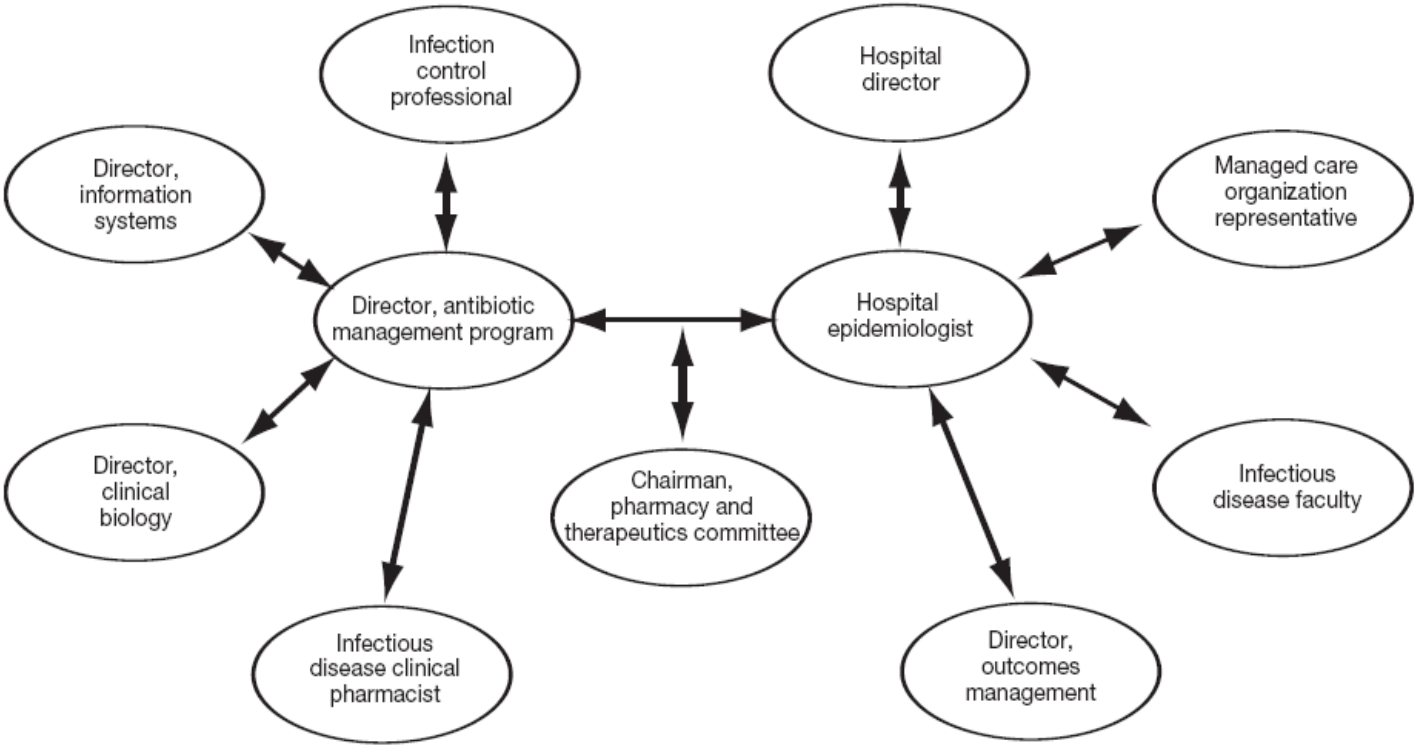


Figure 2. Multidisciplinary members of the antimicrobial stewardship team. (Adapted from reference 6.)

Rybak M. Pharmacotherapy; 27:131S

Strategies for and AMS program

- Education and Guideline Implementation Strategies
- Formulary and Restriction Strategies
- Prospective Audit with Intervention and Feedback (Review and Feedback Strategies)

Antimicrobial Stewardship Strategies summary

Right drug/dose/duration

Obtain cultures/avoid empiric prescribing if possible

Adjust empiric prescribing/stop antibiotic based on lab results

Establishing an AMS program

Considerations

- Leadership
- Scope
- Ownership
- Location
- Tools
- Implementers
- Review and feedback

Scope of AMS program

In setting up an AMS program:

1. Define what the institution considers appropriate antimicrobial use
2. Determine the scope of the program
   - Hospital-wide
   - Departmental
   - Unit
   - Critical care unit

Core elements of AMS

- **Leadership Commitment**: Dedicating necessary human, financial and information technology resources

- **Accountability**: Appointing a single leader responsible for program outcomes. Experience with successful programs show that a physician leader is effective

- **Drug Expertise**: Appointing a single pharmacist leader responsible for working to improve antibiotic use.

Core elements of AMS

- **Action**: Implementing at least one recommended action, such as systemic evaluation of ongoing treatment need after a set period of initial treatment (i.e. “antibiotic time out” after 48 hours)
- **Tracking**: Monitoring antibiotic prescribing and resistance patterns
- **Reporting**: Regular reporting information on antibiotic use and resistance to doctors, nurses and relevant staff
- **Education**: Educating clinicians about resistance and optimal prescribing

Barriers to AMS

Description	Barriers	Possible solutions
Human resources	Poor availability of different specialists to create and maintain a functional AS team.	Raise awareness of hospital directors/ managers/policy makers about benefits of AS.
	Available specialists overloaded with other inherent tasks. AS activities generally are not paid.	Training of relevant medical doctors, clinical microbiologists and pharmacists. Make AS standard of care and hospital accreditation and foresee remuneration for AS activities

Description	Barriers	Possible solutions
Knowledge/ education of rational antibiotic use among health care professionals	Suboptimal undergraduate training on microbiologic, ecologic and pharmacologic aspects of antibiotic resistance.	Revision of the curricula related to antibiotic resistance in Schools of Medicine, Pharmacy and others involved.
	Limited continuous medical education programs for physicians, microbiologists and pharmacists.	Provide and update continuous medical education programs certified by respected institutions
	Many physicians receive medical information mainly from companies. Prescriptions and drug selection often influenced by this information and gifts	Authorities should control and supervise promotional activities of pharmaceutical companies.

Description	Barriers	Possible solution
Prescribing practices	Therapeutic freedom' is highly valued among many	Initial training followed by continuous education, audit and feedback
	Lack of stable drug supply	Respected essential drugs list, hospital formulary. Generate awareness among prescribers and pharmacists of the importance of stable and consistent drug supply

Description	Barriers	Possible solutions
Guidelines and recommenda-tions (clinical decision support)	Multitude of guidelines present, often outdated or inappropriate Lack of ownership on local guidelines Lack of access to up-to-date information	Selection of guidelines most suitable to the institution and adaption. Revision of local guidelines by the AS team jointly with opinion leaders among local prescribers Provide open access templates for common infections that can be locally adapted
	Suboptimal microbiology laboratory diagnostic tools.	Improvement of laboratory performance Introduction of relevant near-patient tests Simple testing guidance for laboratories and quality assurance

Description	Barriers	Possible solutions
Infection control (IC)	Poor availability of medical staff and nurses for IC team Poor interest, knowledge and compliance of health care workers basic IC practices.	Education of health care workers and hospital management on nosocomial infections and role of infection control activities
	IC activities generally have no budget Structural deficiencies of the institution (i.e, scarcity of isolation rooms, lack of basic supplies for hand hygiene, patient care articles)	Provision of resources to maintain a fully functional IC team. Revision and modification of main structural and supply caveats.

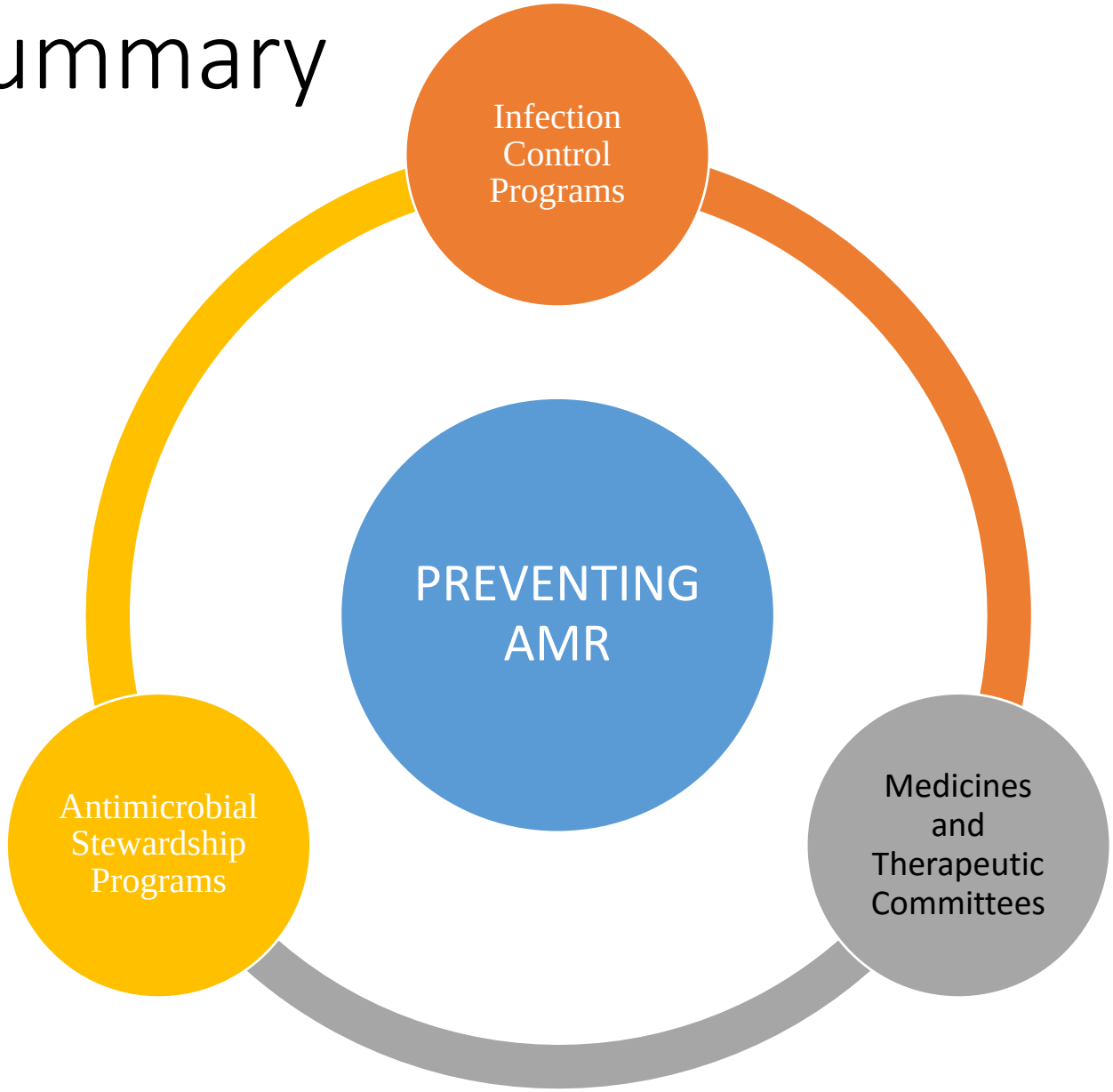
Good Practice on Antimicrobial Use

- Appropriate investigations are recommended for all infections. These are necessary for diagnosis, treatment and follow up.
- Microbiological samples should be collected before initiating antimicrobial therapy.
- The hospital formulary is to be used while choosing antimicrobial therapy.
- Check for factors that will affect drug choice and dose such as renal and hepatic dysfunction, drug interactions and hypersensitivity reactions.

Good Practice on Antimicrobial Use

- Ensure that appropriate dose is prescribed; if uncertain consult the clinical pharmacist or check in the hospital formulary.
- The need for antimicrobial therapy should be reviewed regularly (every 72 hours).
- For most infections 5 to 7 days of antimicrobial therapy is sufficient

Summary


Infection Control Programs
PREVENTING AMR
Antimicrobial Stewardship Programs
Medicines and Therapeutic Committees

In summary:
infection control and prudent use of antimicrobial agents are not only related, but also pivotal steps to stop both selection and dissemination of Multi Drug Resistant organisms.