Rational use of Antibiotics

Contents

- What is Rational use of antibiotics?
- What are the factors influence for irrational antibiotic use (IAU)?
- What are the consequences of IAU?
- How can we improve rational antibiotic use?
- Antibiotic stewardship

What is an antibiotic?

AB are chemical substances **obtained from microbes/microorganisms**

(bacteria, fungi, actinomycetes) that able to **inhibit or eradicate** the **growth**

of the **other microorganisms.**

What is rational use of a drug?

The rational use of drugs requires that patients receive medications **appropriate to their clinical needs**, in **doses** that meet their own **individual requirements** for an **adequate period** of time, and at the **lowest cost** to them and their community.

WHO conference of experts Nairobi 1985

Inappropriate use of antibiotics is a worldwide problem

- **>50%** of all medicines are **prescribed**, **dispensed** or **sold inappropriately**
- **½** of all patients **fail t**o take **medicines correctly**
- **>50%** of all **countries** do **not** implement **basic policies** to promote rational use of medicines
- In **developing countries**, **less** than **40%** of patients in the **public** sector and **30%** in the **private** sector are treated according to **clinical guidelines.**

Antibiotic Misuse - SEA

- Use of antibiotics in the SEA Region, (WHO data)

  50% of viral URTI are treated unnecessarily with **antibiotics**

  Only **53%** of **pneumonia** cases receive an **appropriate antibiotic**

  54% of **acute diarrhoea** cases are treated **unnecessarily** with **antibiotics**

  40% of prescribed **antibiotics** are prescribed in **under-dose**

A multi centre laboratory study of Gram negative bacterial blood stream infections in Sri Lanka

ARSP Working Group, The Sri Lanka College of Microbiologists

(Index words: antibiotic sensitivity, sepsis, antibiotic resistance)

Abstract

Introduction Data on causative agents and antibiotic susceptibility patterns of blood stream infections in Sri Lanka is scarce. Information on trends of antibiotic resistance is necessary for the prescribers to treat patients effectively and policy makers to develop policies and guidelines.

Objectives To lay the foundation for a national data base on antimicrobial resistance in Sri Lanka.

Methods A prospective study was carried out in seven hospitals to study the Gram negative aetiological agents and their susceptibility patterns in patients suspected of having bacteraemia. We reviewed 817 patients with clinically significant blood cultures including both adults and children.

Results Data were complete for analysis in 733 Gram negative isolates only. Of the 733 isolates, 488 were from adults (> 12 years), 109 were from children (1-12 years) and 136 were from infants (<1 year). Intensive care units represented 18.4% of the isolates (123 adult patients and 27 paediatric patients). The highest number of isolates (33.7%) was from patients with septicaemia of unknown origin. Enteric fever, pyelonephritis and respiratory tract infections accounted for 20% of the isolates. Bacteraemia with underline malignancies were responsible for 24.5% of infections. *Salmonella paratyphi* A was the commonest cause of enteric fever in adults with 92% resistance to ciprofloxacin. The prevalence of extended spectrum beta lactamase (ESBL) producing *Escherichia coli* and *Klebsiella pneumoniae* was high in this study population.

Conclusions It is essential to introduce multidisciplinary interventions to reduce the inappropriate use of antibiotics to increase the lifespan of precious antibiotics. Introduction of a National antibiotic policy with strict implementation and a well-planned stewardship programme is essential to control antimicrobial resistance in our country.

Ceylon Medical Journal 2013; **58**: 56-61

Conclusions

It is essential to introduce **multidisciplinary interventions** to reduce the **inappropriate** use of **antibiotics** to increase the lifespan of precious antibiotics.

What are the factors influence for irrational antibiotic use?


Informational
Personal
Knowledge deficits
Unbiased information
Acquired habits
Influence of industry
Cultural beliefs
DRUG USE
Interpersonal
Workload & staffing
Patient demand
Workplace
Infra-structure
Authority & supervision
Relation with peers
Workgroup

Determinants of irrational antibiotic use

- Lack of provider knowledge

  - insufficiently qualified, supervised or supported

- Prescriber habit (guidelines versus habit)

- Poor availability information such as clinical guidelines

- Lack of continuing medical education and supervision in prescribing

Determinants of irrational antibiotic use

- Excessive pharmaceutical promotion

  - emphasising use of the medicines and

  - underplaying the negative consequences (SE, antimicrobial R)

Determinants of irrational antibiotic use

- Very short consultation time (1 minute)

  ? proper diagnosis

- Very short patient-dispenser interaction time (seconds)

  ?explain to patients how to take their medicines

- Peer pressure

  fear to be seen prescribing differently to their colleagues

Determinants of irrational antibiotic use

- Patient demand
- Lack of diagnostic support services such as laboratory services
- Poor infrastructure inability to follow-up of patients
- Economic incentives

  gain income from dispensing or selling the medicines
- Inappropriate medicines supply (appropriate ones are not)

What are the consequences of irrational antibiotic use?

Consequences of inappropriate antibiotic use

1. Antimicrobial resistance

Source: WHO country data 2000-3

Misuse of antimicrobials contributes to antibiotic resistance

- **Tuberculosis -** 0-17 % primary multi-drug R
- **Gonorrhoea -** 5-98 % penicillin R in *N. gonorrhoeae*
- **Pneumonia and bacterial meningitis -** 0-70 % penicillin R in *S. pneumoniae*
- **Diarrhoea: shigellosis** - 10-90% ampicillin R, 5-95% cotrimoxazole resistance
- **Hospital infections -** 0-70% *S. aureus* R to all penicillins & cephalosporins

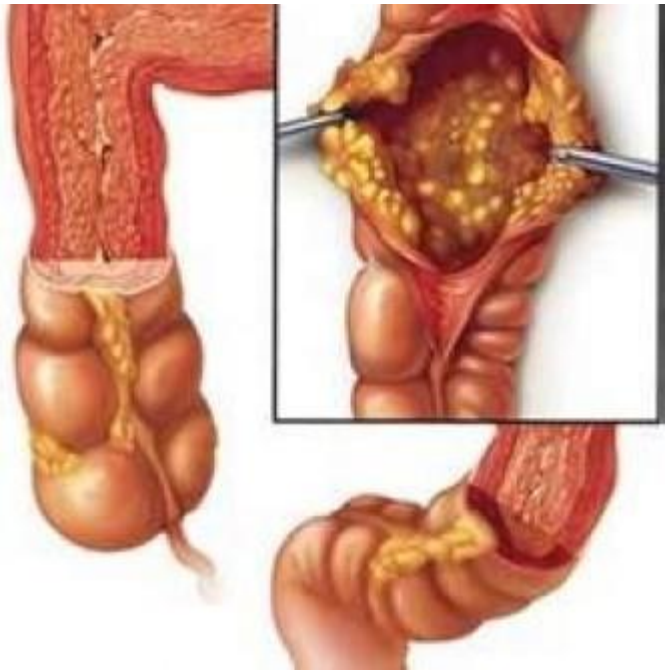
Limited Number of New Antibiotics to Combat Antibiotic Resistance

New Systemic Antibiotics Approved by the FDA

Consequences of inappropriate antibiotic use

2. Adverse drug events

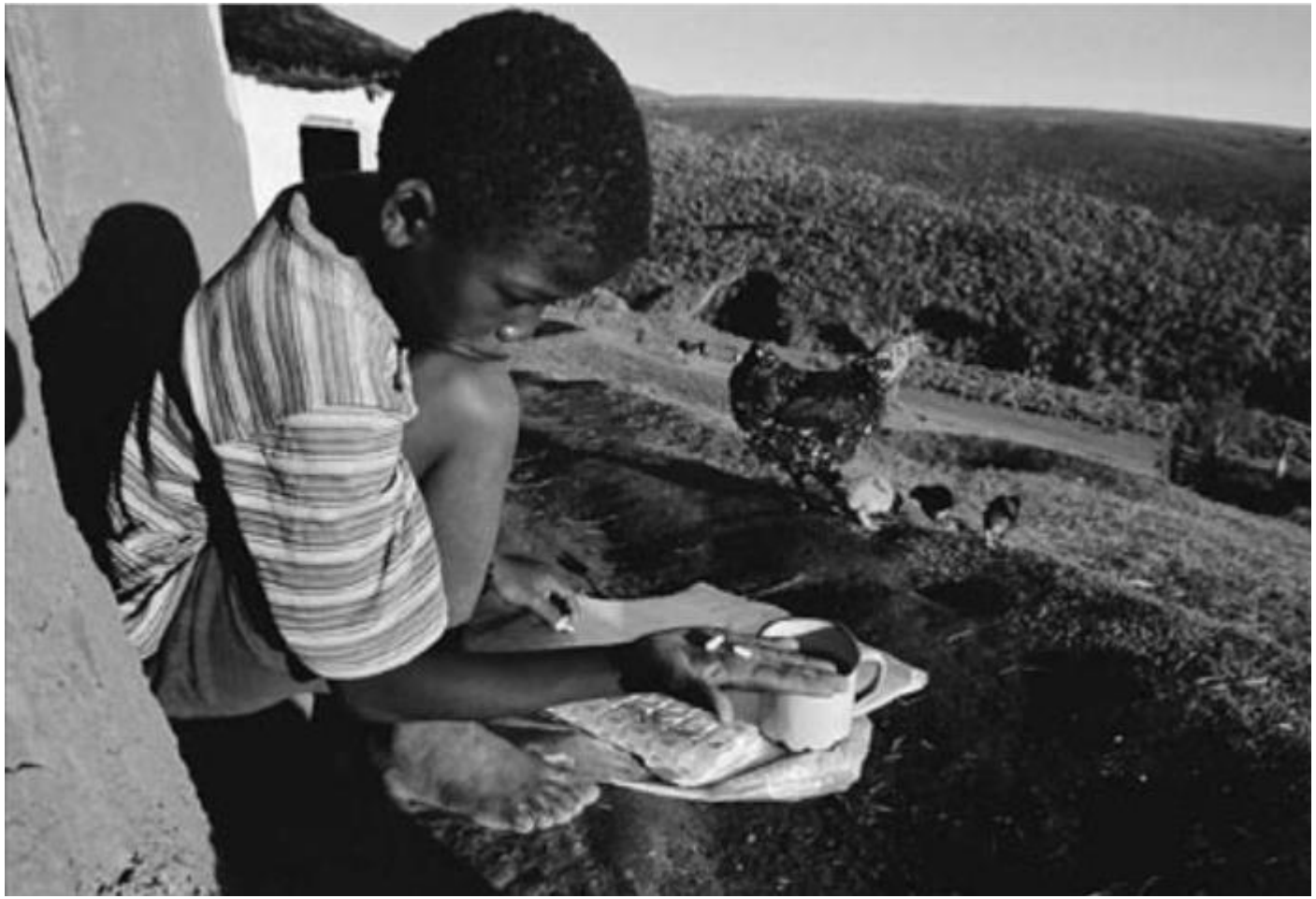
- Hypersensitivity/allergy
- Drug side effects
- *Clostridium difficile* infection
- Antibiotic associated diarrhea/colitis



Consequences of inappropriate antibiotic use

- Antimicrobial resistance
- Adverse drug reactions and medication errors
- Poor patient outcome
- Eroded patient confidence
- wastage of resources
- Increased health-care costs

How can we improve rational antibiotic use?



Ideal antibiotics criteria

1. Most **selective** & most **effective** to infected microorganisms
2. More bactericidal effect in the **site of action**
3. Effect - **not interfered** by body fluid, exudate, plasma protein or enzymes
4. **Minimal toxicity**
5. **Resistance** develops slowly
6. Given by **any route**
7. Reachable **cost**

Antibiotics are use in ----

- **Therapy (Eradication)**

  Definitive therapy

  Empiric therapy

- **Prophylaxis (Prevention in high susceptibility to get infection)**

  non surgical conditions

  surgical conditions

Definitive therapy

- Most effective, least toxicity and narrowest selection
- **Based on :**

  identification of bacteria

  sensitivity test

  interpretation in the content of the

  overall clinical picture

Empiric antibiotic therapy

- Giving AB directly without identification and sensitivity test of bacteria, but…… **obtain specimen for lab.**
- Empiric AB therapy based on **local epidemiological data**

  What is the pathogen **potentially** infected

  AB given based on **susceptibility** pattern

  Initiated after obtaining specimen

  Started with AM **combination** or **single BSAB**

Empiric versus of Directed Antibiotic Therapy

Empiric Therapy

- Infection not well defined
- Broad spectrum
- Multiple drugs
- More adverse reactions
- More expensive

Directed Therapy

- Infection well defined
- Narrow spectrum
- One, seldom two drugs
- Less adverse reactions
- Less expensive

Patient history

- Age → baby, child, adult, old age
- Immune system → immunocompromised! Who?
- Renal dysfunction → accumulation! How ?
- Hepatic dysfunction → metabolism! How ?
- Genetic factors → G6-PD. Attention, contraindication
- Pregnancy → teratogenic, embryogenic
- Lactation → vulnerable AB for new born

Common causes of failure of antibiotic therapy

DRUGS :

- inappropriate drug
- inadequate dose
- improper route of administration
- accelerated inactivation
- poor penetration

Common causes of failure of antibiotic therapy

HOST :

- poor host defense
- undrained pus
- retained infected foreign bodies
- crust/necrotic tissues

Pathogen

- drug resistance
  - super-infection
  - dual infection initially

Laboratory

- erroneous report of susceptible pathogen

Drug:

Antagonism:

1. **Inhibition of cidal activity by static agent**

   - Tetracyclines – Betalactam AB

2. **Induction of enzymatic inactivation**

   - Ampicillin - Piperacillin

Considerations before prescribing

1. Is an antibiotic necessary?
2. What is the most appropriate antibiotic?
3. What dose, frequency, route and duration?
4. How to improvethe chances that the tretament will be effective?

Is an antibiotic necessary?

- Useful only for the treatment of bacterial infections
- Not all fevers are due to infection
- Not all infections are due to bacteria
- No evidence that antibiotics prevent secondary bacterial infection in viral infection

Choice of antimicrobial agent

Based on three main factors:

- Etiological agent
- Patient-related factors
- Antibiotic-related factors

Antibiotic choice: etiological agent

- **Be careful of the identification of the agent by the laboratory**
  - Example: UTI
    - How was sample collected?
    - Contamination of sample is frequent, even in the best conditions
    - Consider the symptoms…
    - Consider the urinalysis…

Antibiotic choice: Etiological agent

- Most probable agents: based on epidemiology and clinical experience
- As per local antibiotic resistance data

  Resistance patterns vary

  - From hospital to hospital in the same country
  - From unit to unit in the same hospital
  - With time

Antibiotic choice: Patient-related factors

- Age
- Physiological factors
- Comorbidoties
- Genetic factors
- Pregnancy
- Site and severity of infection
- Allergies

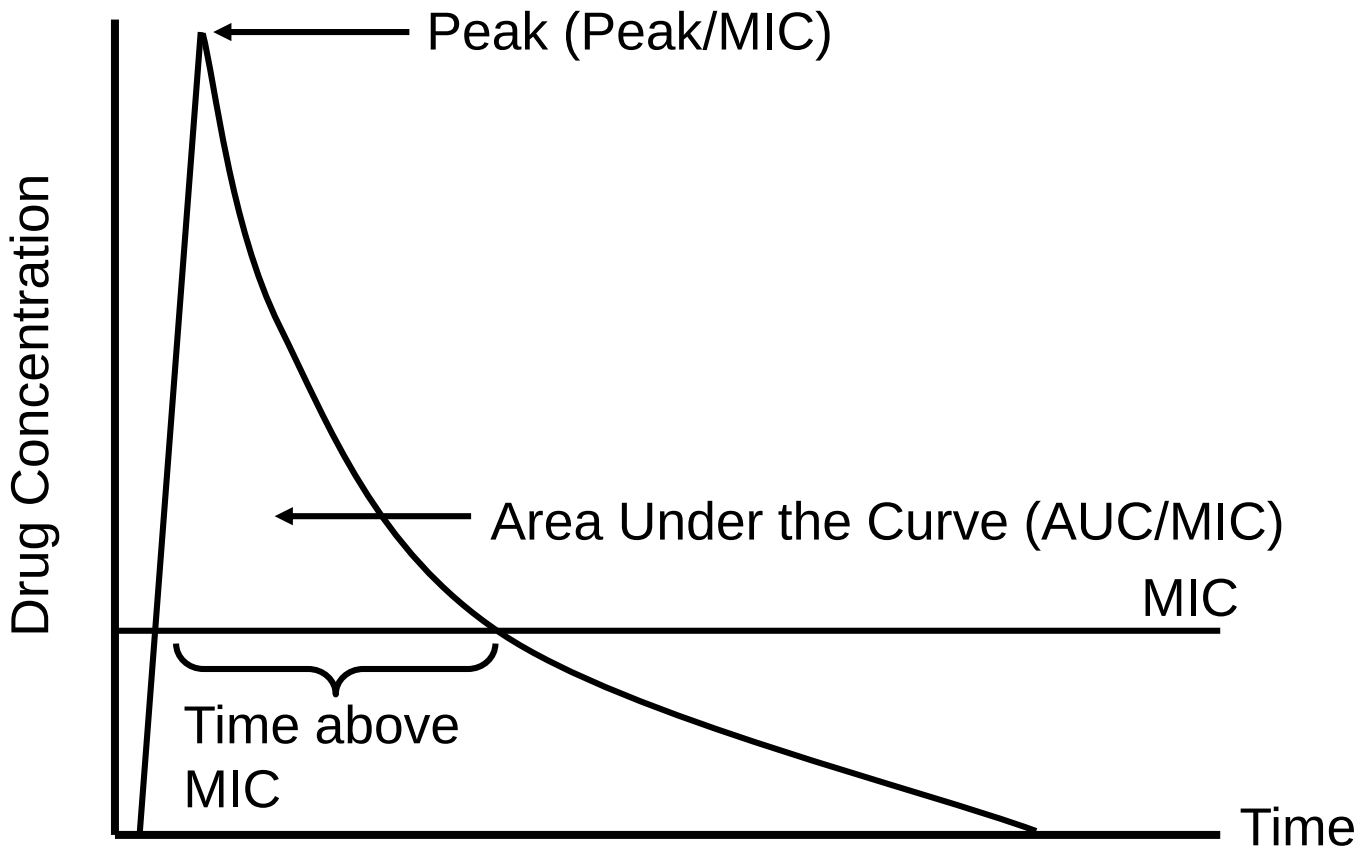
Antibiotic choice: Antibiotic-related factors

- Pharmacokinetic/pharmacodynamic (PK/PD) profile
  - Absorption
  - Excretion
  - tissue levels, peak levels, AUC,
  - Time above MIC
- Toxicity and other adverse effects
- Drug-drug interactions
- Cost

PK/PD factors

- Increasing knowledge on the association between PK/PD parameters on
  - clinical efficacy
  - preventing emergence of resistance
- Enables optimization of dosage regimens

Antimicrobial activity



Pharmacodynamic properties of antibiotics

Type of bactericidal profile	Important parameter	Dosage optimization
Dose-dependent *Aminoglycosides, quinolones*	Cmax / MIC Prolonged PAE	Single daily dose
Time-dependent *Penicillin, cephalosporins*	T > MIC No PAE	Multiple DD or continuous infusion
Cumulative-dose dependent *Clarithromycin, clindamycin*	AUC / MIC Prolonged PAE	Total dose and duration

PAE: Post-Antibiotic Activity

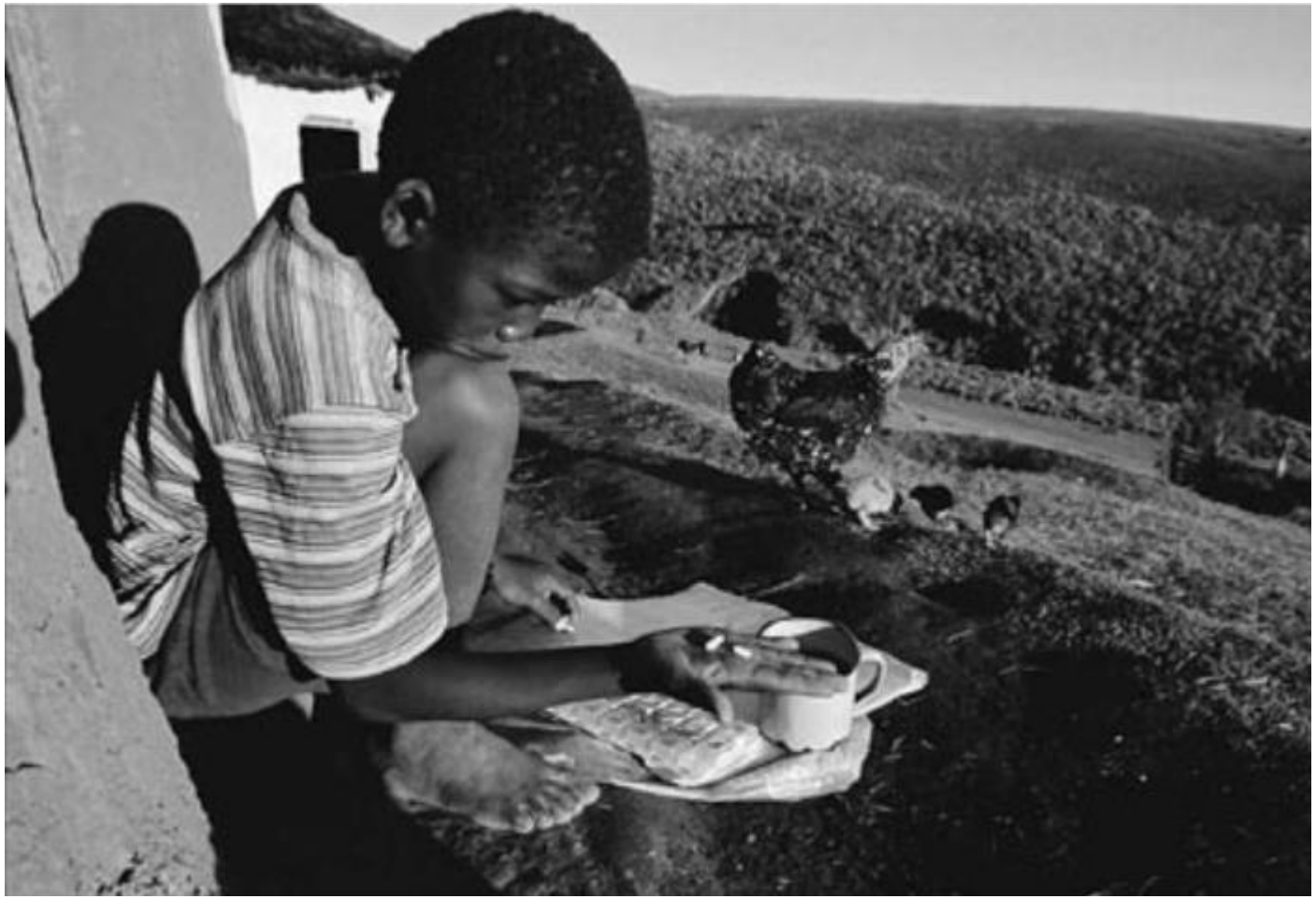
Antibiotic-related factors: Cost

- Not just the unit cost of the antibiotic
- Materials for administration of drug
- Labour costs
- Expected duration of stay in hospital
- Cost of monitoring drug levels
- Expected compliance

Choice of regimen: Advantages of oral treatment

- Eliminates risks of complications associated with intravascular lines
- Shorter duration of hospital stay
- Savings in nursing time
- Savings in overall costs
- Greater patient satisfaction

How can we improve rational antibiotic use?



Treat Bacterial Infection, not Colonization

- Many patients become colonized with potentially pathogenic bacteria but are not infected
  - Catheter colonization
  - Tracheostomy colonization in chronic respiratory failure
  - Chronic wounds and decubiti
  - Lower extremity stasis ulcers
  - Chronic bronchitis
- Can be difficult to differentiate : Assess clinically

Do not Treat Viral Infections with Antibiotics

- Acute bronchitis
- Common colds
- Sinusitis with symptoms less than 7 days
- Pharyngitis not due to Group A *Streptococcus spp.*

Limit Duration of Antibiotic Therapy to the Appropriate Length

- Ventilator-associated pneumonia: 8 days
- Most community-acquired pneumonia: 5 days
- Cystitis: 3 days
- Pyelonephritis: 7 days if fluoroquinolone used
- Intra-abdominal with source control: 4-7 days
- Cellulitis: 5-7 days

depending on clinical response

- Re-evaluate, de-escalate or stop therapy at 48-72 hours based on diagnosis and microbiologic results
- Re-evaluate, de-escalate or stop therapy with transitions of care (e.g. ICU to step-down or ward)
- Do not give antibiotic with overlapping activity
- Do not “double-cover” gram-negative rods (i.e. *Pseudomonas sp.*) with 2 drugs with overlapping activity

- Limit duration of surgical prophylaxis to <24 hours perioperatively
- Use rapid diagnostics if available

  (e.g. respiratory viral PCR)
- Obtain expert opinion if needed
- Prevent infection
  - Use good hand hygiene and infection control practices
  - Remove catheters

Antibiotic Stewardship

- Definition: A system of informatics, data collection, personnel, and policy/procedures which promotes the optimal selection, dosing, and duration of therapy for antimicrobial agents throughout the course of their use
- Purpose:
  - Limit inappropriate and excessive antibiotic use
  - Improve and optimize therapy and clinical outcomes for the individual infected patient


Antibiotics
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we have to save antibiotics
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