Use of Antibiotics

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Introduction

Antibiotic: Chemical produced by a microorganism that kills or inhibits the growth of another microorganism

Antimicrobial agent: Chemical that kills or inhibits the growth of microorganisms

Important considerations when prescribing antibiotics:

- 1) Obtain accurate diagnosis of infection.
- 2) Empiric and definitive therapy.
- 3) Identifying opportunities to switch to narrow-spectrum.
- 4) Cost-effective oral agents for the shortest duration necessary.

Important considerations when prescribing antibiotics:

- 5) Understanding drug pharmacodynamics and efficacy at the site of infection..
- 6) Host characteristics that influence antimicrobial activity
- 7) Adverse effects of antimicrobial agents on the host.

1) Obtaining an Accurate Infectious Disease Diagnosis

- Determining the site of infection,
- Defining the host (e.g., immunocompromised)
- Establishing, when possible, a microbiological diagnosis.
- especially for:

  Endocarditis, septic arthritis, meningitis..

- Additional investigations to exclude noninfectious diagnoses

- Microbiological diagnosis :

  Bacterial or fungal culture or

  Serologic testing..

- Frequently the "Most likely"

  microbiological etiology can be inferred from the clinical

  presentation:

- Cellulitis (streptococci or staphylococci)

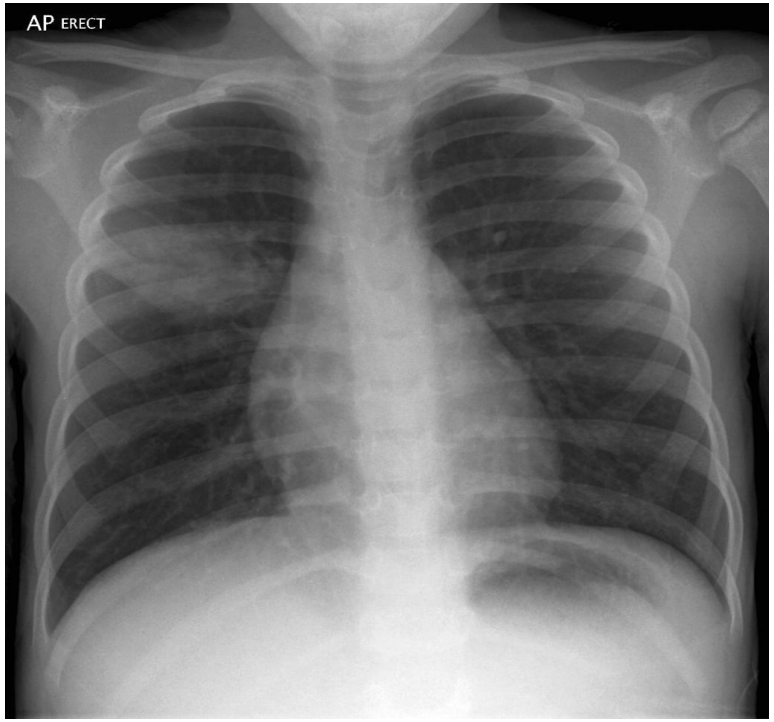
  No need for positive culture.

Cellulitis

Use of antibiotics

- **Is An Antibiotic Indicated?**
- **Clinical diagnosis of bacterial infection.**

- **Pneumonia (CAP)**
- can also be treated empirically—Macrolide or fluoroquinolone antibiotic—without performing specific diagnostic test



Pneumonia

Timing of Initiation of Antimicrobial Therapy

- **Urgent situation:**
  1) Acute meningitis
  2) Septic shock
  3) Febrile neutropenia..
- **Empiric therapy should be initiated immediately after or concurrently with collection of diagnostic specimens.**

- **None urgent**:
- 1) febrile and stable patient with fever for several days with no clue to diagnosis..

- In more stable clinical circumstances..
- Hold antibiotics until appropriate specimens have been collected and submitted:
- Example:
- subacute bacterial endocarditis ……. multiple sets of blood cultures

Urgent vs non urgent

- 16 year old boy who presented with 3 days H/O high grade fever and severe headache ..examination revealed T: 39 and patient has neck stiffness, otherwise fully conscious and has no neurological deficit :

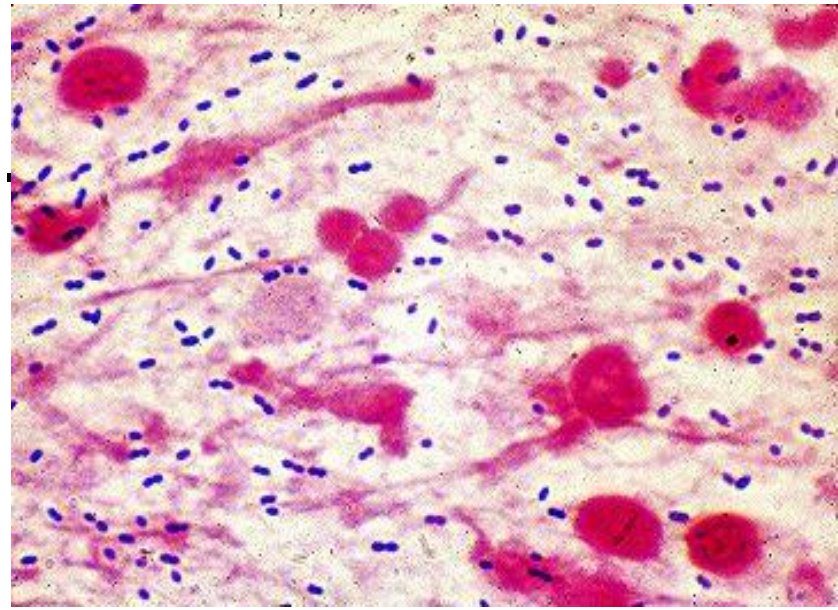
What is the most appropriate steps of approach:

- A) Start combination of antibiotic and arrange for CSF study.
- B) Arrange for urgent CT-scan brain ,
- C) Perform urgent LP and give the first dose of antibiotics.
- D) perform urgent LP and if csf is abnormal ,start RX…

…… A OR C ……

Use of antibiotics

- Patient was prescribed a dose of :
  cefetriaxone and vanocmycin and urgent LP is done:
- Result:
- WBC : 1230 cells/mm…90% polymorph.
- RBC : NIL ..
- Gram stain:
- **Gram positive intracellular dipplococci**..
- What you will do?
  To continue the same antibiotics? **Yes or No.**



- Premature initiation of antimicrobial therapy…any harm ?

1] can suppress bacterial growth

2] Preclude the opportunity to establish a microbiological diagnosis,

3] Require several weeks of directed antimicrobial therapy to achieve cure.

Empiric vs Definitive Antimicrobial Therapy

- Microbiological results do not become available
- for 24 to 72 hours

- Empiric and guided by the clinical presentation..

- Inadequate therapy for infections in critically ill, hospitalized patients is associated with greater morbidity and mortality

- Use broad-spectrum antimicrobial agents as initial empiric therapy

Use of antibiotics

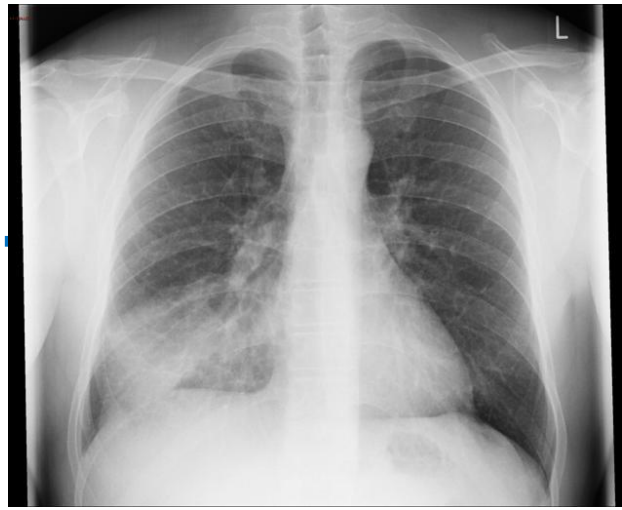
What organisms are likely to be responsible:

Best Educated Guess?

- Based on:
  - **Hx & P.E…. You might have a clue to DX.**
  - **Epidemiological data**
    - **Hospital-acquired vs. community-acquired**
    - **Prior antibiotic use**

- **Best Educated Guess?**
- Patient with dyspnoea and cough …..

  Streptococcal pneumonia and atypical organism.



- Patient with fever and urinary symptomes :

  E.coli ….

- Patient with erythema over the right leg associated
- with pain and tenderness …

  Group A Streptococcus and Staphylococcus

- **Hospital-acquired infections**
- Related to the presence of invasive devices and procedures

- A] **Catherter related bacteremia**:,
  Coagulase negative staph..
  Methicillin-resistant Staphylococcus aureus [MRSA]

- B] **Catheter related UTI**:
  Gram negative (eg, Pseudomonas aeruginosa)

- Once :
- 1) Microbiology have identified the etiologic pathogen and
- 2) Antimicrobial susceptibility data are available..
- Then…

Every attempt should be made to narrow the antibiotic spectrum. :

1) It can reduce cost and toxicity and
2) Prevent the emergence of antimicrobial resistance in the community

Interpretation of Antimicrobial Susceptibility Testing Results

- Antimicrobial susceptibility testing measures the ability of a specific organism to grow in the presence of a particular drug in vitro:

  susceptible, resistant, or intermediate

- Data are reported in the form of minimum inhibitory concentration (MIC):

  The lowest concentration of an antibiotic that inhibits visible growth of a microorganism..

antimicrobial susceptibility testing (AST).

- **Susceptible**:
- indicates that the isolate is likely to be inhibited by the usually achievable concentration of a particular antimicrobial agent when the recommended dosage is used..
- Different antibiotics has different MIC.

CASE SCENARIO

- 23 years old man who has surgery at the base of the skull
- After trauma . Presented few days later with meningitis
- CSF has revealed :

- WBC 1200 mainly poly
- Culture : staph aureus ..
- RX cephazolin..

- it does not achieve therapeutic concentrations in the CSF

Bactericidal vs Bacteriostatic Therapy

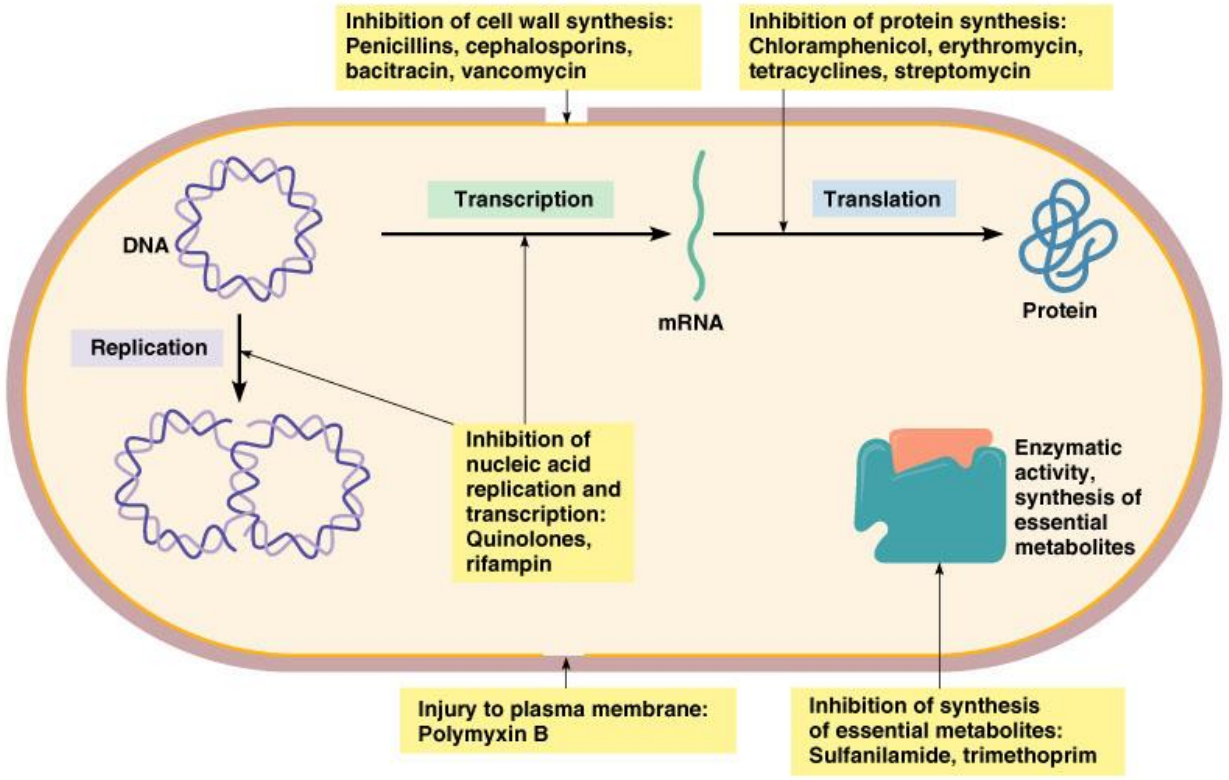
- **Bactericidal**
- Cause death and disruption of the bacterial cell. Drugs act on :

1) The cell wall …….β-lactams
2) **Cell membrane ….. Daptomycin**
3) **Bacterial DNA ……. Fluoroquinolones**

- Preferred in the case of serious infections such as endocarditis & meningitis to achieve rapid cure…

- **Bacteriostatic**
- Inhibit bacterial replication without killing the organism.
- act by inhibiting protein synthesis: SUCH AS :

- Sulfonamides.
- Tetracyclines.
- Macrolides.

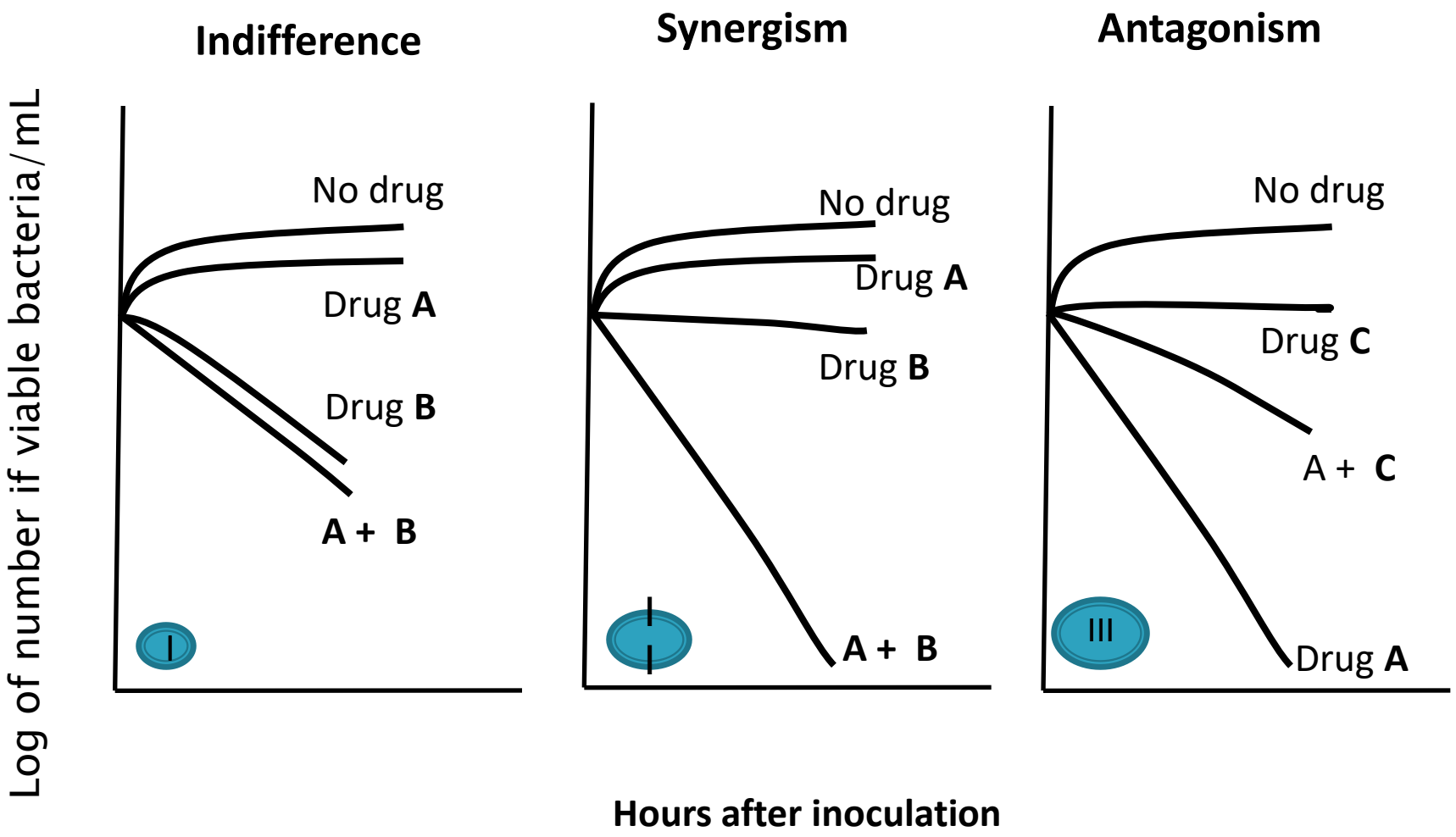


Use of Antimicrobial Combinations

Exhibits synergistic activity
is used in the treatment of serious Infections:
A] Rapid killing is essential
Endocarditis caused by *Enterococcus* species with
a combination of penicillin and gentamicin: bactericidal,
activity…

- B] shorten the course:
- Endocarditis due to viridans group streptococci,
penicillin or ceftriaxone with
gentamicin for 2 weeks can be as effective as penicillin or
ceftriaxone alone for 4 weeks).

- **D] Polymicrobial Infections:**
- Antimicrobial combinations, such as a third-generation cephalosporin or a fluoroquinolone **plus** metronidazole,


Indifference
Synergism
Antagonism
Log of number if viable bacteria/mL
No drug
Drug A
Drug B
A + B
I
No drug
Drug A
Drug B
A + B
II
No drug
Drug C
A + C
Drug A
III
Hours after inoculation

Host Factors to Be Considered in Selection of Antimicrobial Agents

1) Renal and Hepatic Function..
2) Pregnancy and Lactation… Special considerations .. teratogenicity or otherwise toxic to the fetus.

:

Sulphonamides : A risk to develop kernicterus, especially preterm infants..

Tetracycline : Staining of the teeth..

Fluoroquinolone: Cartilage damage to the fetus..

3) History of Allergy or Intolerance.

Pencillin and anaphylaxis

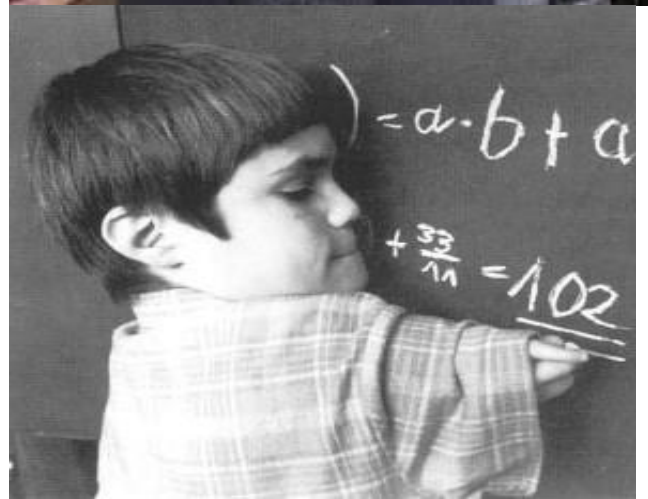
Consider Special Host Factors

- Genetic e.g. G6PD
- Renal function
- Liver function
- Pregnancy & Lactation
- Drug interaction

Thalidomide-induced teratogenesis

- Phacomelia..
- Thalidomide was released in the late 1950's
- It was very effective :
- anti-emetic and used to treat morning sickness
- and emesis in pregnant women..

- The biggest man-made medical disaster ever, Over 10,000 children were born with a range of severe and debilitating malformations…



Oral vs Intravenous Therapy

- Candidates for treatment mild to moderate infections
- well-absorbed oral antimicrobial agents :

A] **Pyelonephritis**
Fluoroquinolones ..

B] Community-acquired pneumonia
Augmentin and macrolides coverage

- **Bioavailability**

The percentage of the oral dose that is available unchanged in the serum).

Examples of antibiotics with excellent bioavailability are:

Trimethoprim-sulfamethoxazole

.

- The efficacy of antimicrobial agents depends on their capacity to achieve :

  Concentration equal to or greater than the MIC at the site of infection..

- Ocular fluid, CSF, abscess cavity, prostate, and bone) are often much lower than serum levels

For example:

First- and second- generation cephalosporins do not cross the blood-brain barrier

- **Aminoglycosides**: **are less active** in the :
  low-oxygen, low-pH, **of Abscesses**

- **Fluoroquinolones** achieve high concentrations in the prostate
  preferred oral agents for the treatment of **Prostatitis..**

- **Moxifloxacin** does not achieve significant urinary concentrations
  therefore **not suitable** for treatment of **UTIs.**

Assessment of Response to Treatment

- Response to treatment of an infection:

Clinical parameters

- improvement of symptoms and signs (eg, **fever, tachycardia, or confusion**

- laboratory values
- decreasing leukocyte count
- radiologic decrease in the size of an abscess).,

Antimicrobial Agents as Prophylactic

- 1) Presurgical Antimicrobial Prophylaxis
- is used to reduce the incidence of postoperative surgical site infections..

- A single dose of a cephalosporin (such as cefazolin) administered
- within 1 hour before the initial incision is appropriate for
- most surgical procedures..

Antimicrobial Agents as Prophylactic

2) **Prevent Transmission of Communicable Pathogens to Susceptible Contacts**

- **ciprofloxacin** for close contacts of a patient with N.meningitis

3) Antimicrobial Prophylaxis Before Dental Procedures:

- Prosthetic valves
- Rheumatic heart..
- to prevents Endocaridits

NONE INFECTIOUS CAUSES :...PROLONGED USE

- Examples :
- **Adult onset Still disease**
- **Drug-induced fever**
- **fever associated with pulmonary embolism**
- **lymphoma**

Treatment of a Positive Clinical Culture in the Absence of Disease:

- **Colonization** without any associated manifestation
- of disease occurs frequently in certain populations:

Colonization of :

- Old women with indwelling urinary catheter:
  Active infection are absent
  (asymptomatic bacteriuria)

- Endotracheal tubes in mechanically ventilated patients,
- chronic wounds..

Conclusion

- Appropriate use of antimicrobial agents involves:
- **Obtaining an accurate diagnosis,**
- **Determining the need for and timing of antimicrobial therapy.**
- **Understanding how dosing affects the antimicrobial activities of different agents,**
- **Tailoring treatment to host characteristics,**

- Sign for the narrowest spectrum and shortest duration of therapy, and:
  switching to oral agents as soon as possible.
- In addition,
- Nonantimicrobial interventions, such as abscess drainage, are equally or more important in some cases and should be
- pursued diligently in comprehensive infectious disease management.

What is the appropriate dose?

- **The lowest dose that is effective..**

- AVOID SUB-THERAPEUTIC DOSES
- DETERMINED BY:
  - SERIOUS VS NON-SERIOUS INFECTIONS
  - SITE OF INFECTION
  - DRUG PK/PD PROPERTIES
  - OTHER HOST FACTORS (E.G. RENAL FUNCTION … ETC)

Any Modification Needed?

Principles:

- Narrow vs broad spectrum agents.
- Least toxic agent.
- Cheaper.

Criteria for Use of New Agent

- Antimicrobial activity is superior
- Have a therapeutic advantage
- Better pharmacokinetics
  - Site penetration
  - Longer t ½
  - Shorter duration
- Less toxic
- Better tolerance

Thank you