



Use of Antibiotics

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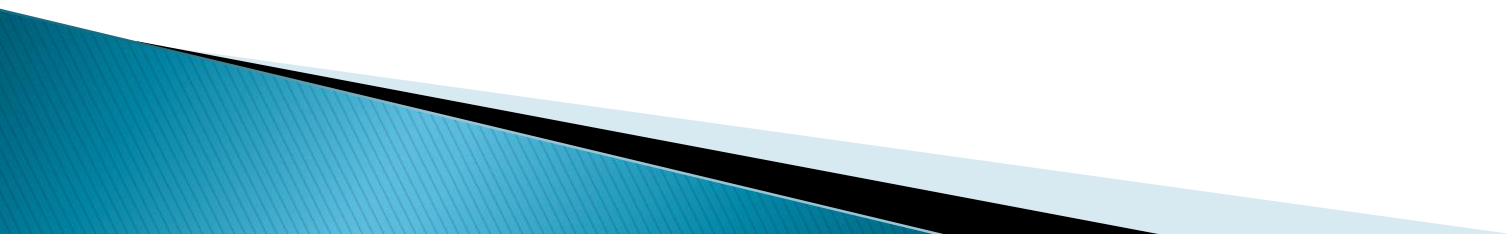


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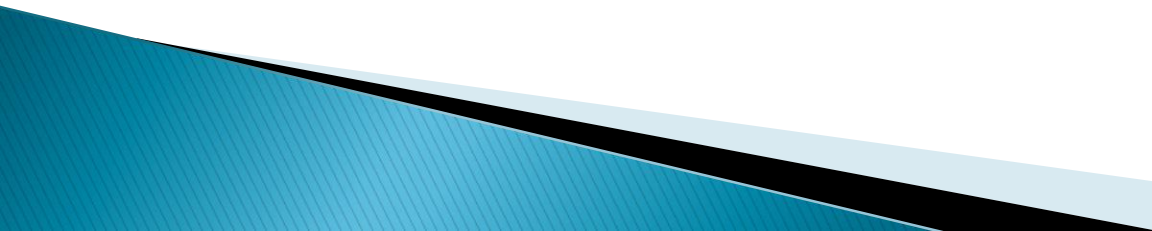
Introduction

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

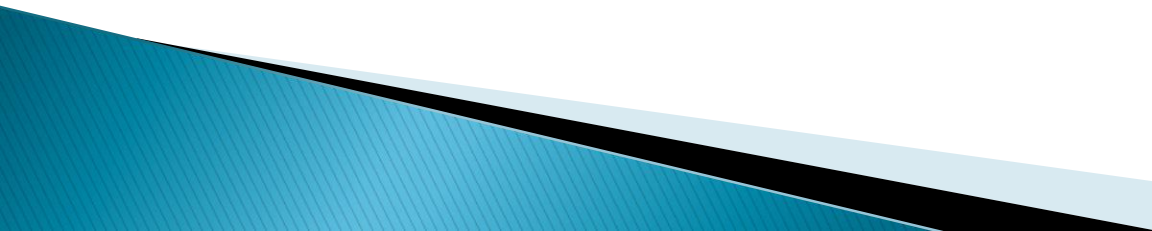
Antimicrobial agent: Chemical that kills or inhibits the growth of microorganisms



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.
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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.
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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

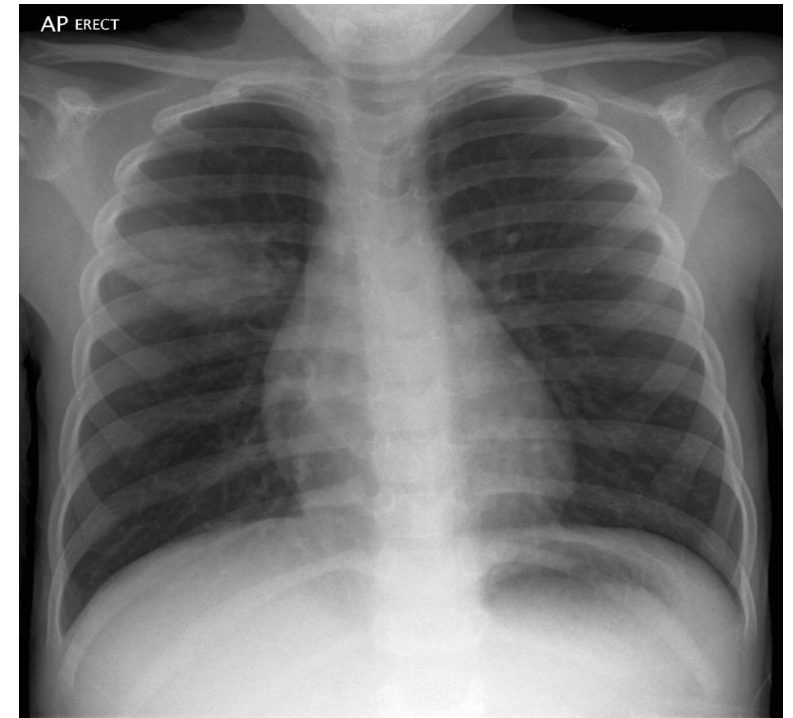


Use of antibiotics

- ▶ **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

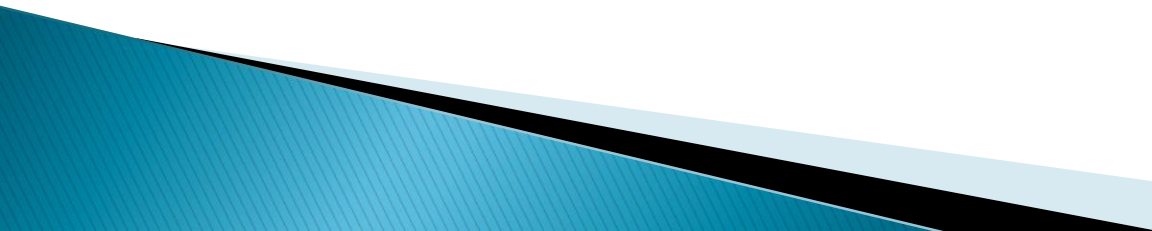
- ▶ **Urgent situation:**

- 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**
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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 :

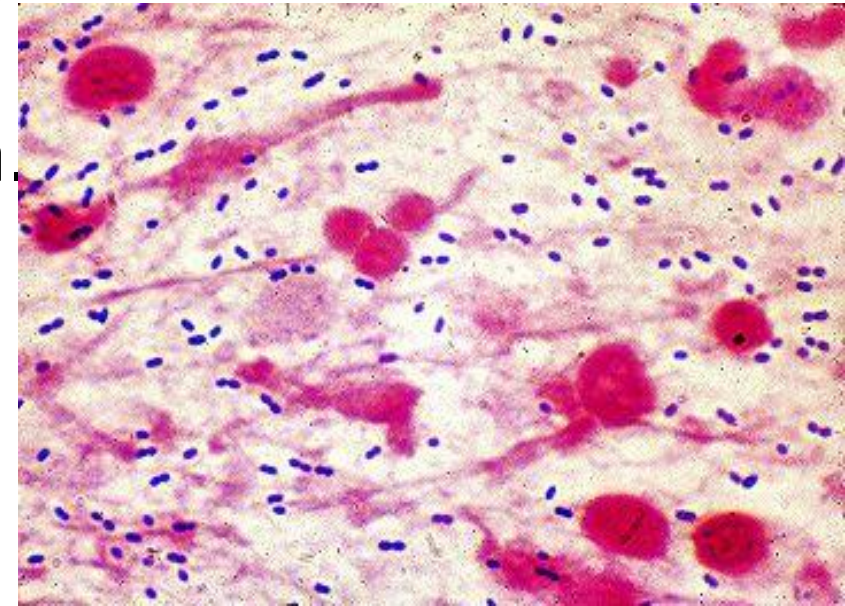
What is the most appropriate steps of approach:

- ▶ 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 :
ceftriaxone and vanocmycin and urgent LP is done:
- ▶ Result:
- ▶ WBC : 1230 cells/mm...90% polymorph
- ▶ RBC : NIL ..
- ▶ Gram stain:
- ▶ **Gram positive intracellular diplococci..**
- ▶ What you will do?
To continue the same antibiotics?



Yes or No.

▶ Premature initiation of antimicrobial therapy...any harm ?

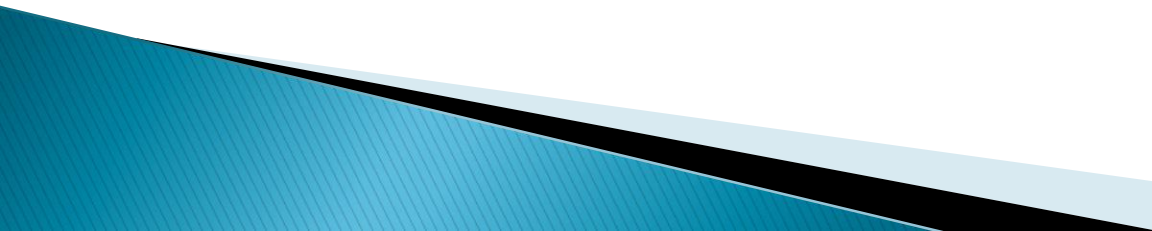
1] can suppress bacterial growth

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

- ▶ **Best Educated Guess?**
- ▶ Patient with dyspnoea and cough
Streptococcal pneumonia and atypical organism
- ▶ Patient with fever and urinary symptoms :
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] **Catheter 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

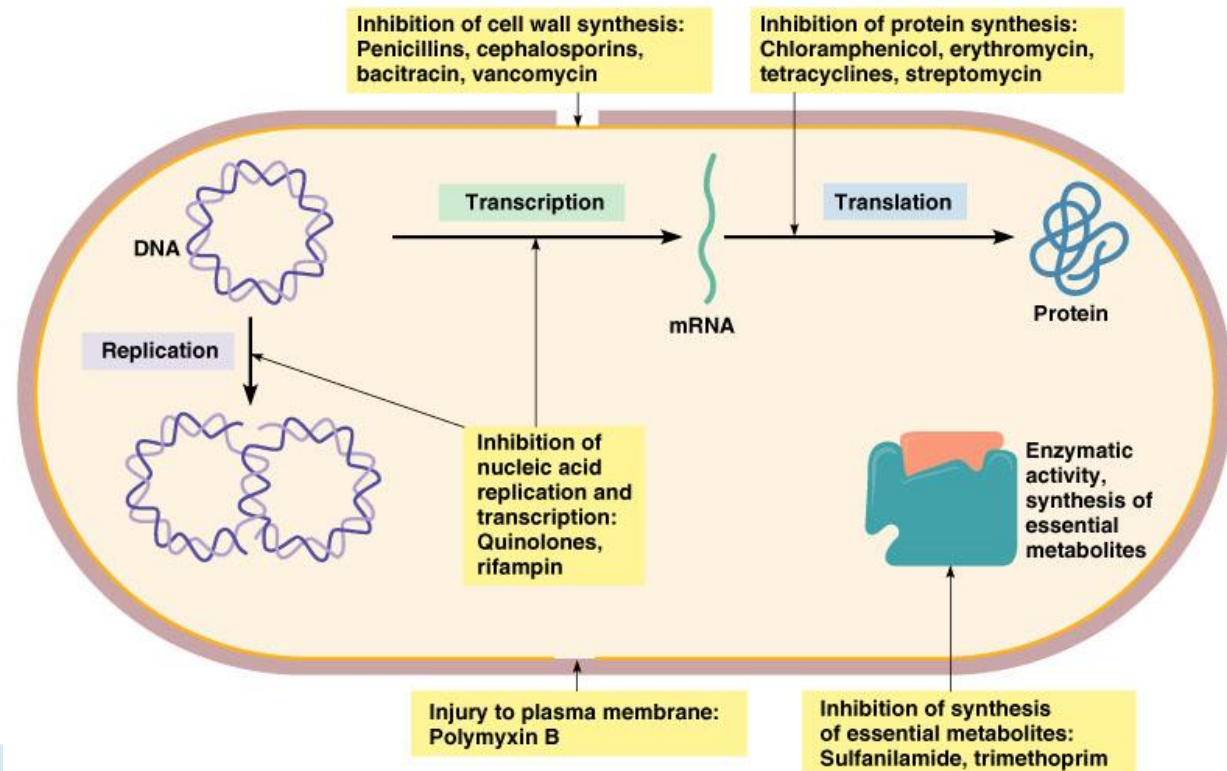
- 3) Bacterial DNA Fluoroquinolones

- ▶ 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:

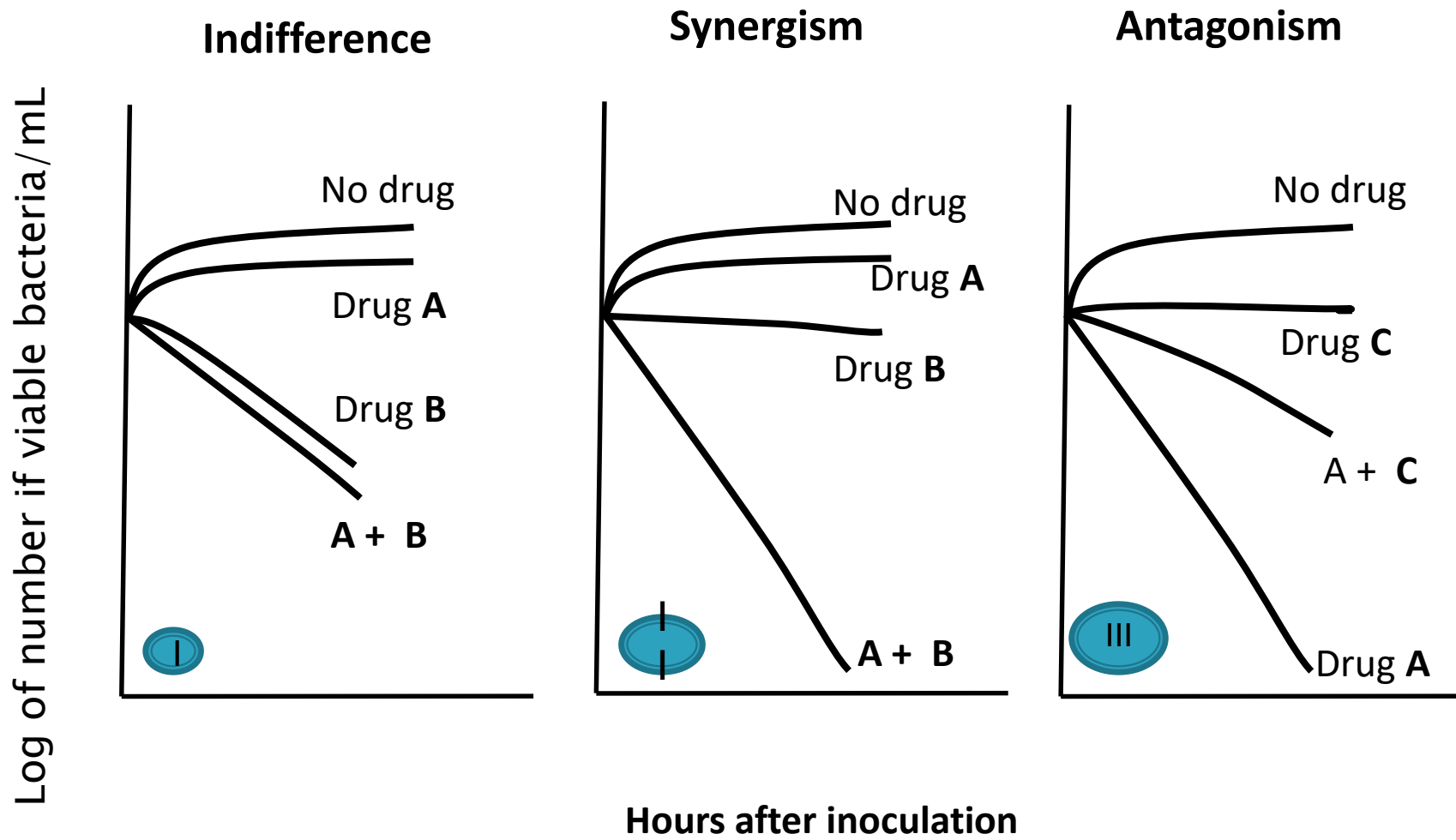
A] **Rapid killing is essential**

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,
- 



Host Factors to Be Considered in Selection of Antimicrobial Agents

1) Renal and Hepatic Function..

2) Pregnancy and Lactation... Special considerations ..

Teratogenicity or **Toxic to the foetus.**

:

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

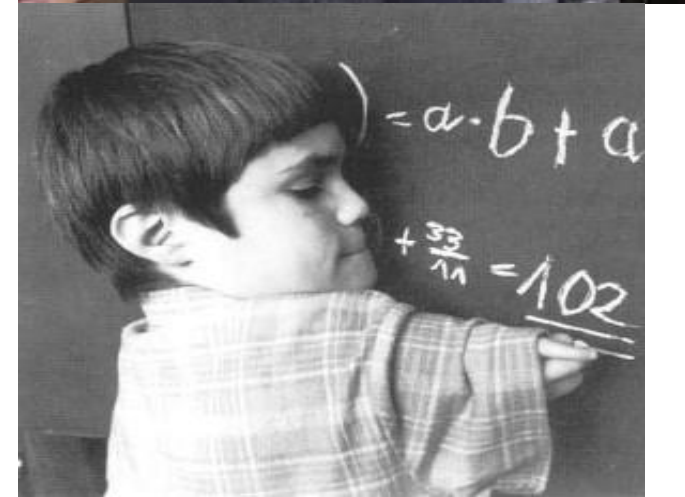
Consider Special Host Factors

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

Thalidomide-induced teratogenesis

- ▶ Phocomelia..
- ▶ 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.

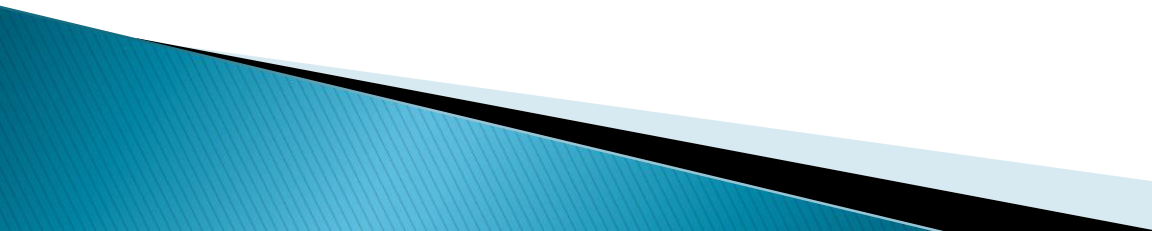
Assessment of Response to Treatment

- ▶ 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..
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Antimicrobial Agents as Prophylactic

2) Prevent Transmission

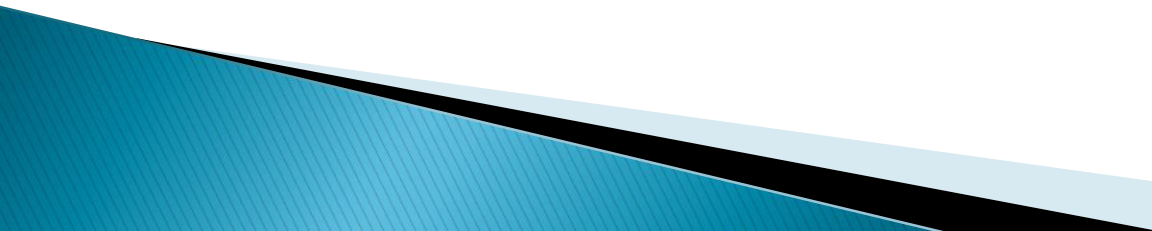
of Communicable Pathogens to Susceptible Contacts

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

3) Antimicrobial Prophylaxis Before Dental Procedures:

- ▶ Prosthetic valves
- ▶ Rheumatic heart..
- ▶ to prevents Endocarditis

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 $t_{1/2}$
 - Shorter duration
 - ▶ Less toxic
 - ▶ Better tolerance
- 

Thank you

