BASIC PRINCIPLES OF ANTIMICROBIAL THERAPY

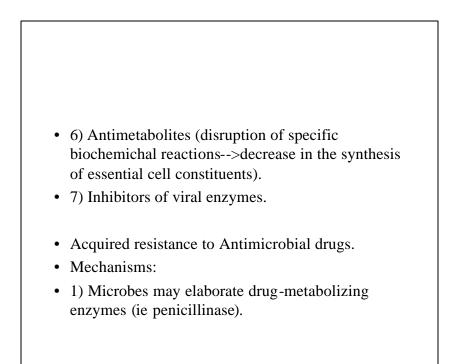
- Chemotherapy = the use of chemicals against invading organisms (ie bacteria).The term is used for both treatment of cancer and treatment of infection.
- Antibiotic = a chemical that is produced by one microorganism and has the ability to harm other microbes.
- Selective toxicity = the ability of a drug to injure a target cell or organism without injuring other cells or organisms that are in intimate contact .

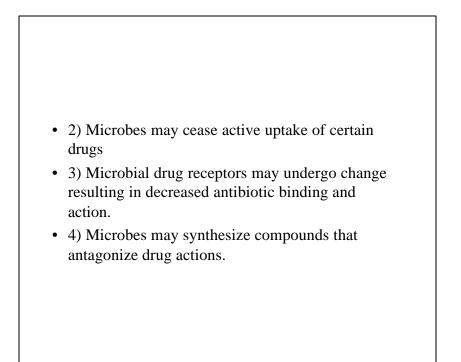
CLASSIFICATION OF ANTIMICROBIAL DRUGS BY SUSCEPTIBLE ORGANISMS

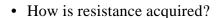
- 1) Antibacterial drugs (narrow and broad spectrum).Examples: Penicillin G, erythromycin,cephalosporins,sulfonamides
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- 2) Antiviral drugs (examples:acyclovir,amantadine)
- 3) Antifungal drugs
- (examples : amphotericin,ketoconazole)

CLASSIFICATION BY MECHANISM OF ACTION

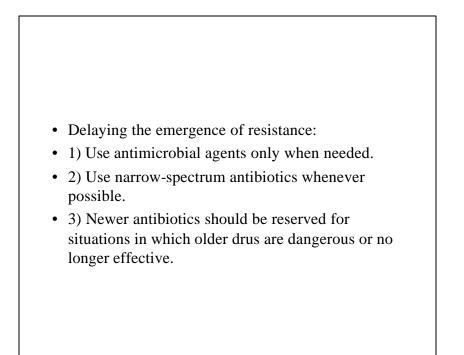
- 1) Drugs that inhibit bacterial wall synthesis or activate enzymes that disrupt the cell wall.
- 2) Drugs that increase cell membrane permeability (causing leakage of intracellular material)
- 3) Drugs that cause lethal inhibition of bacterial protein synthesis.
- 4) Drugs that cause nonlethal inhibition of protein synthesis (bacteriostatics).
- 5) Drugs that inhibit bacterial synthesis of nucleic acids

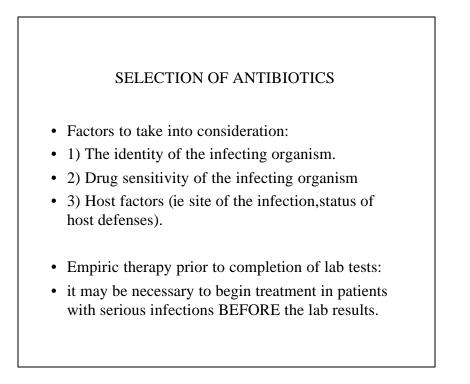


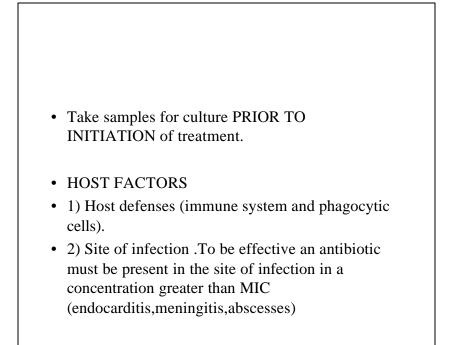


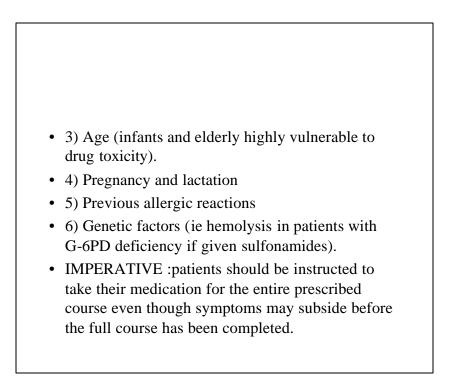


- A) Spontaneous mutation
- B) Conjugation
- Use of antibiotics PROMOTES the emergence of drug-resistant microbes.
- Suprainfection (or supeinfection) : a new infection that appears through the course of treatment for a primary infection.

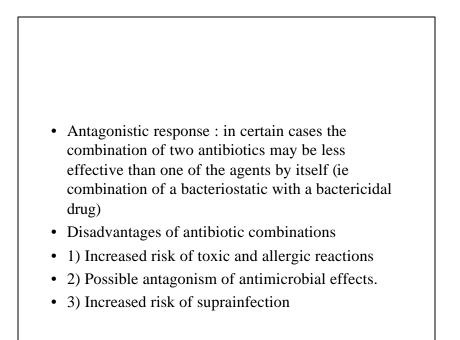


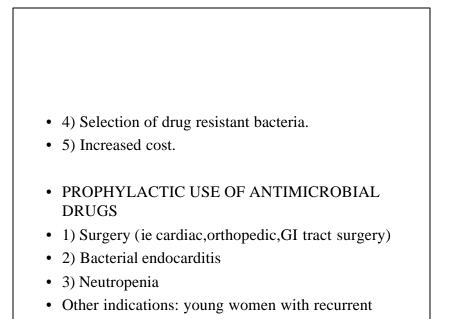




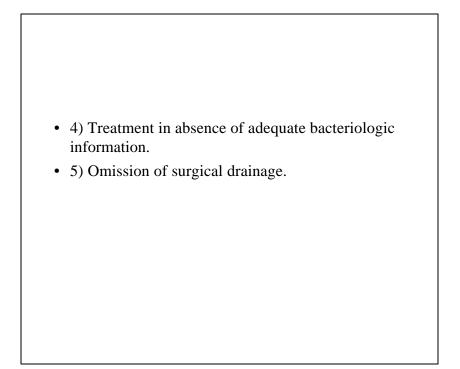


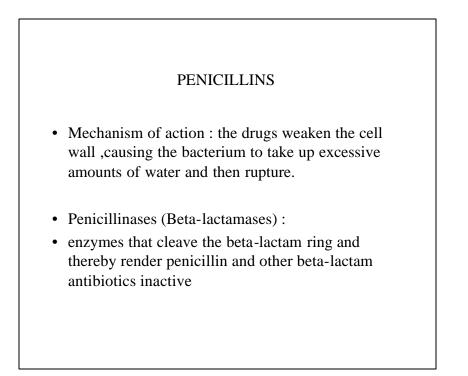
Antibiotic combinations : the result may be additive,potentiative or antagonistic. Additive response :one in which the antimicrobial effect of the combination is equal to the sum of the effects of the two drugs alone. Potentiative interaction :one in which the effect of the combination is GREATER than the sum of the effects of the individual agents.





urinary tract infection, prophylaxis against type A influenza with amantadine, lifelong prophylaxis of individuals who have had severe rheumatic carditis.
Misuses of antibiotics
1) Attempted treatment of untreatable infection (viral infections)
2) FUO
3) Improper dosage





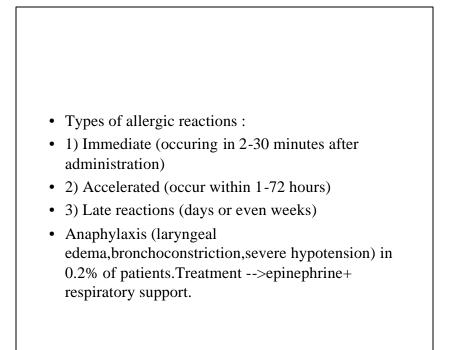
Classification : 1) Narrow-spectrum (penicillinase sensitive) 2) Narrow-spectrum that are penicillinase resistant (antistaphylococcal) 3) Broad-spectrum penicillins (aminopenicillins) 4) Extended-spectrum penicillins (antipseudomonal)

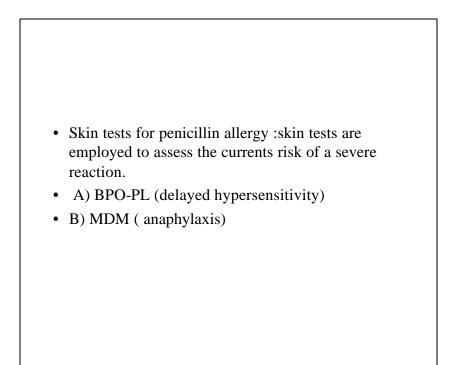
PENICILLIN G Antimicrobial spectrum : active against most gram-positive bacteria,gram-negative cocci (ie neisseria meningitis) and spirochetes.With few exceptions gram-negative bacteria are resistant. Therapeutic uses : 1)Pneumonia and meningitis caused by Streptococcus pneumonia 2) Pharyngitis caused by Streptococcus Pyogenes 3) Infectious endocarditisis (Streptococcus viridans)

4) Gangrene ,tetanus
5) Syphilis (treponema pallidum).
Side Effects and toxicities :pain at the site of injection,neurotoxicity with too high plasma levels.Inadvertent intra-arterial injection can produce severe reactions (gangrene,necrosis) and must be avoided .

PENICILLIN ALLERGY

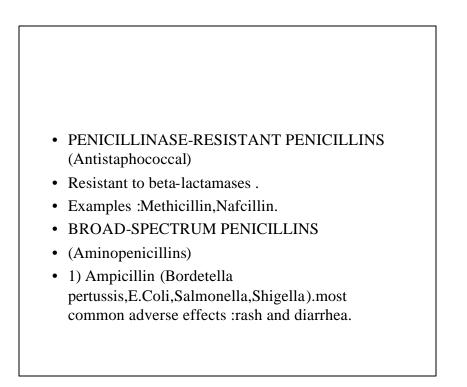
- Penicillins are the most common cause of drug allergy (1-10% of the patients will experience an allergic response). There is no direct relationship between the size of the dose and the intensity of allergic response.
- Cross-sensitivity :5-10% of patients allergic to penicillins are also allergic to cephalosporins.

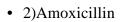




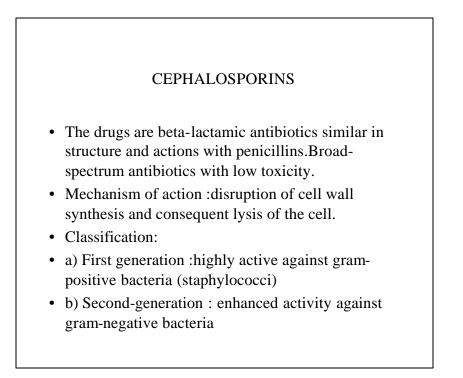
MANAGEMENT OF PATIENTS WITH HISTORY OF PENICILLIN ALLERGY

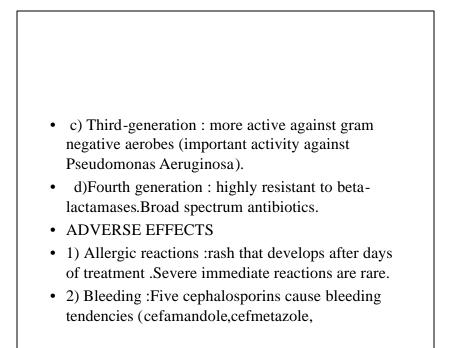
- ASK patients for previous history of allergy to penicillin.
- If the patient refers to a positive history of allergy AVOID PENICILLINS entirely.
- If the allergy is mild a CEPHALOSPORINE is often appropriate as alternative.
- If the allergy is severe AVOID CEPHALOSPORINS.
- For many infections VANCOMYCIN AND ERYTHROMYCIN are effective and safe.

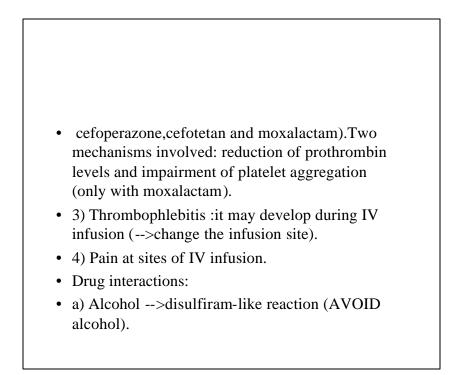


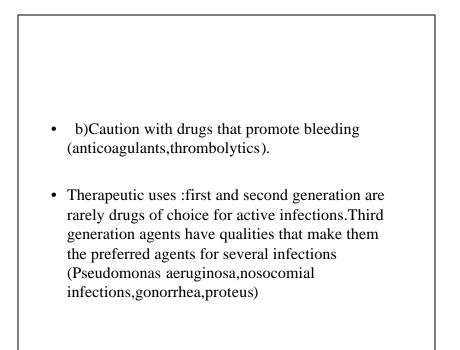


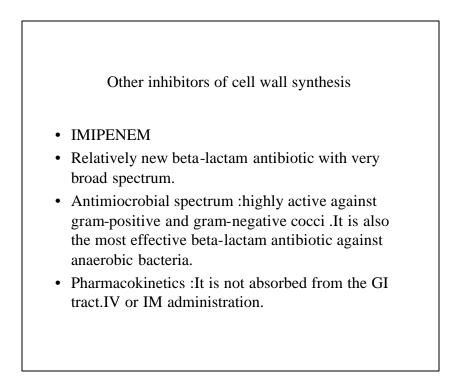
- EXTENDED-SPECTRUM PENICILLINS
- (Antipseudomonal)
- Used to treat infections with Pseudomonas Aeruginosa (ie Ticarcillin)
- Penicillins combined with a beta-lactamase inhibitor :
- ie Amoxicillin+ clavulanic acid =Augmentin











• ADVERSE EFFECTS

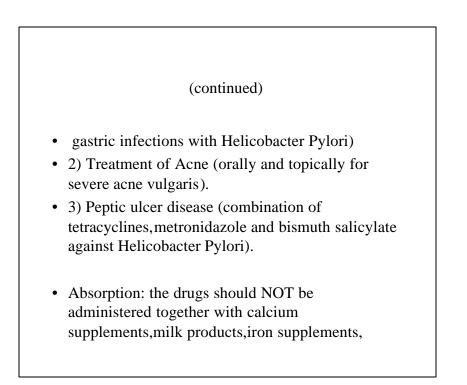
- (generally well tolerated)
- 1) GI effects (nausea, vomiting, diarrhea)
- 2) Hypersensivity reactions (rashes, pruritus) have occurred.
- 3) Suprainfections with bacteria or fungi develop in about 4% of patients.
- 4)Rarely seizures have occurred.

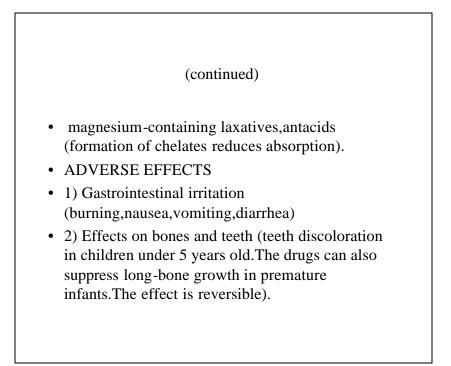
- VANCOMYCIN
- It is used only for serious infections due to toxicity.
- Principal indications : antibiotic-associated pseudomembranous colitis (Clostridium difficile),infection with methicillin-resistant Staphylococcus aureus.
- Adverse effects: ototoxicity, thrombophlebitis.

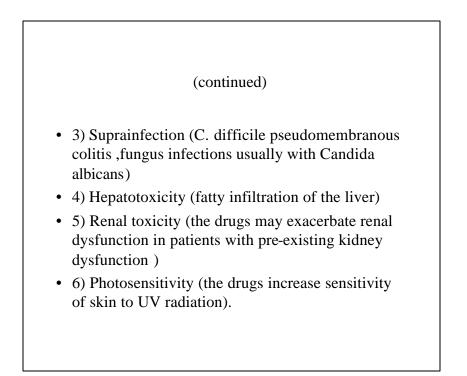
BACTERIOSTATIC INHIBITORS OF PROTEIN SYNTHESIS

• TETRACYCLINS

- Broad spectrum antibiotics.
- Mechanism of action : supression of bacterial growth by inhibiting protein synthesis.
- Therapeutic uses
- 1) Treatment of infectious diseases (rickettsial diseases--> Rocky mountain spotty fever,typhus fever,Q fever,infections caused by chlamydia trachomatis,brucellosis,cholera,pneumonia caused by Mucoplasma pneumonia,Lyme disease,



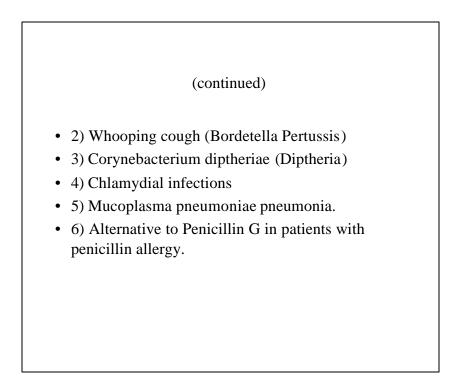


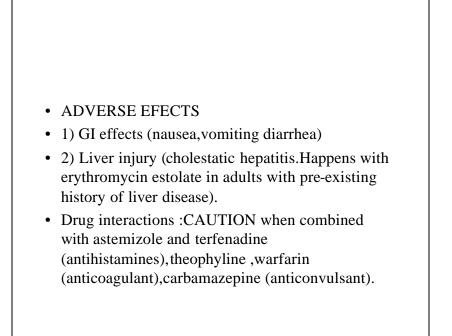


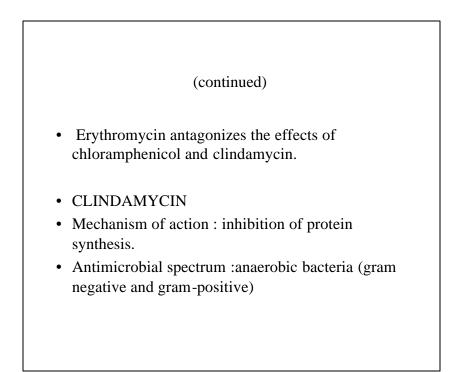
MACROLIDES

• ERYTHROMYCIN

- Mechanism of action : inhibition of protein synthesis.
- Antimicrobial spectrum :(similar to penicillins) effective against most gram-positive bacteria and against some gram-negative.
- Therapeutic uses
- 1) Legionella pneumophila pneumonia (legionnaires' disease).

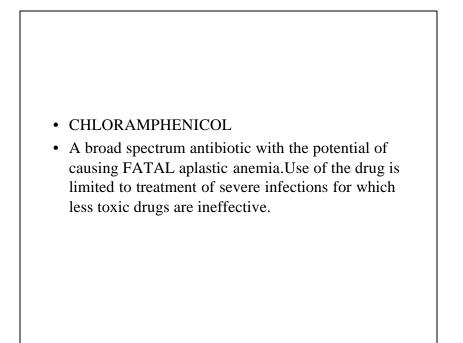






• ADVERSE EFFECTS

- 1) Antibiotic associated pseudomembranous colitis (symptoms include profuse watery diarrhea, abdominal pain, fever and leucocytosis). Stools often contain mucus and blood).
- 2) Hypersensitivity reactions (rashes).



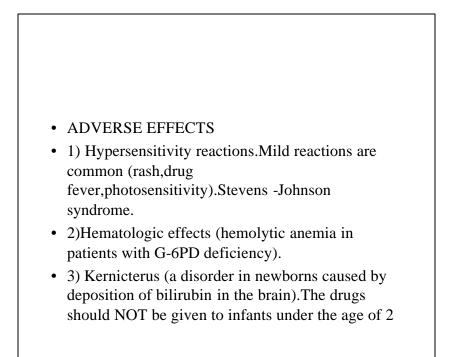
AMINOGLYCOSIDES

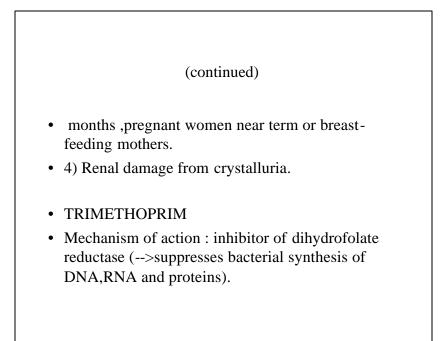
- Mechanism of action :disruption of bacterial protein synthesis.
- Antimicrobial spectrum : aerobic gram-negative bacilli (E.Coli,Klebsiella pneumoniae,Proteus Mirabilis,Pseudomonas Aeruginosa).The drugs are inactive against most gram-positive bacteria.the drugs are ineffective against anaerobes.

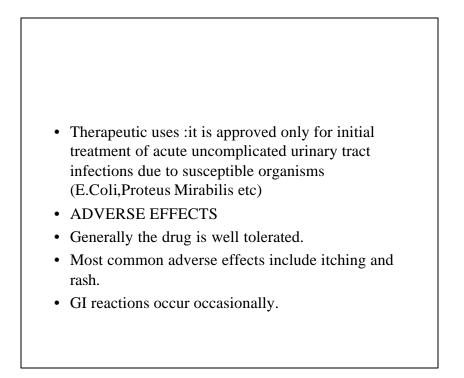
- ADVERSE EFFECTS
- 1) Ototoxicity
- 2) Nephrotoxicity
- Examples of drugs :Gentamicin,Tobramycin,Amicacin.

SULFONAMIDES AND TRIMETHOPRIM

- SULFONAMIDES
- Mechanism of action :suppression of bacterial growth by inhibiting synthesis of of folic acid (required for the synthesis of DNA,RNA,proteins)
- Antimicrobial spectrum :broad antibiotics
- Therapeutic uses :urinary tract infections

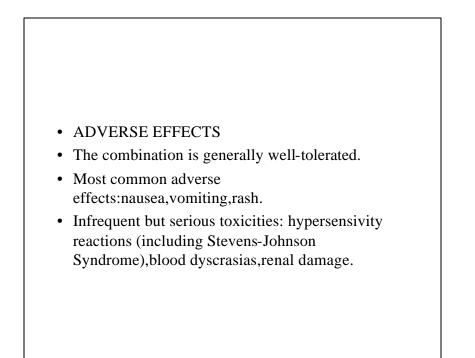






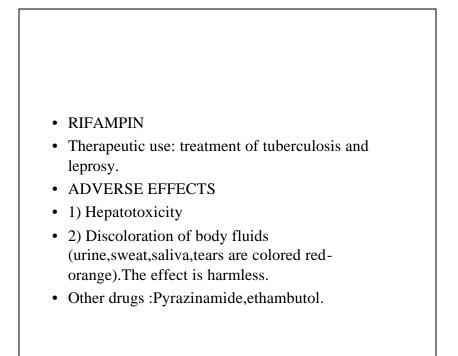
(continued)

- Caution when administering the drug to patients with suspected folate deficiency-->danger of bone marrow suppression (thrombocytopenia, neutropenia, anemia).
- TRIMETHOPRIM-SULFAMETHOXAZOLE
- Therapeutic uses: urinary tract infections, otitis media, bronchitis, shingellosis, pneumonia , Pneumocystis Carinii pneumonia.



ANTITUBERCULUS DRUGS

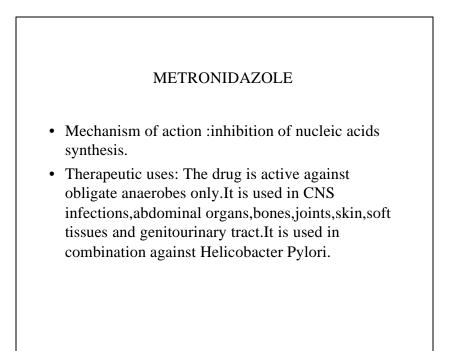
- ISONIAZID
- Therapeutic uses : prophylaxis and treatment of tuberculosis.
- ADVERSE EFFECTS
- 1) Peripheral Neuropathy (dose-related) :peripheral paresthesias of hands and feet,cluminess,unsteadiness,muscle aches (-->administer pyridoxine).
- 2) Hepatotoxicity (incidence increases with age)



FLUOROQUINOLONES

• CIPROFLOXACIN

- Mechanism of action : inhibits DNA replication
- Therapeutic uses :infections of respiratory tract,GI tract,bones,joints,skin and soft tissues.
- ADVERSE EFFECTS
- Mild reactions include nausea,vomiting,diarrhea and CNS effects (dizziness,headache).Candida infections of the pharynx and the vagina may result.Rarely -->Achilles tendon rupture.



MANAGEMENT OF POISONING

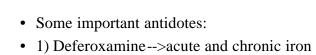
- 1) Supportive care
- 2) Poison identification
- 3) Prevention of further absorption
- 4) Promotion of poison removal
- 5) Use of specific antidotes



- Action:induction of emesis.
- Contraindications : following ingestion of strong acids or bases. Also it is contraindicated in comatose or delirious patients.

• ACTIVATED CHARCOAL

- It is a substance that absorbs drugs and other chemicals .Charcoal particles cannot be absorbed into the blood.The charcoal-poison complex is eliminated in the stool.
- GASTRIC LAVAGE



- toxicity.2) Dimercaprol-->metal poisoning
 - (mercury,arsenic,gold,lead)
- 3) Penicillamine-->Wilson's disease.